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Hand/Peripheral Nerve

Regenerative Peripheral Nerve Interfaces for the Treatment of Postamputation Neuroma Pain: A Pilot Study

Shoshana L. Woo, MD*
Theodore A. Kung, MD*
David L. Brown, MD*
James A. Leonard, MD†
Brian M. Kelly, DO†
Paul S. Cederna, MD*

Background: Originally designed for prosthetic control, regenerative peripheral nerve interfaces (RPNIs) prevent neuroma formation by providing free muscle grafts as physiological targets for peripheral nerve ingrowth. We report the first series of patients undergoing RPNI implantation for treatment of symptomatic postamputation neuromas.

Methods: A retrospective case series of all amputees undergoing RPNI implantation for treatment of symptomatic neuromas between November 2013 and June 2015 is presented. Data were obtained via chart review and phone interviews using questions derived from the Patient Reported Outcomes Measurement Information System instruments. Statistical analyses were performed using dependent sample t tests with a significance threshold of $P < 0.01$.

Results: Forty-six RPNIs were implanted into 16 amputees for neuroma relief (3 upper extremities and 14 lower extremities). Mean age was 53.5 years (6 females and 10 males). All patients participated in postoperative phone interviews at 7.5 ± 3.4 (range: 3–15) months. Patients reported a 71% reduction in neuroma pain and a 53% reduction in phantom pain. Most patients felt satisfied or highly satisfied with RPNI surgery (75%), reporting decreased (56%) or stable (44%) levels of analgesic use. Most patients would strongly recommend RPNI surgery to a friend (88%) and would do it again if given the option (94%). Complications included delayed wound healing ($n = 4$) and neuroma pain at a different site ($n = 2$).

Conclusions: RPNI implantation carries a reasonable complication profile while offering a simple, effective treatment for symptomatic neuromas. Most patients report a significant reduction in neuroma and phantom pain with a high level of satisfaction. The physiological basis for preventing neuroma recurrence is an intriguing benefit to this approach. *(Plast Reconstr Surg Glob Open 2016;4:e1038; doi: 10.1097/GOX.0000000000001038; Published online 27 December 2016.)*

More than 500 Americans sustain major amputations each day[1] and almost 2 million people in the United States currently live with major extremity loss.[2] Painful neuromas develop in 12.5% to 50% of cases,[3,4] preventing or limiting prosthetic restoration and diminishing quality of life. Up to 30% of patients abandon their prostheses for reasons including neuroma pain.[5] The fact that over 150 different methods of neuroma treatment have been described in the literature[6] indicates the absence of a reliable and efficacious treatment modality.

Neuromas form when injured axons sprout in a discordant fashion, creating swellings of disorganized tissue containing axons, Schwann cells, endoneurial cells, perineurial cells, and fibroblasts in a dense collagenous matrix.[7] The neuroma's afferent fibers develop ectopic activity, mechanical sensitivity, and chemosensitivity to catecholamines.[8] The altered expression of transduction molecules, upregulation of sodium channels, downregulation of potassium channels, and development of nonfunctional connections between axons all contribute to the hyperexcitability and spontaneous discharge witnessed within injured nerves.[9] Nonsurgical

From the [*]Section of Plastic Surgery, University of Michigan Health System, Ann Arbor, Mich.; and [†]Department of Physical Medicine and Rehabilitation, University of Michigan Health System, Ann Arbor, Mich.

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treatment includes desensitization, chemical or anesthetic injections, transcutaneous electrical nerve stimulation, topical lidocaine, and adjuvant pain medications such as antidepressants and anticonvulsants.[7] Recalcitrant cases are subject to various surgical treatments such as simple neuroma excision,[4] nerve capping,[10–12] and nerve relocation into bone,[13] muscle,[13–15] or vein.[7] Fibrin patch application with placement of a local pain catheter has also been described.[16] The long-term outcomes of such methods are mixed,[6,8] likely because of the nonphysiological nature of these treatments.

We propose a simple, straightforward, and reproducible method of neuroma management using regenerative peripheral nerve interfaces (RPNIs). RPNIs are constructed by implanting severed peripheral nerve ends into free, devascularized muscle grafts,[17,18] which serve as denervated targets for nerve ingrowth and survive through a process of degeneration, regeneration, revascularization, and reinnervation.[18–25] Muscle graft survival has been demonstrated in numerous animal experiments in which RPNIs have been studied for use in prosthetic control.[17,18,26] Muscle graft reinnervation occurs as early as 1 month postoperatively[27] and can occur with sensory nerves[28–30] in addition to motor nerves. By providing a physiological target for regenerating axons, RPNI surgery prevents neuroma formation by taking advantage of fundamental nerve and muscle biology.

Here, we describe our initial experience treating patients with symptomatic postamputation neuromas by neuroma excision and RPNI implantation.

