OPEN
PRS GLOBAL OPEN
IDEAS AND INNOVATIONS
Hand/Peripheral Nerve

# Neuroma Implantation into Long Bones: Clinical Foundation for a Novel Osseointegrated Peripheral Nerve Interface

Jacqueline S. Israel, MD*
Aaron M. Dingle, PhD*
Ruston J. Sanchez, MD*
Sahil K. Kapur, MD†
Sarah Brodnick, BS‡
Thomas J. Richner, PhD§
Jared P. Ness, MS‡
Joseph Novello, MS‡
Justin C. Williams, PhD‡
Samuel O. Poore, MD, PhD*‡

**Summary:** Symptomatic neuroma after major extremity amputation is a challenging clinical problem for which there are many described treatment options. Neuroma excision and implantation into the medullary canal of long bones offers durability and insulation, and minimizes chronic pain. Another challenge in amputees is impaired function and an ongoing need for accessible and functional prostheses that are "bidirectional," in that they provide both fine motor control and sensory feedback. Drawing on clinical experience with neuroma implantation into the medullary canal of long bones, the authors propose a novel neural interface whereby a terminal nerve end is redirected into the medullary canal of a nearby long bone and interfaced with an electrode array. The osseointegrated neural interface aims to exploit electrical signals from peripheral nerves to control advanced prosthetic devices for amputees. The purpose of this article is to present 2 clinical cases of nerve translocation into bone that serve as the clinical foundation of the osseointegrated neural interface as an innovative interface for prosthetic control. *(Plast Reconstr Surg Glob Open 2018;6:e1788; doi: 10.1097/GOX.0000000000001788; Published online 21 May 2018.)*

## INTRODUCTION

The physical and psychological effects of major limb loss are profound. It is estimated that at least 1.6 million Americans have undergone major upper or lower extremity amputation, and this number is expected to double by 2050.[1] Throughout the past several decades, prosthetic limbs have become increasingly sophisticated. Despite many advances, a neural prosthetic that is "bidirectional," providing both fine motor control (via efferent input from the central to peripheral nervous system) and sensory feedback (via afferent input), is not yet available for amputees. Peripheral nerve interfaces (PNIs) may be the key to developing an advanced prosthetic with both motor and sensory control. Drawing on our clinical experience with the surgical management of painful neuromas, we have developed the osseointegrated neural interface (ONI), whereby a mixed sensory-motor nerve is redirected into the medullary canal of long bones and interfaced with an electrode array.

## CLINICAL BASIS

The idea for the ONI emerged from the senior author's clinical experience treating individuals with debilitating postamputation neuromas. There are numerous described techniques for surgically treating neuromas including the implantation of the nerve into surrounding soft tissue, muscle, and/or bone.[2] The implantation of a peripheral nerve into bone after neuroma resection remains a viable methodology for the treatment of postamputation neuromas.[2,3] We present 2 case examples illustrating the senior author's experience with the translocation of peripheral nerves into the medullary canal of long bones, which provided the clinical foundation for the ONI.

*From the *Division of Plastic Surgery, Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, Wis.; †Department of Plastic Surgery, The University of Texas MD Anderson Cancer Center, Houston, Tex.; ‡Department of Biomedical Engineering, College of Engineering, University of Wisconsin – Madison, Madison, Wis.; and §Department of Biomedical Engineering, University of Minnesota Twin Cities, Minneapolis, Minn.*
*Received for publication February 5, 2018; accepted March 26, 2018.*
*Supported by the Defense Advanced Research Projects Agency (DARPA) Biological Hand Proprioception and Touch Interfaces program under the auspices of Dr. Doug Weber through the DARPA Contracts Management Office Grant/Contract No. HR0011-15-2-0008.*

DOI: 10.1097/GOX.0000000000001788

**Disclosure:** *The authors have no financial interest to declare in relation to the content of this article. The Article Processing Charge was paid for by the authors.*


