

POSTAMPUTATION PAIN TREATED WITH PULSED RADIOFREQUENCY - A CASE REPORT

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Background: Transmetatarsal amputation (TMA) is a commonly performed procedure that can result in residual limb and phantom pain. Neuromodulation using pulsed radiofrequency (PRF) is a growing area of research in the management of refractory postamputation pain (PAP).

Case Report: A veteran in his sixties with a history of diabetes required a left TMA due to gas gangrene, subsequently complicated by severe, prolonged postoperative pain. PRF was performed first on the saphenous nerve using ultrasound guidance, then 12 weeks later on the saphenous, peroneal, and sural nerves. This resulted in analgesic effects lasting over 3 months and affording him an improved quality of life and function with his prosthetic.

Conclusions: The use of PRF for refractory PAP is not widely reported in pain literature and limited primarily to a handful of case reports; therefore, this case serves an important role in exploring the benefit this modality may provide for an otherwise refractory condition.

Key words: Pulsed radiofrequency, amputation pain, transmetatarsal amputation, neuromodulation, case report

BACKGROUND

Chronic postamputation pain (PAP) is a significant risk following amputations. A number of musculoskeletal and neurological factors play into the development of this potentially debilitating condition. Though a significant degree of heterogeneity exists, the estimated overall prevalence is 61% as reported in a meta-analysis of lower extremity amputations by Schwingler et al (1). The most common forms of PAP include phantom limb pain and residual limb pain, with an estimated prevalence of 53% and 32%, respectively (1). Residual limb pain can be further classified as either somatic (e.g., musculoskeletal, chronic infection, or wound inflammation related) or neuropathic (e.g., sympathetically mediated, neuroma driven, or postamputation neuralgia) (2). As the number of US individuals living with an amputation is estimated to double to 3.6 million by 2050, management of this risk is an incredibly important area of research (3).

Transmetatarsal amputation (TMA) is a commonly performed procedure for the management of severe foot pathologies, including peripheral vascular disease or diabetic foot infections (4). While the prevalence of PAP after a TMA varies, it is commonly reported that PAP is more common in individuals with nontraumatic lower extremity amputations (1). The management of PAP is multimodal and multidisciplinary, including pharmacological, rehabilitation, integrative therapies (e.g., acupuncture), as well as interventional techniques including neuromodulation (5).

Pulsed radiofrequency (PRF) is a form of neuromodulation and an important tool in the management of PAP. PRF involves the creation of a strong electrical stimulation around a nerve to ultimately provide analgesic relief, most commonly for joint, muscular, and neuropathic pain (6). Unlike conventional RF, which

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results in the thermal ablation of neural tissue around the RF needle tip, PRF provides a cooler temperature (often at or below 42 °C) with brief electrical stimulation and pauses to facilitate heat dissipation and thus preserves neural structures (6,7). There are multiple theories on the mechanism of PRF. One theory is that PRF results in neuromodulatory changes to gene expression in pain-processing neurons (8). Alternatively, PRF is proposed to lead to selective long-term depression of C-fiber-mediated spinal sensitization, reducing C-fiber efficiency, and thus inhibiting pain signal transmission to the central nervous system. Animal models of lumbar radiculitis have demonstrated that the analgesic effects of PRF may involve enhancement of the noradrenergic and serotonergic descending inhibitory pathways. The analgesic effects of PRF are dependent on both electrical dose and duration, which is thought to be due to modulation of electroporation and rectification (9). Additionally, on the cellular level, OX-42 and phosphorylated extracellular signaling-regulated kinase expression in the dorsal column is downregulated, reducing pain generation by attenuating astrocyte and microglial activation (10).

The use of PRF for PAP is not widely reported in pain literature. One case series (11) found 2 patients experienced 50% pain relief after PRF to the dorsal root ganglia. Another case (12) reported relief after application of PRF to the sciatic nerve after a favorable but brief response to a diagnostic block with bupivacaine and clonidine. PRF can even be applied using an electromagnetic field device, with 66% of patients reporting moderate or better pain improvement after 30 days in a study of 12 patients (13). Here, we report the use of PRF in a patient with chronic PAP following a TMA, applied to the left saphenous nerve, sural nerve, and superficial peroneal nerves of the residual limb.