METHODS

Patient Registry

With institutional review board approval, a retrospective registry was created, comprising all patients treated for postamputation symptomatic neuromas via neuroma excision and immediate RPNI implantation by the senior author (PSC) between November 2013 and June 2015. Demographic and clinical data were extracted from the electronic medical record. Inclusion criteria were the diagnosis of symptomatic neuromas within a residual limb and a postoperative follow-up greater than 3 months. Patients were excluded if RPNIs were performed prophylactically during primary amputation or if the neuroma was not associated with limb amputation.

Surgical Technique

An RPNI is constructed by excising the neuroma bulb and wrapping the proximal nerve end with a small free muscle graft (Fig. 1). Previous work from our laboratory has shown that any further manipulations are unnecessary, such as wrapping the RPNI with a biological tissue cover for insulation[31] or anchoring the RPNI to surrounding tissues.[32] The free muscle graft (approximately 3×1 × 1.5cm) is harvested sharply from a muscle near the neuroma or from a muscle at a distant site. Care is taken to avoid harvesting muscle that would otherwise serve as crucial padding for the residual limb. Donor muscle fiber–type composition, whether slow-twitch or fast-twitch, has not be shown to make a significant difference in muscle graft reinnervation when implanted with a peripheral nerve.[17] Grafts are harvested along the axis of the muscle fibers to avoid unnecessary tissue trauma, thereby optimizing the viability of muscle fibers within the graft. A single RPNI takes approximately 7 to 10 minutes to construct under 2.5× to 3.5× loupe magnification.

In general, neuromas are exposed under tourniquet control through existing scars. In some cases, such as superficial and deep peroneal neuromas after below-knee amputations, a separate incision in normal tissue at the lateral knee can be used to identify the common peroneal nerve proximally. The common peroneal nerve is transected, and an intrafascicular dissection is performed to separate the nerve into 2 fascicles to construct 2 separate RPNIs. For sciatic neuromas in above-knee amputations, the sciatic nerve is split into 3 fascicles to construct 3 separate RPNIs (Fig. 2). In theory, splitting large nerves into separate fascicles for RPNI construction improves the axon number–to-muscle graft volume ratio, promoting muscle graft reinnervation and therefore neuroma prevention. Notably, nerve splitting is performed without the need for distinguishing between motor and sensory axons, as either type can reinnervate a denervated muscle graft.[29,30] Furthermore, there is no practical way to distinguish between motor and sensory axons in a residual limb, as these axons lack normal end targets from prior amputation, precluding the ability to test by nerve stimulation.

All suturing is performed with 6-0 nonabsorbable monofilament. The nerve end is first secured to the center of the muscle graft using 2 or 3 epineural-to-epimysial stitches. The muscle graft is then wrapped and secured around the nerve with additional epimysial stitches. Finally, 2 more stitches are placed for extra support from the proximal edge of the muscle graft to the adjacent epineurium, taking care to avoid kinking of the nerve or disruption of the axons within the epineurium. Once all RPNIs are constructed, primary closure of the surgical site is performed.

Phone Interviews

Postoperative phone interviews were conducted by the same author (SLW) using a short questionnaire (Fig. 3) to

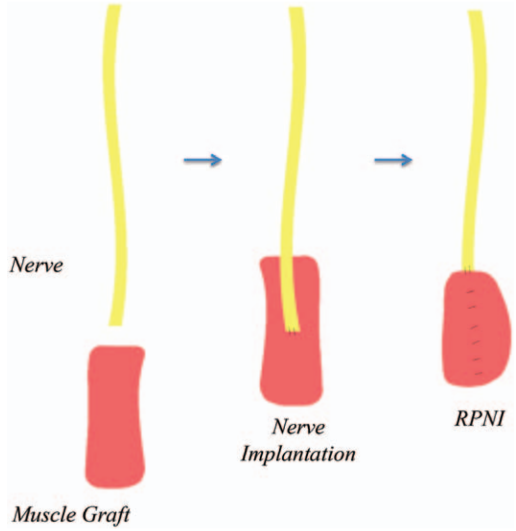


Fig. 1. Illustration of RPNI construction.