**Fig. 1.** Case one: Dissection and resection of a painful tibial nerve neuroma.

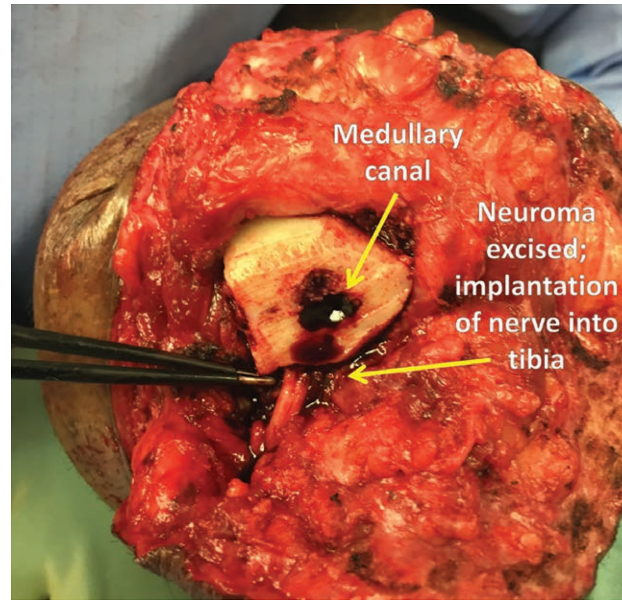


**Fig. 2.** Case one: Translocation of the tibial nerve (status post resection of the terminal neuroma) into the medullary canal of the tibia via a corticotomy.

## CASE ONE

A 42-year-old male sustained a crush injury to his right lower extremity after being pinned by a truck. He sustained a severely comminuted ankle fracture resulting in a significant soft-tissue defect. Limb salvage was unsuccessful, and the patient underwent below-knee amputation 2 months following the initial injury. One year postamputation, he developed a painful, debilitating neuroma at the medial aspect of the residual limb with an anatomic location suggestive of the saphenous nerve. He underwent neuroma excision and implantation into nearby muscle. Five months later, he underwent neuroplasty of a neuroma at a different site, this time consistent with the tibial nerve. The tibial neuroma was excised (Fig. 1) and implanted into the medullary canal of the tibia (Fig. 2), and did not recur. He was relieved of his pain and achieved excellent function and use of a prosthetic.

## CASE TWO

A 61-year-old female with a history of right total knee replacement complicated by infection and need for multiple revisions ultimately elected to undergo above-knee amputation. Approximately 1 year later, she developed profound refractory phantom limb pain and a symptomatic sciatic nerve neuroma. She ultimately underwent exploration with neuroma excision and implantation into the medullary canal of the femur utilizing a posteromedial corticotomy and 2 smaller adjacent corticotomies to facilitate suture anchoring. Shortly after surgery, she was completely relieved of her phantom limb pain.

## THE OSSEOINTEGRATED NEURAL INTERFACE FOR PROSTHETIC CONTROL

The ONI draws on a technique for surgically managing painful neuromas that was first described in 1943.[3] When implanted into the medullary canal of a long bone, neuromas are placed into an environment of mechanical insulation that limits axons' ability to aberrantly reinnervate surrounding tissue. Specific to the ONI, we hypothesize that the intramedullary placement of the nerve provides insulation and durability that minimizes motion artifact and electrical "cross-talk" from surrounding soft tissue. Furthermore, the terminal nerve may be positively influenced by the vascular, stem-cell–rich environment of the medullary cavity.[4] The ONI aims to provide a durable niche for harnessing electrical signals for control of a neural prosthetic device (Fig. 3).[5]

The technique for the ONI animal model involves transfemoral amputation and sciatic nerve transection with translocation into the medullary cavity of the femur via a corticotomy in rabbits. The distal nerve can then be secured to a variety of electrodes, from basic cuff to multichannel custom electrodes for electrophysiology (Fig. 4). A muscle flap is sutured over the distal femur before skin closure. The refined surgical model is feasible and repeatable, based on results of a pilot study of 4 animals. Electrophysiology can be performed immediately (for terminal procedures) or after a period of postoperative recovery (for survival procedures). In subsequent studies, we have observed histologic viability of the nerve-electrode interface and stable neurophysiologic signals, at 5 and 12 weeks postamputation.

