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Quick Review and Technical Approach for Regenerative Peripheral Nerve Interface Surgery

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Abstract

Regenerative peripheral nerve interface RPNI's surgery was originally designed for prosthetic control. RPNI's has demonstrated to be an effective tool to prevent neuroma formation by providing free muscle grafts as physiological targets for peripheral nerve ingrowth. Nerve transection injuries can result in painful neuromas that adversely affect patient recovery. This is especially significant following amputation surgeries, but they can also be used in surgeries in which the nerves can be visualized with a noticeable lesion. The first series of patients undergoing RPNI implantation for treatment of symptomatic postamputation neuromas was published in 2016. The series included a report of 46 patients undergoing RPNI. The clinical outcomes of RPNI have been optimistic with a reduction in neuroma pain up to 73% and phantom pain reduction of 53% along the uniformly high patient satisfaction. Since then, studies have been expanded, and knowledge regarding physiology has increased, providing us with new tools for a better understanding and giving these procedures more benefits and applications.

Keywords

Component, Formatting, Style, Styling, Insert

1. Introduction

Painful neuromas result from traumatic injuries to nerves and cause substantial physical disability, psychological distress, and decreased quality of life. Pain can be a major issue after total or partial amputation, with reported incidences up to 8% for finger amputation and 85% for major limb amputation. Pain can originate in the amputated stump which is mostly described as residual limb pain (RLP) or as a result of phantom limb pain (PLP). Symptomatic neuromas result from a disorganized proliferation of transected peripheral nerves [1]. The origin of RLP lies in the peripheral nerve system and can be caused by skin problems, infections, poor prosthetics, and poor soft tissue coverage, but the principal cause of neuropathic pain due to a scar-tethered residual nerve stump or end neuroma at the site of transection. These neuromas cause neuropathic pain. PLP occurs in both peripheral and central nervous system. Psychological factors have an influence on this as well as on the severity, frequency, and impact of the pain. It is not understood why some neuromas remain asymptomatic and further investigation into the pathophysiology is needed [1] [2]. Components of the nociceptive response of painful neuromas have been identified, including central sensitization, accumulation of ion channels, and an inflammatory response that sensitizes the neurons, leading to hypersensitivity. Importantly, painful neuroma development after primary nerve repair is rare because the nerve has a target to innervate.

Nonsurgical management of symptomatic neuromas includes desensitization, anesthetic and or steroid injection, electrical nerve stimulation, and opioids. Conservative treatment for post-amputation pain shows a little effect [3]. Opposite, the prevention of a painful neuroma after amputation by means of nerve surgery in the same session has promising results [4] [5]. However, there is no clear consensus of which surgical technique provides the best surgical outcome in terms of pain prevention [5]. The Regenerative Peripheral Nerve Interface (RPNI) was developed to overcome these limitations. The RPNI consists of an autologous free muscle graft secured around the end of a transected nerve. The muscle graft provides regenerating axons with end organs to reinnervate, thereby preventing neuroma formation [6]. We have shown that this simple and safe surgical technique successfully treats and prevents neuroma formation in major limb amputations. In this paper, we describe RPNI surgery in the setting of major limb amputation and highlight the promising results of RPNIs in animal and clinical studies [7].

2. The Regenerative Peripheral Nerve Interface

RPNI is a surgical treatment approach for management and prevention of painful neuromas. RPNI is a simple surgical solution and constructed by implanting the distal end of a transected peripheral nerve into a free skeletal muscle graft.

The muscle graft initially de-vascularized at the time of the harvest undergoes a process of degeneration followed by regeneration. The muscle graft at the time of the implantation is supported by imbibition. After the regeneration process becomes revascularized just as any free tissue graft would be. The skeletal muscle becomes a perfect target for the denervated axons for regenerating spouting from the end of the peripheral nerve. As a result, substantially fewer regenerating axons will be part of the inflammatory process and undergo a problematic neuroma. After peripheral nerve transection injury, the nerve undergoes 3 biological processes Wallerian degeneration, axonal sprouting/regeneration, and muscle reinnervation if end organs are present.

In the context of amputation, the end organs are missing, and the end of the peripheral nerve continues to sprout and regenerate until they form a neuroma.

The RPNI surgery provides ample denervated muscle fiber to facilitate the reestablishment of neuromuscular junction. The muscle graft displays dispersion of acetylcholine receptors along the sarcolemma and expresses a variety of neurotrophic factors. An environment conducive to reinnervation [8].

A regenerating axon contacts a denervated muscle fiber and provides necessary trophic support to prevent atrophy. Electrophysiologic experiments confirmed that these new neuromuscular junctions were functional and capable of transducing nerve signals to muscle action potentials [9].

3. Description of Technique

Multiple descriptions of the surgical technique have been made. The free skeleton muscle graft that is used to create RPNI's is ideally harvested from the amputated limb but at times a separate incision will need to be made to harvest healthy free muscle graft from another site.

Following completion of the limb amputation, the specimen is passed off the field but kept sterile so that it can be used for free muscle graft harvest if appropriate.

It is important to avoid placing too large of graft as this can interfere with perfusion of the muscle from the wound bed and lead to greater necrosis.