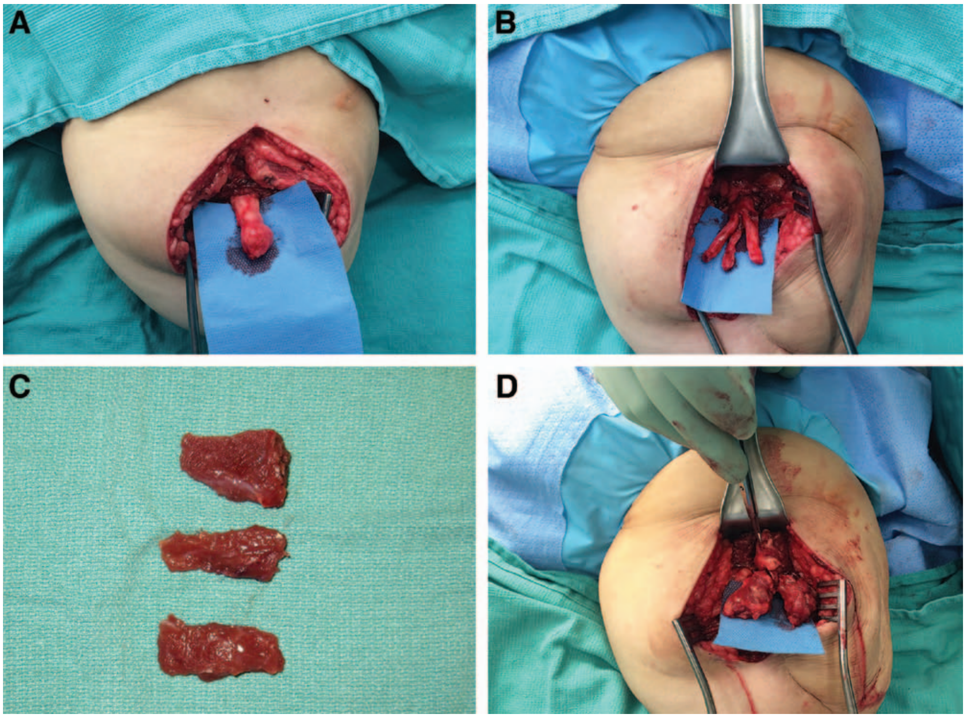


Fig. 2. Excision of sciatic neuroma with construction of 3 RPNIs. A, Sciatic neuroma is identified. B, Sciatic nerve is split into 3 fascicles after neuroma excision. C, Three small muscle grafts are harvested from the adjacent biceps femoris muscle. D, Three RPNIs are constructed.

elicit patient-reported pain scores both before and after surgery, while also distinguishing neuroma pain from phantom pain. Pain interference questions were adapted from the publically available Patient Reported Outcomes Measurement Information System (PROMIS) instruments.[33] The PROMIS instruments facilitate patient communication regarding outcomes related to injury or illness[34,35] and are useful in evaluating pain, disability, and quality of life in patients with amputations involving the upper extremity[36] and lower extremity.[37] Because shortened pain inventories have been shown to be roughly equivalent or slightly more effective than more exhaustive inventories in detecting patient-reported pain scores,[38] our questionnaire was fashioned to simplify reporting, decrease interviewee fatigue, and optimize response rate. Although not validated, our questionnaire was effectual for the purposes of this study.

Statistical Analyses

Descriptive statistics were employed to quantitatively describe the characteristics of this patient population. Further analyses were performed using dependent sample t tests with a significance threshold of $P < 0.01$, where applicable.

