OPEN

PRS GLOBAL OPEN

VIEWPOINT
Peripheral Nerve

Brief Intraoperative Electrical Stimulation to Enhance Nerve Regeneration

Tiam M. Saffari, MD, PhD, MSc*; Eric R. Walker, PhD†; Mitchell A. Pet, MD‡; Amy M. Moore, MD, FACS*

INTRODUCTION

Peripheral nerves regenerate slowly and often must regrow over long distances. Many therapeutic and surgical adjuncts have been explored to augment nerve regeneration and to overcome the challenges that currently limit achievable outcomes.[1] Intraoperative electrical stimulation is a new technology in nerve surgery that may enhance nerve regeneration.

MECHANISM OF ACTION

Electrical stimulation acts through a calcium-dependent mechanism, which activates cyclic adenosine monophosphate to stimulate axonal sprouting and neuron survival. Decades of animal studies have demonstrated that 20 Hz delivered postsurgically enhances axonal outgrowth and muscle reinnervation.[1,2] In 2020, Power et al found that 1 hour of stimulation postoperatively (20 Hz, 0.1 ms) after cubital tunnel decompression significantly increased compound muscle action potential amplitude, grip, and pinch strength.[3] However, prolonged postoperative delivery of stimulation poses a logistical challenge.

PILOT DATA BRIEF ELECTRICAL STIMULATION

Brief intraoperative electrical stimulation could overcome practical limitations. Roh et al found that 10 minutes of stimulation (16 Hz, 100 μs) with a handheld device (Checkpoint Surgical Inc.) was equally beneficial to 1 hour of continuous stimulation in rodents,[4] highlighting the possibility that the advantages of electrical stimulation may be achieved with a brief intraoperative treatment alone.

To evaluate the benefits of brief intraoperative electrical stimulation in humans, we conducted a pilot randomized controlled trial (RCT) to investigate the safety and feasibility of brief electrical stimulation (16 Hz, 100 μs) after cubital tunnel decompression. After institutional review board approval, 10 patients were randomized in a 2:1 fashion between decompression + 10 minutes of stimulation (treatment) versus surgical decompression only (control). Baseline patient characteristics were similar between groups. Once the nerve was decompressed and the tourniquet released, the handheld device stimulated the ulnar nerve on its anterior surface proximally to the site of compression for 10 minutes. Visible contraction of the distal muscle confirmed adequate contact with the nerve. Outcomes included two-point discrimination, Semmes-Weinstein monofilaments, grip, and pinch force. Electromyography was included to evaluate nerve conduction over time. Furthermore, questionnaires were included to assess quality of life and pain (Fig. 1). During surgery and follow-up, no adverse events related to treatment were reported (0%), including nerve injury or damage from the nerve stimulator to surrounding tissue. Our data suggest that brief intraoperative electrical stimulation is safe and feasible. This study serves as pilot data for a current large multicenter study to evaluate the efficacy of this treatment.[5]

FUTURE DIRECTIONS

Many clinical trials are currently exploring the benefits of electrical stimulation in nerve surgery. These studies are investigating electrical stimulation for a multitude of indications: nerve transfers for brachial plexus injuries, digital nerve transection, nerve decompressions (carpal and cubital tunnel), and two-staged facial reanimation for facial palsy.[1] Given the challenges associated with prolonged and/or postoperative delivery of electrical stimulation, it is of critical importance to determine whether a brief intraoperative stimulus can augment nerve regeneration. The multicenter effort now underway has potential to drastically impact the practice of peripheral nerve surgery by offering a simple and practicable method to improve patient outcomes.

Amy M. Moore, MD, FACS
Professor and Chair, Department of Plastic and Reconstructive Surgery
The Ohio State University Wexner Medical Center
915 Olentangy River Road, Suite 2100
Columbus, IL 43212
E-mail: amy.m.moore@osumc.edu

Disclosure statements are at the end of this article, following the correspondence information.

*From *Department of Plastic Surgery and Reconstructive Surgery, Ohio State University Wexner Medical Center, Columbus, Ohio; †Checkpoint Surgical, Inc., Cleveland, Ohio; and ‡Division of Plastic Surgery, Washington University School of Medicine, Saint Louis, Mo.*

Received for publication November 17, 2023; accepted February 16, 2024.

Plast Reconstr Surg Glob Open 2024; 12:e5730; doi: 10.1097/GOX.0000000000005730; Published online 10 April 2024.