CASE PRESENTATION

A veteran in his sixties with a pertinent past medical history of diabetes mellitus type II required a left TMA secondary to gas gangrene. The patient's TMA was complicated by delayed wound healing requiring numerous debridement revisions, in addition to severe and prolonged postoperative pain. He had tried multiple pharmacologic therapies, including neuropathic agents and opioids with insufficient relief. He had also completed extensive postoperative physical therapy.

The patient was referred to our Veterans Affairs pain clinic 13 months after his surgery with severe, persistent postoperative left lower leg and foot pain. He described the pain as sharp, stabbing, and radiating from his medial left knee to his left foot and ankle. On exam, he demonstrated full strength in bilateral lower extremities. He was noted to have allodynia with pain reproduction via palpation along the medial leg to ankle. Additionally, pain was reproduced via Tinel's sign at the proximal medial tibia.

Utilizing a linear ultrasound probe, a saphenous nerve block was performed. At the medial aspect of the proximal tibia at the level of the tubercle, the saphenous vein was visualized (Fig. 1A and 1B). Using an in-plane approach, a 25G 1.5-inch needle (BD PrecisionGlide, Becton Dickinson & Co, Franklin Lakes, NJ) was guided to the perisaphenous nerve area and 5 mL of 0.5% ropivacaine (NDC 63323-286-11) was injected. The patient reported near immediate pain relief of his medial leg and foot pain following this injection.

At a follow-up appointment 12 weeks later, the patient reported 6 weeks of marked pain relief following his saphenous nerve block. Given his improvement, PRF of the saphenous nerve was performed (Avanos, COOLIEF* Cooled RF Advanced Generator paired with COOLIEF* Quad Pump Unit, Alpharetta, GA). The tibia was visualized under ultrasound guidance at the level of the tibial tubercle and scanned medially until the saphenous vein was visible. Then, a 22G 54-mm cannula (Avanos, REF PMF22-54-10CS) was placed beneath the saphenous vein at the location of the saphenous nerve. An RF 22G 54-mm probe with 10-mm tip (Avanos, REF PMP-22-54C-SU) was placed into the cannula, upon which sensory and motor testing were conducted at 50 Hz and 2 Hz, respectively. Two lesions were made at 42°C for 150 seconds each. A mixture of 1 mL of 40 mg triamcinolone (NDC 0003-0293-28) and 1 mL of 0.5% ropivacaine (NDC 63323-286-11) were subsequently injected.

At another follow-up appointment 12 weeks later, the patient reported marked improvement of his medial leg pain with a new, increased diffuse foot and ankle pain in his residual limb. A repeat PRF of the saphenous nerve was performed, in addition to PRF of the sural and peroneal nerves. His saphenous nerve PRF was completed utilizing the same procedural protocol as previously. For his superficial peroneal nerve PRF, an ultrasound probe was placed over the distal anterior tibia (Fig. 2A) where the superficial peroneal nerve was visualized (Fig. 2B).