RESULTS

Patients

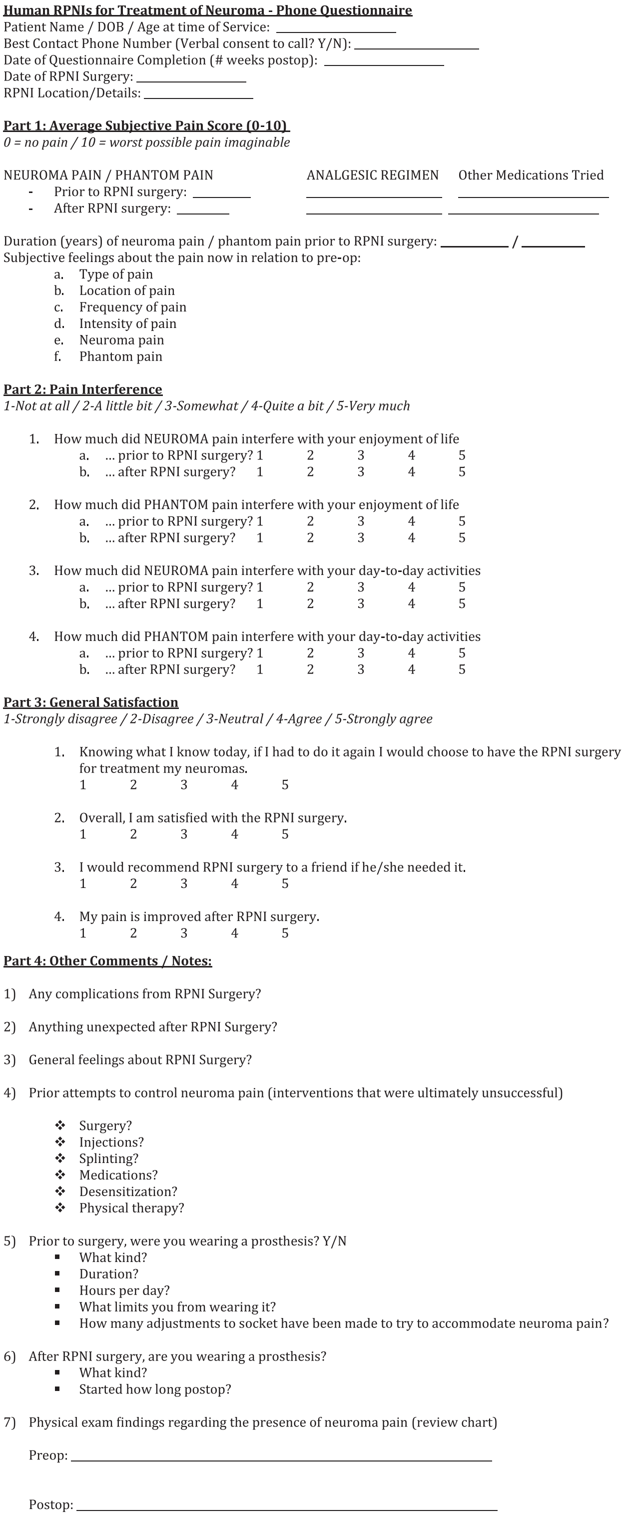
Sixteen patients ($n = 16$) met inclusion criteria during the study period (Table 1). All underwent RPNI implantation for postamputation neuroma treatment and had at least 3 months of postoperative follow-up documented in the medical record. Mean age was 53.5 ± 12.8 (range: 30–76) years, with 6 females (38%) and 10 males (63%). Four patients (25%) had documented peripheral vascular occlusive disease. Five patients (31%) had diabetes. Three patients (19%) were recent smokers who, after preoperative counseling, quit smoking 4 to 6 weeks before surgery. Ten patients had below-knee amputations, 4 patients had above-knee amputations, 2 patients had below-elbow amputations, and 1 patient had an above-elbow amputation. Duration of neuroma pain before RPNI surgery was an average of 6.1 ± 7.2 (range: 1–29) years. Patients reported that their neuroma pain was refractory to multiple prior treatments, including desensitization exercises, electrical stimulation, physical therapy, steroid injections, and surgical neurectomy.

Operative Details

In these 16 patients, a total of 17 residual limbs were treated for symptomatic neuromas (3 upper extremity and 14 lower extremity). Forty-six RPNIs were constructed with an average of 2.7 RPNIs per limb (Table 2). All patients received preincisional intravenous antibiotics. Mean operative time was 132 ± 42 (range: 69–209) minutes. There were no intraoperative complications. The most commonly used donor muscles were the vastus lateralis ($n = 14$), gastrocnemius ($n = 11$), and biceps femoris ($n = 10$) muscles. Other donor sites included the gluteus maximus, semitendinosus, soleus, and flexor digitorum superficialis muscles.

Postoperative Course

Postoperatively, patients were admitted to the hospital for an average of 1.9 ± 1.2 (range: 0–4) days. Mean follow-up time



Human RPNIs for Treatment of Neuroma - Phone Questionnaire
Patient Name / DOB / Age at time of Service: ____________________
Best Contact Phone Number (Verbal consent to call? Y/N): ____________________
Date of Questionnaire Completion (# weeks postop): ____________________
Date of RPNI Surgery: __________________
RPNI Location/Details: __________________

Part 1: Average Subjective Pain Score (0-10)
0 = no pain / 10 = worst possible pain imaginable

NEUROMA PAIN / PHANTOM PAIN	ANALGESIC REGIMEN	Other Medications Tried
- Prior to RPNI surgery: _________	______________________	________________________
- After RPNI surgery: ________	______________________	________________________

Duration (years) of neuroma pain / phantom pain prior to RPNI surgery: ___________ / __________
Subjective feelings about the pain now in relation to pre-op:
a. Type of pain
b. Location of pain
c. Frequency of pain
d. Intensity of pain
e. Neuroma pain
f. Phantom pain

Part 2: Pain Interference
1-Not at all / 2-A little bit / 3-Somewhat / 4-Quite a bit / 5-Very much

1. How much did NEUROMA pain interfere with your enjoyment of life
    a. … prior to RPNI surgery? 1 2 3 4 5
    b. … after RPNI surgery? 1 2 3 4 5

2. How much did PHANTOM pain interfere with your enjoyment of life
    a. … prior to RPNI surgery? 1 2 3 4 5
    b. … after RPNI surgery? 1 2 3 4 5

3. How much did NEUROMA pain interfere with your day-to-day activities
    a. … prior to RPNI surgery? 1 2 3 4 5
    b. … after RPNI surgery? 1 2 3 4 5