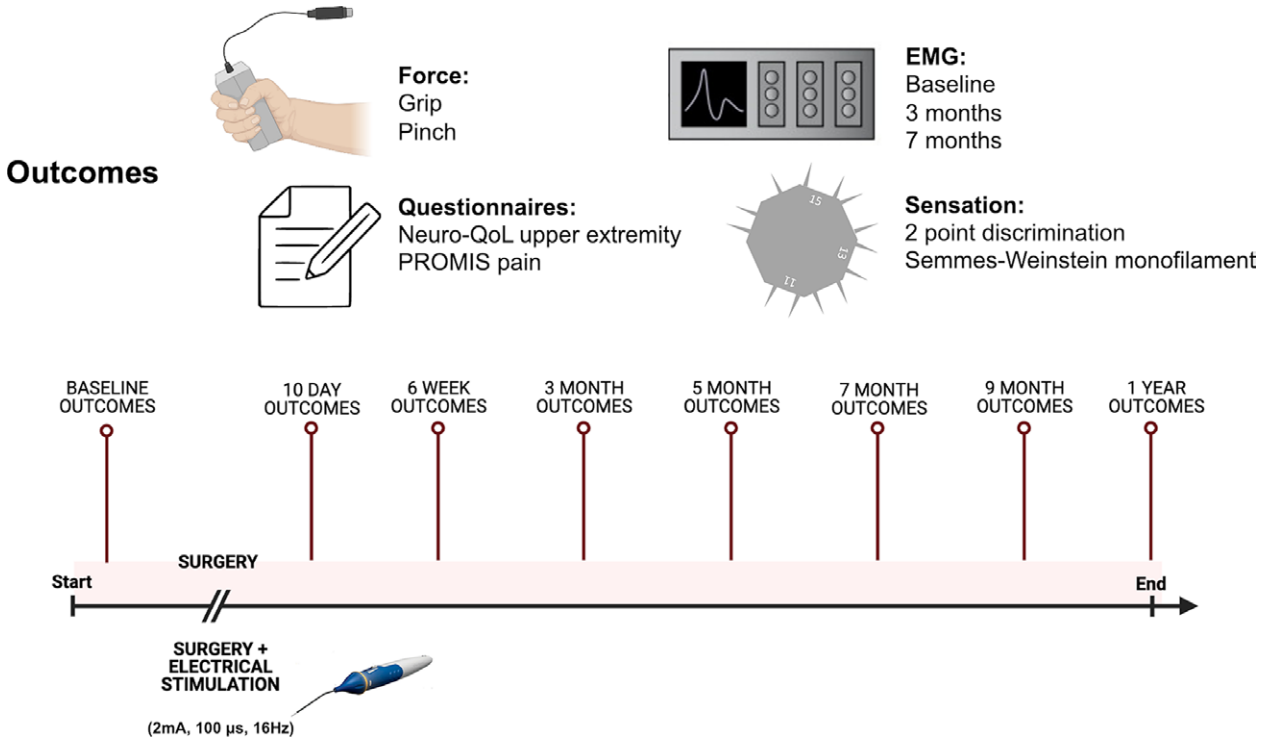

Fig. 1. A schematic overview of the outcomes and timepoints of the RCT to investigate brief electrical stimulation. This figure presents the timeline and outcomes of the RCT that evaluates electrical stimulation. Patient-reported outcomes included the Neurology Quality of Life upper extremity instrument and Patient-Reported Outcomes Measurement Information System questionnaires for pain interference. Sensation was tested using two-point discrimination and Semmes-Weinstein monofilaments, and force was tested using grip and pinch force. These outcomes are assessed at each of the timepoints presented in the figure. Electromyography (EMG) was included to evaluate nerve conduction over time.

DISCLOSURES

Dr. Walker is an employee of Checkpoint Surgical. Dr. Pet receives support from Checkpoint Surgical, 3M, and Kent Imaging, and is a consultant for KLISBio. Dr. Moore is a consultant for Checkpoint Surgical, but does not receive royalties. Dr. Saffari has no financial interest to declare in relation to the content of this article. This study was funded in part by Checkpoint Surgical.

REFERENCES

1. Juckett L, Saffari TM, Ormseth B, et al. The effect of electrical stimulation on nerve regeneration following peripheral nerve injury. *Biomolecules*. 2022;12:1856.
2. Zuo KJ, Gordon T, Chan KM, et al. Electrical stimulation to enhance peripheral nerve regeneration: update in molecular investigations and clinical translation. *Exp Neurol*. 2020;332:113397.
3. Power HA, Morhart MJ, Olson JL, et al. Postsurgical electrical stimulation enhances recovery following surgery for severe cubital tunnel syndrome: a double-blind randomized controlled trial. *Neurosurgery*. 2020;86:769–777.
4. Roh J, Schellhardt L, Keane GC, et al. Short-duration, pulsatile, electrical stimulation therapy accelerates axon regeneration and recovery following tibial nerve injury and repair in rats. *Plast Reconstr Surg*. 2022;149:681e–690e.
5. Moore, AM. Promoting healing of nerves through electrical stimulation (PHONES). Available at https://classic.clinicaltrials.gov/ct2/show/NCT04662320. Published 2020. Accessed December 15, 2023.