PNIs are likely the key to bidirectional (eg, motor and sensory) prosthetic control. Remarkable advances have emerged in the last 2 decades, including targeted muscle reinnervation (TMR) and regenerative peripheral nerve

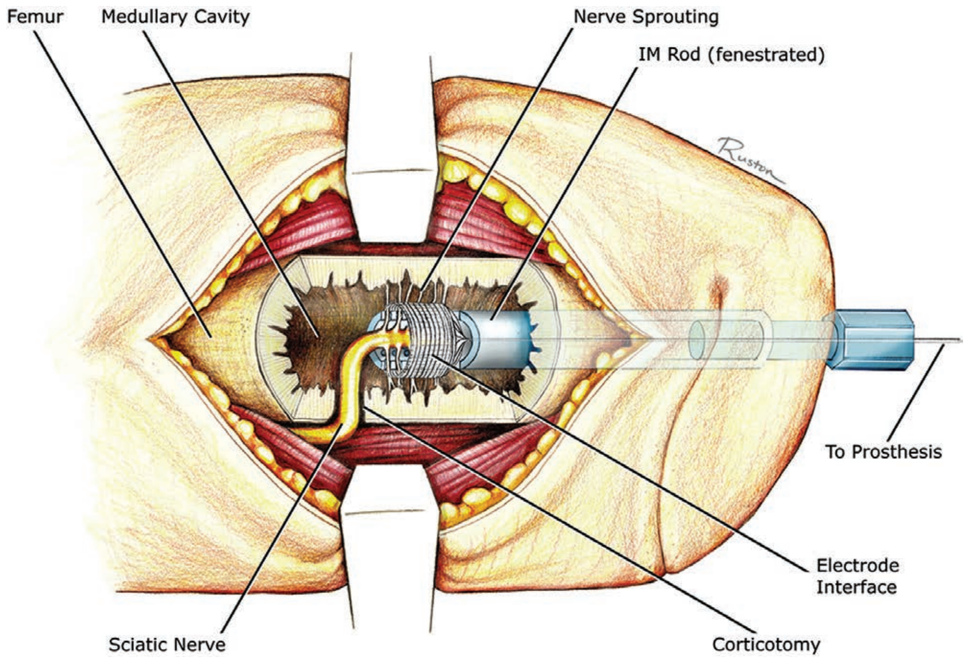


**Fig. 3.** Illustration of the ONI. Following neuroma excision, the distal nerve is implanted into the medullary canal of a long bone. The terminal nerve, when attached to an electrode, creates a PNI within the medullary canal, which may be connected to an osseointegrated prosthesis. Thus, the ONI aims to provide a durable, highly vascular environment for harnessing electrical signals to drive an osseointegrated neural prosthesis. Artwork by Ruston Sanchez, MD. IM = Intramedullary.

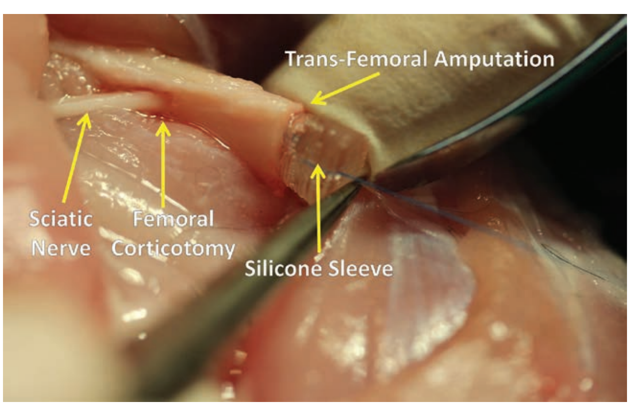


**Fig. 4.** Demonstration of the surgical preparation for establishing the ONI in a New Zealand white rabbit cadaver. Transfemoral amputation was performed and the nerve was translocated into the medullary canal through a mid-shaft corticotomy and a silicone sleeve (which in this case serves as a "mock" electrode and femoral plug). Utilizing this surgical configuration, with both intra- and extracortical recording electrodes, we have recorded stable electrophysiology signals at 5 and 12 weeks postoperatively and have demonstrated stable, nonpathologic histology. All animal work was approved by the University of Wisconsin Animal Care and Use Committee and United States Army Medical Research and Materiel Command Animal Care and Use Review Office.