4. How much did PHANTOM pain interfere with your day-to-day activities
    a. … prior to RPNI surgery? 1 2 3 4 5
    b. … after RPNI surgery? 1 2 3 4 5

Part 3: General Satisfaction
1-Strongly disagree / 2-Disagree / 3-Neutral / 4-Agree / 5-Strongly agree

1. Knowing what I know today, if I had to do it again I would choose to have the RPNI surgery for treatment my neuromas.
    1 2 3 4 5

2. Overall, I am satisfied with the RPNI surgery.
    1 2 3 4 5

3. I would recommend RPNI surgery to a friend if he/she needed it.
    1 2 3 4 5

4. My pain is improved after RPNI surgery.
    1 2 3 4 5

Part 4: Other Comments / Notes:

1) Any complications from RPNI Surgery?

2) Anything unexpected after RPNI Surgery?

3) General feelings about RPNI Surgery?

4) Prior attempts to control neuroma pain (interventions that were ultimately unsuccessful)

    - Surgery?
    - Injections?
    - Splinting?
    - Medications?
    - Desensitization?
    - Physical therapy?

5) Prior to surgery, were you wearing a prosthesis? Y/N
    - What kind?
    - Duration?
    - Hours per day?
    - What limits you from wearing it?
    - How many adjustments to socket have been made to try to accommodate neuroma pain?

6) After RPNI surgery, are you wearing a prosthesis?
    - What kind?
    - Started how long postop?

7) Physical exam findings regarding the presence of neuroma pain (review chart)

Preop: ____

Postop: ____

Fig. 3. Phone interview questionnaire.

for chart review was 11.3±5.5 (range: 3–23) months. Before RPNI surgery, 9 of 16 patients (56%) reported being able to use prostheses. After RPNI surgery, 13 of 16 patients (81%) reported being able to wear prostheses. Average time to wearing prostheses after surgery was 4.6±4.0 (range: 1–15) months.

Table 1. Patient Characteristics

Patients (*N*)	*N* = 16 Amputees
Age	53.5 ± 12.8 y (range: 30–76)
Females, *n* (%)	6 (38%)
Males, *n* (%)	10 (63%)
PVOD, *n* (%)	4 (25%)
Diabetes, *n* (%)	5 (31%)
Recent smoking history, *n* (%)	3 (19%)
Pain duration (y)	6.1 ± 7.2 y (range: 1–29)

PVOD, peripheral vascular occlusive disease.

Table 2. Nerves Treated with RPNI Construction

RPNIs Implanted (*n*)	46
Upper extremity nerves	8
Musculocutaneous	1
Medial brachial cutaneous	1
Median	2
Ulnar	2
Dorsal radial sensory	2
Lower extremity nerves	38
Sciatic (no. fascicles)	7
Common peroneal	3
Tibial	10
Superficial peroneal	8
Deep peroneal	9
Saphenous	1

Complications

Five of 16 patients (31%) experienced surgical complications (Table 3).

One patient with a history of severe peripheral thromboembolic disease, due to a prothrombin G20210A mutation, developed acute bilateral lower extremity ischemia on postoperative day 1, requiring aortic and bilateral iliac thombectomies. Five days later while on a therapeutic heparin drip, she was diagnosed with an acute deep venous thrombosis of the contralateral lower extremity, and an inferior vena cava filter was placed. She was eventually discharged on warfarin for lifelong therapeutic anticoagulation. Two weeks later in clinic, a hematoma at the RPNI surgical site was detected, opened, and drained to allow for dressing changes. No further intervention was required.

Four patients (25%) experienced wound dehiscence and delayed wound healing. Three were in the setting of preoperative infection such as chronic osteomyelitis and/or recent cellulitis. One was in the setting of postoperative hematoma as described above. All were treated with topical dressings until fully healed

Two patients (13%) complained of new neuroma pain, each at a previously unaddressed site within the operated residual limb. One was confirmed by ultrasound at 7 months, involving a small branch of the peroneal nerve. This was treated with RPNI implantation at 9 months, with resolution of the neuroma pain documented at a follow-up of an

Table 3. RPNI Surgery Complication Profile

Patients Experiencing Complications, *n* (%)	5 (31%)
Wound healing delay	4 (25%)
Acute limb ischemia and deep venous thrombosis	1 (6%)
Hematoma	1 (6%)
Neuroma at different site	2 (13%)

additional 5 months. The other neuroma was detected during routine follow-up at 8 months and involved the lateral antebrachial cutaneous nerve. This patient elected to avoid further surgery and wished to proceed with prosthetic fitting.

Patient-reported Outcomes

All 16 patients were contacted for postoperative phone interviews with a 100% response rate. These interviews were conducted at an average of 7.5 ± 3.4 (range: 3–15) months after RPNI surgery.