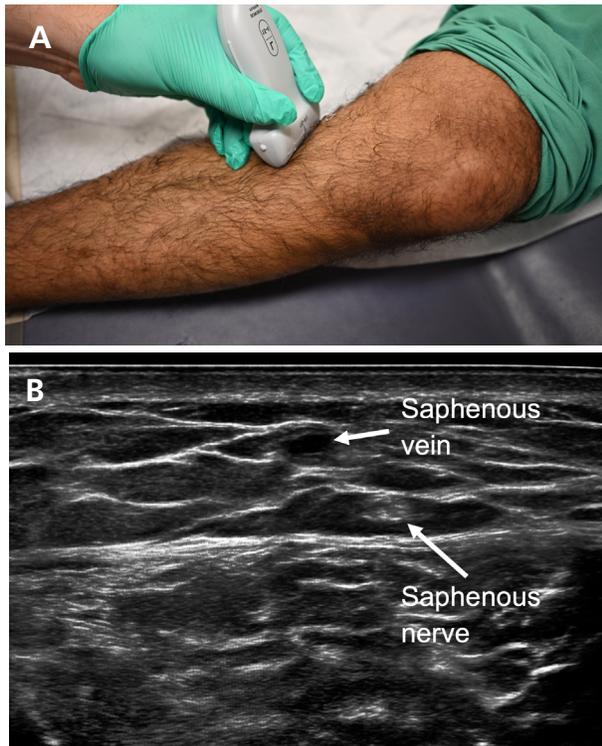


Fig. 1. A) Patient and ultrasound positioning to visualize the saphenous nerve. B) Ultrasound visualization of the saphenous nerve via the saphenous vein.

A 22G 54-mm cannula (Avanos, REF PMF22-54-10CS) was placed by the nerve, an RF 22G 54-mm probe with 10-mm tip (Avanos, REF PMP-22-54C-SU) was inserted, and sensory and motor tests were conducted at 50 Hz and 2 Hz, respectively. A lesion was made at 42°C for 150 seconds and 2 mL of 0.5% ropivacaine (NDC 63323-286-11) was administered. For the sural PRF, the distal lateral fibula was visualized under ultrasound guidance (Fig. 3A and 3B). A 22G 54-mm cannula (Avanos, REF PMF22-54-10CS) was placed by the nerve, an RF probe with 54-mm tip (Avanos, REF PMP-22-54C-SU) was inserted, and confirmatory sensory and motor testing were again performed. A lesion was then made at 42°C for 150 seconds, followed by administration of 1 mL of 1% lidocaine (NDC 63323-492-09).

At 11 weeks follow-up, the patient reported continued substantial pain relief and functional improvement. He was able to increase his ambulation from half a block to 3 blocks and noted improved tolerance of activities of daily living, such as getting dressed. Additionally, he was able to return to hobbies he previously enjoyed, including playing music.

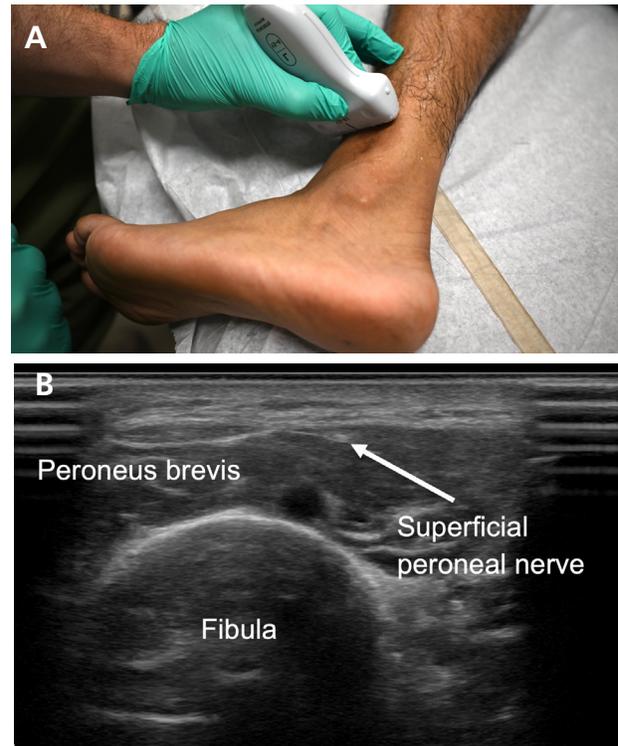


Fig. 2. A) Patient and ultrasound positioning to visualize the superficial peroneal nerve. B) Ultrasound visualization of the superficial peroneal nerve via the fibula and peroneus brevis.

DISCUSSION

This case report suggests that intractable PAP after a TMA that is refractory to oral medications and physical therapy can be effectively treated with PRF to the saphenous, sural, and peroneal nerves. The analgesic effects lasted for ≥ 12 weeks for this patient and afforded him an improved quality of life and function. The saphenous nerve is a terminal branch of the femoral nerve formed from L3 and L4 spinal roots and innervates the medial calf; the sural nerve from S1 and S2 innervates the lateral calf, ankle, and foot; and the peroneal nerve from L4, L5, S1, and S2, via its branches into the deep and superficial peroneal nerves, innervates the anterior calf and dorsal foot (14). Though the saphenous and sural nerves are pure sensory nerves, the peroneal nerve has both sensory and motor function, the latter of which was unaffected by the application of PRF: the patient retained function of ankle dorsiflexion and ankle eversion before and after the procedure.