interfaces (RPNIs).[2,6–9] Both TMR and RPNI offer a clinical technique for neuroma management and serve as experimental models for prosthetic control.[6–10] In TMR, terminal nerve ends are coapted to nearby intact "motor points."[8,9] After a period of recovery, muscle innervated by the previously amputated nerves acts as an internal biologic amplifier, and signals can be recorded by skin electrodes and translated into intuitive muscle action.[8–10] RPNIs involve the creation of discrete interfaces using free muscle grafts wrapped around terminal nerve ends. Electrodes may be placed internally, directly interfacing with the reinnervated muscle.[6,7] By placing electrodes directly within the muscle, higher signal amplitudes can be recorded.[7,11]

The ONI complements both TMR and RPNI. It proposes an alternative mechanism for both the treatment of painful neuromas and the promotion of nerve regeneration in an environment that facilitates isolation of neural signals and can potentially be used to power advanced neural prosthetic devices. With decades of successful use throughout Europe and Australia and recent FDA approval as a Humanitarian Device, osseointegration represents the future of limb reconstruction following amputation. From a PNI perspective, the osseointegrated implant offers a potential percutaneous connection point for directly connecting electrode arrays to prostheses for higher fidelity signaling, ultimately providing greater functionality.

## CONCLUSIONS

Similar to the multidisciplinary management of post-amputation pain and symptomatic neuroma, ongoing collaborations in the fields of regenerative medicine, biomedical engineering, and peripheral nerve surgery are essential to the development and refinement of advanced prostheses. The ONI for prosthetic control draws inspiration from techniques for managing neuromas and existing PNI technologies such as TMR and RPNI, and aims to one day improve clinical outcomes in individuals who have sustained major extremity amputation.

***Samuel O. Poore, MD, PhD***
University of Wisconsin School of
Medicine and Public Health
600 Highland Avenue
Madison, WI 53792
E-mail: poore@surgery.wisc.edu

## ACKNOWLEDGMENTS

*The authors greatly appreciate the veterinary and surgical assistance of Brett Nemke, BS, Yan Lu, MD, and Lisa Krugner-Higby, MD, PhD.*

## REFERENCES

1. Ziegler-Graham K, MacKenzie EJ, Ephraim PL, et al. Estimating the prevalence of limb loss in the United States: 2005 to 2050. *Arch Phys Med Rehabil.* 2008;89:422–429. doi:10.1016/j.apmr.2007.11.005.
2. Ives GC, Kung TA, Nghiem BT, et al. Current state of the surgical treatment of terminal neuromas. *Neurosurgery.* 2017. doi:10.1093/neuros/nyx500.
3. Boldrey E. Amputation neuroma in nerves implanted in bone. *Ann Surg.* 1943;118:1052–1057.
4. Ren Z, Wang Y, Peng J, et al. Role of stem cells in the regeneration and repair of peripheral nerves. *Rev Neurosci.* 2012;23:135–143.
5. Dingle AM, Novello J, Ness JP, et al. Osseointegrated neural interface (ONI): rethinking a conventional surgical treatment for amputation neuromas in the digital age. *Plast Reconstr Surg.* 2017;5:42–43.
6. Woo SL, Kung TA, Brown DL, et al. Regenerative peripheral nerve interfaces for the treatment of postamputation neuroma pain: a pilot study. *Plast Reconstr Surg Glob Open.* 2016;4:e1038.
7. 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.
8. Kuiken TA, Miller LA, Lipschutz RD, et al. Targeted reinnervation for enhanced prosthetic arm function in a woman with a proximal amputation: a case study. *Lancet.* 2007;369:371–380.
9. 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.
10. 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.
11. Langhals NB, Woo SL, Moon JD, et al. Electrically stimulated signals from a long-term regenerative peripheral nerve interface. *Conf Proc IEEE Eng Med Biol Soc.* 2014;2014:1989–1992.