3.1. Preparation of Peripheral Nerves

RPNI surgery can be performed any time peripheral nerves are transected and direct nerve repair cannot reapproximate these axons back to their native targets. In immediate RPNI surgery, major peripheral nerves are isolated, marked and sharply transected in the residual limb during the amputation. Traction neurectomy is not performed to purposefully avoid proximal retraction of the nerve end [10].

During a Below-knee amputation (BKA) surgery the tibial nerve is identified in the deep posterior compartment adjacent to the posterior tibial vessel. The nerve is transected and dissected free from surrounding soft tissues to allow creation of an RPNI around the end of the nerve.

For superficial and deep peroneal nerves, RPNI can be created within the BKA site.

To isolate SPN and DPN prior to segmentation and decrease the number of free muscle grafts placed distally in the residual limb after BKA, the common peroneal nerve (CPN) can be exposed through a proximal separate incision between the fibular head and the distal lateral thigh.

3.2. Skeleton Muscle Graft Harvest

In general, an approximately 3 cm × 2 cm × 0.5 cm free skeleton muscle graft is used of as many nerves fascicles as needed depending on the nerve size. For example, the sciatic nerve may require up to 5 fascicles obtained through interneural dissection. Thus, for larger caliber nerves fascicular dissection is performed to enable multiple fascicular RPNI's rather than creating a single large RPNI. Grafts that are too thick will undergo central necrosis. Doing so, also improves the ratio of denervated muscle fibers to regenerating axons to maximize reinnervation. For each isolated nerve a small free muscle graft is harvested from healthy, autologous skeletal muscle. In the case of major limb amputation, these free muscle grafts can be harvested directly from the amputated limb unless this is not appropriate due to ischemia tumor or infection. If no healthy muscle can be obtained from the amputated limb, the muscle grafts can be obtained from a more proximal donor muscle (e.g., vastus lateralis) through a separate incision [10].

3.3. RPNI Surgery

After all nerves are isolated and free muscle graft are obtained, The RPNIs are created by implanting each distal nerve end into a corresponding muscle graft.

The transected peripheral nerve end is placed in the center of the muscle graft parallel to the muscle fibers. At the interface between transected axons and the muscle graft, 6-0 non absorbable monofilament sutures are placed. Only the epineural portion and a minuscule portion of muscle are incorporated into each stitch.

The nerve is them wrapped circumferentially around the nerve and secured with interrupted 6-0 monofilament sutures (**Figure 1**).

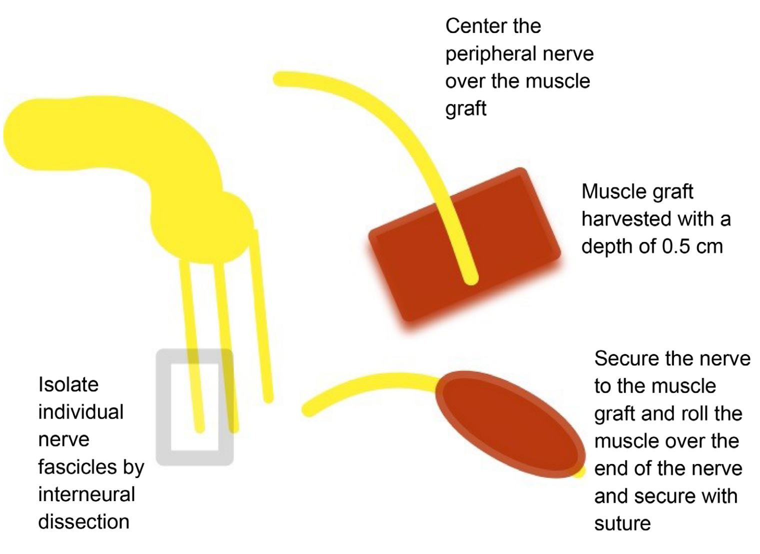

Figure 1. Diagram illustrating the steps of RNPI procedure.

Finally, a space is created for the placement of RPNI in an area remote from the surgical incision and away from the weight bearing surface.

3.4. RPNI Outcomes

The clinical outcomes of RPNI have been favorable with a reduction in neuroma pain up to 73% and phantom pain reduction of 53% along the uniformly high patient satisfaction. A decrease at painkillers intake and the improvement in chronic pain in everyday activities, and Most of the patients were satisfied with the RPNI surgery [11].

4. Conclusions

Patients whose limbs have been amputated are at high risk for neuropathic pain and phantom limb pain, which can generate a decrease in the quality of life. It can be prevented by performing RPNI at the same time as surgery.

Current clinical and experimental studies are promising and have shown a decrease in pain, patient satisfaction, and lower consumption of analgesics. Therefore, RPNI surgery should be considered in patients who are going to undergo amputation of a limb.

They should also be considered in any peripheral nerve injury such as inguinal hernia repair surgery, in case of ilioinguinal or iliohypogastric nerve injury.

RPNI surgery may be considered in any peripheral nerve injury for pain prevention, but further study is required.

Conflicts of Interest

The authors have no financial interest to declare in relation to the content of this article.

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