In patients that have incomplete or ineffective treatment with PRF to the nerves above, one consideration is involvement of the tibial nerve, which is a continuation

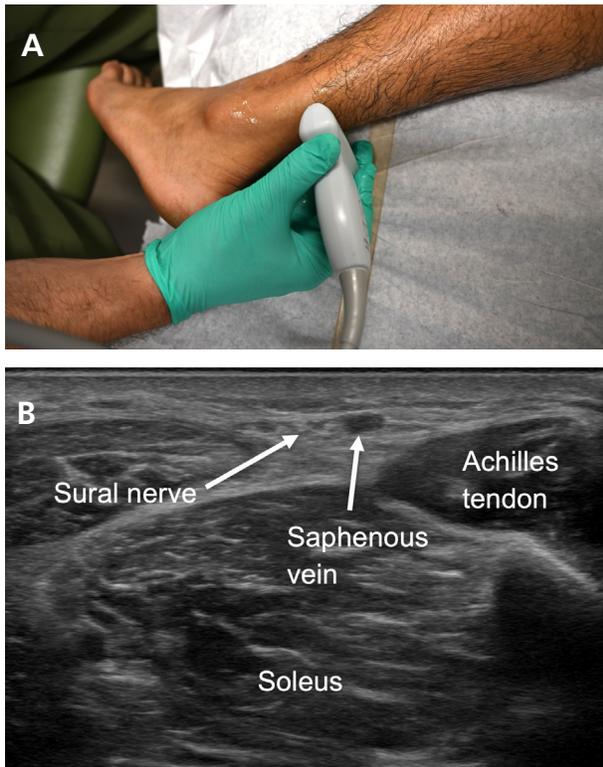


Fig. 3. A) Patient and ultrasound positioning to visualize the sural nerve. B) Ultrasound visualization of the sural nerve via the saphenous vein.

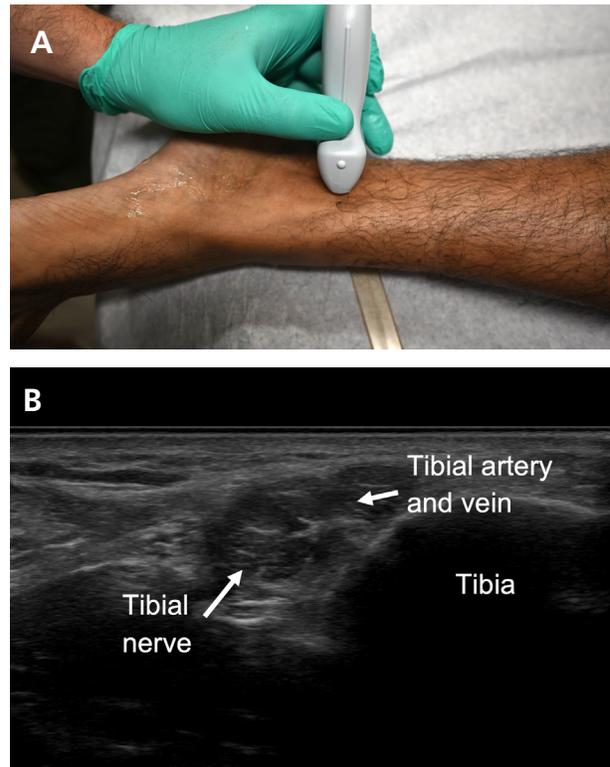


Fig. 4. A) Patient and ultrasound positioning to visualize the superficial peroneal nerve. B) Ultrasound visualization of the superficial peroneal nerve via the fibula and peroneus brevis.

of the sciatic nerve at the distal posterior thigh, formed from the spinal roots of L4, L5, S1, S2, and S3. It runs to the medial malleolus where it splits into the medial and lateral branches, the entrapments of which could result in pain in similar distributions as this patient, though he did not have pain classically in the plantar foot distribution. As seen in Fig. 4A and 4B, the tibial nerve can be assessed for entrapment neuropathy and neuroma formation prior to the application of PRF to the appropriate pain generator.