Using the numeric pain rating scale (0–10), patients reported an average reduction of neuroma pain score 71%, from 8.7 ± 1.4 preoperatively to 2.5 ± 2.1 postoperatively ($P = 0.000001$) (Fig. 4A). Twelve of the 16 patients (75%) reported at least a 50% decrease in neuroma pain score after surgery. Patients also reported an average reduction of

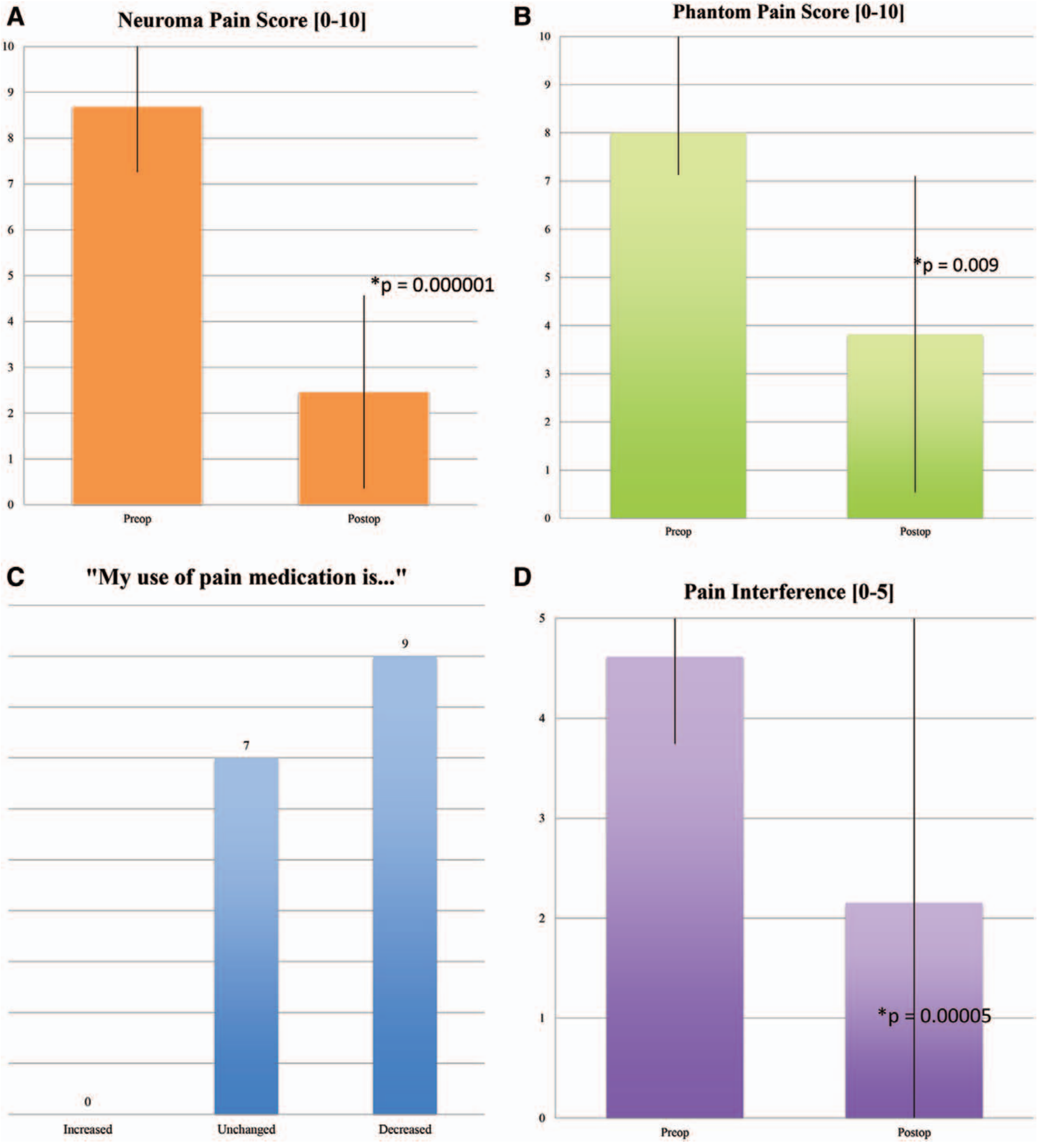


Fig. 4. Patient-reported outcomes: A, neuroma pain score; (B) phantom pain score; (C) pain medication use; (D) pain interference.

phantom pain score by 53%, from 8.0 ± 2.1 preoperatively to 3.8 ± 3.3 postoperatively ($P = 0.009$). Five of 11 patients (45%) presenting with phantom pain reported at least a 50% decrease in phantom pain score after surgery (Fig. 4B). There was no association detected between preoperative duration of symptoms and reduction in pain scores.

Nine patients (56%) reported a reduction in pain medication use postoperatively, whereas 7 patients (44%) reported no change. No patients required an increased use of pain medications (Fig. 4C).

Aggregate pain interference scores, for both neuroma and phantom pain, dropped from 4.6 ± 0.9 preoperatively to 2.15 ± 1.3 postoperatively ($P = 0.00005$) (Fig. 4D). An interference score of 5 indicates that pain interferes "very much" with enjoyment of life and daily activities, whereas a score of 1 indicates that pain interferes "not at all" with enjoyment of life and daily activities.

Most patients (75%) felt satisfied or highly satisfied with RPNI surgery (Fig. 5A), and 94% would choose to undergo surgery again if given the option (Fig. 5B). Eighty-eight percent would strongly recommend the surgery to a friend (Fig. 5C).

DISCUSSION

General Considerations

We propose the novel use of RPNIs for the treatment of symptomatic neuromas in amputation patients. RPNI construction is simple to perform, by wrapping the distal end of a severed peripheral nerve with a free muscle graft. Free muscle grafts survive by a process of degeneration followed by regeneration and concomitant reinnervation in the presence of nerve implantation,[24,39] hence the "regenerative" nature of RPNIs.[17,40–42] Unlike the many existing methods to surgically treat neuromas, the RPNI is a physiological technique: the free muscle graft serves as a denervated target for regenerating axons, and reinnervation occurs through a well-described series of neurotrophin-mediated events.[20,25,43] This process results in the formation of new neuromuscular junctions[21–23] and precludes the formation of neuromas.

RPNIs were originally designed to harness voluntary motor nerve signals for neuroprosthetic control.[26,41] Indeed, RPNIs can conduct and amplify nerve signals[44] to support real-time intuitive control of advanced myoprostheses.[45,46] More recent studies have demonstrated muscle reinnervation by sensory nerves as well, which may prove useful in achieving bioprosthetic somatosensory feedback.[28] In general, RPNIs take advantage of basic nerve sprouting behavior, which favors the organized reinnervation of denervated targets. Without a target for nerve ingrowth, injured axons embark on an uncoordinated path toward neuroma formation, which may explain why other methods for neuroma treatment such as nerve relocation[7,13–15] or nerve capping[10–12] have not achieved widespread success.

In our case series, RPNI surgery was associated with reasonably positive outcomes. Sixteen patients were treated for symptomatic postamputation neuromas. On average, patients reported a 71% reduction in their neuroma pain scores and a 53% reduction in their phantom pain scores, along with a significant improvement in pain interference scores. More patients were able to use their prosthesis postoperatively, indicating an improvement in quality of life. Furthermore, the overwhelming majority patients felt satisfied or highly satisfied with the RPNI surgery, would do it again if given the option, and would recommend the surgery to a friend. Although subjective, these patient-reported outcomes highlight the promise that RPNIs hold in the treatment of amputation neuromas.

In addition to RPNI surgery, other neuroma treatments more recently described in the literature include targeted nerve implantation (TNI)[47] and targeted muscle reinnervation (TMR).[48] TNI involves securing nerve endings to transected intramuscular motor nerve branches within surgically denervated muscle in the residual limb. TMR involves coapting nerve endings to recipient motor nerve stumps or performing direct muscle neurotization. Based on the published case series, both methods show great promise in both neuroma treatment and prevention by taking advantage of basic nerve sprouting behavior. Still, these methods do require microsurgical techniques that may not be available to all surgeons, may prove challenging to perform, and may lead to longer operative times. Furthermore, both TNI and TMR require living muscle targets at the site of nerve coaptation, which may not be available in the presence of significant scar tissue or if faced with preoperative soft-tissue deficiencies. In contrast, RPNIs can easily be constructed without specialized microsurgical or peripheral nerve training. Furthermore, if suitable tissue is not present at the recipient site, muscle grafts can be harvested from a distant donor site with minimal morbidity.[17,18] Finally,