In addition to topical anesthetic, triamcinolone was also injected after the first application of electrical stimulation to the saphenous nerve. In the subsequent application, it was withheld with only local anesthetic administration. One may argue that the effect of corticosteroid application confounds the effect of PRF, especially given a possible similar mechanism of action in suppressing C-fiber transmission of pain signals and reduction in neuronal firing, and may even interfere with the intended neuromodulatory mechanisms of PRF (15). Corticosteroids can exert their effect for days to

months, and even years, and may have contributed to this patient's substantial pain relief that may be effectually indistinguishable from the effects of PRF. However, the anti-inflammatory and edema reduction effects of corticosteroids have conversely significantly higher risk of local and systemic adverse effects, including cutaneous atrophy, hyperglycemia, increased blood pressure, weight gain, and adrenal suppression over long-term use. For this patient, to optimize his pain relief given his severe pain on presentation, he was initially treated with both corticosteroids and PRF. Considering the patient's comorbid diabetes and favorable effect of PRF after the second application to the saphenous, sural, and peroneal nerves, and the possible confounding effects described above, we have proceeded with only PRF for repeat stimulation.

Our case demonstrates effective treatment of PAP after TMA with a diagnostic block and 2 PRF treatments spaced 12 weeks apart. The reported frequency of treatment and length of effect varies in the literature. Studies (16) of ≤ 5 treatments to the dorsal root

ganglia for lumbar radicular pain lasted \leq 25 months. Another study (17) using PRF to the occipital nerve for ventriculoperitoneal shunt-related headache reported relief lasting 2 and 4 months for 2 patients. A study (18) of 100 patients using PRF to the second and third thoracic dorsal root ganglia for postmastectomy pain syndrome was repeated 3 times one week apart with no serious complications and was effective, measured by the Visual Analog Scale and Quality-of-Life Scale. Though there are no consensus guidelines, and only case reports of PRF use in select conditions in the field, current literature suggests that it can be repeated with shortest interval of one week apart, with a range of one to five treatments, pain-relieving effect lasting months to years, and with none to minimal adverse effects.

PRF can be compared against other forms of neuromodulation, including percutaneous peripheral nerve stimulation (PNS). One pilot study (19) looking at 60-day percutaneous PNS in the acute postamputation phase reported a greater reduction of pain and medication requirements for individuals provided a PNS postoperatively. Similarly, a randomized control trial (20) of 28 lower extremity amputees with PAP demonstrated a significantly greater proportion of individuals reporting substantial pain reduction in individuals provided PNS compared to placebo over a 4-week study. These results were similarly supported in a study (21) demonstrating a majority of patients

with chronic PAP (18/24) reporting $>$ 50% reduction of pain following PNS. To these authors' knowledge, there are no direct comparison studies assessing PRF and PNS in the management of PAP. However, there are comparisons (22,23) looking at PRF and PNS for herpes zoster ophthalmicus and postherpetic neuralgia.

While this case offers a promising example of the potential therapeutic benefits of PRF in the management of refractory PAP, it is important to recognize limitations that exist. Primarily, as this is a case report and derived from a single patient's experience, its broader applicability may be limited. Future research is crucial to better understand the efficacy of PRF in the management of PAP and, in particular, in comparison to other forms of neuromodulation, including PNS. Further research to better define consensus guidelines for PRF, including intervals between treatment, number of treatments, and expected relief duration, are all key to optimizing the use of this modality.

CONCLUSIONS

PAP is a commonly encountered complication of lower extremity amputations and can be debilitating. When conservative modalities fail to provide relief, PRF is a neuromodulation technique that may offer analgesic relief by helping to disrupt central processing changes that result from chronic painful stimuli.

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