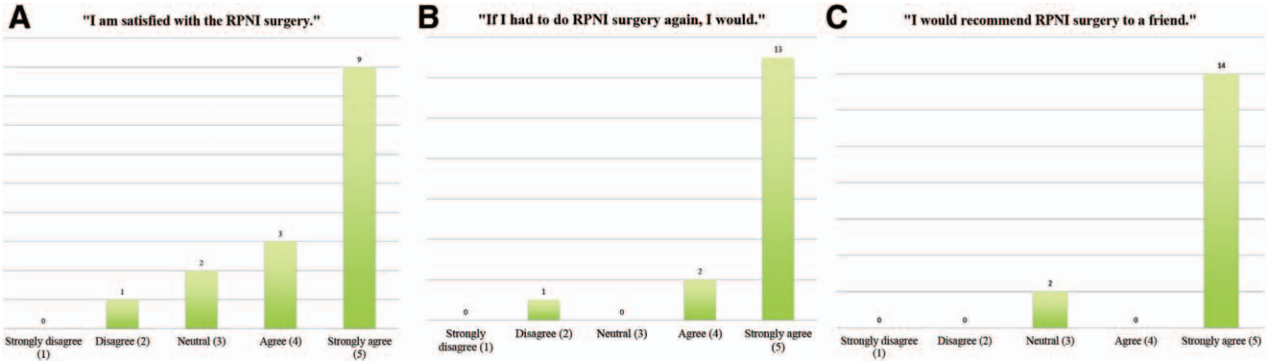


Fig. 5. Patient-reported outcomes: A, satisfaction; (B) do it again?; (C) recommend to a friend?

RPNIs may potentially be used for downstream control of advanced myoprostheses in the future[17,18]; RPNIs have the ability to harness and transduce discrete motor nerve signals that would otherwise be lost in a neuroma.

Future Directions

As this is a pilot study, further studies are warranted to better understand the outcomes and implications of RPNI surgery for neuroma treatment and prevention.

First, from a technical standpoint, the optimal ratio of axons-to-muscle graft volume has yet to be determined. This would affect the size of the nerve fascicles and/or the size of the muscle grafts used for RPNI construction.

Second, the impact of RPNI surgery on upper extremity versus lower extremity neuromas should be more closely evaluated, as there may be response differences that cannot be detected in this study because of small sample size.

Third, despite relatively short operative times, patients stayed an average of 2 days in the hospital after RPNI surgery. We have observed that these chronic pain patients require intensive postoperative pain management strategies to ensure that they are comfortable before discharge. Oftentimes, help from the Acute Pain Service is solicited. Further study regarding the mechanisms driving pain perception after RPNI surgery and regarding perioperative pain management is warranted.

Fourth, further investigation is needed regarding reasons why only half of all patients decreased their use of pain medications after surgery. Although an association between duration of symptoms and pain reduction was not detected in this study, likely because of small sample size, it is possible that patients with longer symptom duration possessed a larger central component to their pain that was unaddressed by peripheral nerve surgery. Indeed, the 6-year average duration of preoperative neuroma pain in this sample of patients may be indicative of this phenomenon. In addition, patients can be reluctant to change their habits of taking pain medication out of fear of more pain. Finally, as follow-up time was only 7.5 months, any medication changes that would occur beyond that time frame could not be captured. Regardless, patient quality of life still appeared to improve as indicated by reduced pain interference scores, independent of medication adjustments or lack thereof.

Fifth, 2 patients developed new neuroma pain at different sites at 7 and 8 months. These new sites were likely unmasked after RPNI treatment of more dominant painful neuromas in the area. By better understanding the incidence of new neuroma formation versus delayed presentation of less symptomatic neuromas, an improved algorithm can be developed to avoid such pitfalls.

Finally, RPNI surgery may also be beneficial for neuroma prophylaxis during primary amputations and for treatment of painful end neuromas and neuromas-in-continuity in patients without amputations. Studies focused on these particular patient populations are needed to explore the potential indications for RPNI surgery.

Limitations

This study is limited in that it is a retrospective, descriptive case series with a small number of patients, no control group, and relatively short follow-up time. Furthermore, the patient questionnaire was administered postoperatively, subjecting the data to recall bias. A more optimal approach for future study would be to administer both pre- and postoperative validated PROMIS instruments.

Despite its limitations, this pilot study has provided valuable data necessary to lay the foundation for a larger prospective study, which is now underway. While demonstrating the feasibility of performing such a study in this particular patient population,[49] the study has also raised new, important questions pertaining to the optimization of RPNI design and its potential use not only for neuroma treatment but also for prophylaxis.

CONCLUSIONS

This pilot study serves to introduce a safe, novel, and potentially effective surgical technique in the form of RPNIs that may benefit patients with symptomatic postamputation neuromas who have otherwise failed all other treatment options. By providing free muscle grafts as targets for peripheral nerve ingrowth, RPNI implantation is physiological in nature by taking advantage of basic nerve sprouting behavior. The surgery is straightforward to perform, appears to be associated with a significant reduction in neuroma and phantom pain scores, results in a high level of patient-reported satisfaction, and has a reasonable complication profile. Further study is warranted, as RPNI implantation may also be indicated for the treatment of refractory neuromas in patients without amputations and for neuroma prophylaxis at the time of primary amputation.

Paul S. Cederna, MD
University of Michigan Health System
Department of Surgery
Section of Plastic Surgery
2130 Taubman Health Center
1500 E. Medical Center Drive
Ann Arbor, MI 48109
E-mail: cederna@med.umich.edu

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