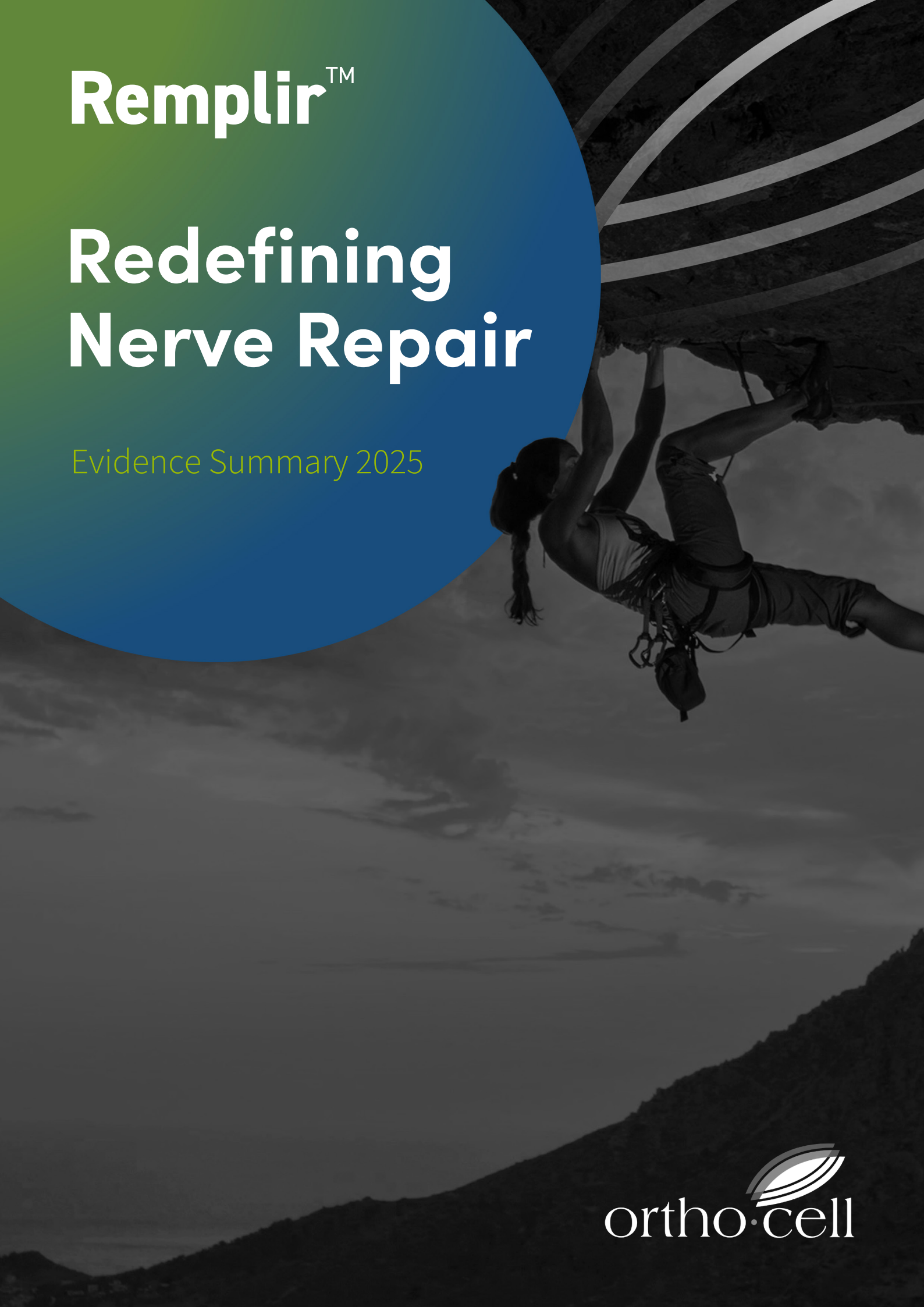
Remplir™

Redefining Nerve Repair

Evidence Summary 2025



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Remplir™ Redefining Nerve Repair

Remplir™ is a collagen nerve wrap used in the repair of peripheral nerve injuries. It provides compression-free protection to the nerve, generating an ideal microenvironment to aid nerve healing.

Remplir was approved for sale by the Australian Therapeutic Goods Administration in 2022. Since then, over 3000 patients have received treatment with Remplir for a diverse range of peripheral nerve repair procedures with no adverse events/serious incidents, no usability complaints, no field safety actions or recall and no safety signals reported.

The strong adoption of this product by plastic reconstructive and orthopedic surgeons has been driven by the excellent outcomes observed in pre-clinical studies, published clinical data and case reports.

For Example

1. **Clinical study showed 85% of nerve repairs resulted in functional recovery of muscles controlled by the repaired nerve** – Study included patients with injuries to the upper extremities, brachial plexus and cervical spinal cord. Nerve reconstruction with Remplir resulted in functional recovery of muscles controlled by the repaired nerve in 76% of nerve repairs within 12 months, increasing to 85% nerve repairs by 24 months post-treatment. Improvements in strength and range of motion of target muscles was observed between 12- and 24-months post-treatment.

2. **Pre-clinical animal study showed no abnormal inflammation or scarring after implantation of Remplir, which remodeled into epineurial-like tissue at the repair site.** Nerve regeneration, demonstrated by the presence of myelinated (mature) axons downstream of the repair site, correlated with sensory and motor recovery.

Feedback from plastic reconstructive and orthopaedic surgeons is that Remplir is easy to use straight out of the box, provides compression free sealing around the repaired nerve and is likely to reduce need for multiple sutures at the coaptation site and surgical time.

A multi-center post-market clinical study is underway to collect more safety and performance data for Remplir™ in peripheral nerve surgery. **First reports for the study will be released in Q4 CY 2025.**

"We are now seeing a consistent return of arm and hand function following nerve transfer surgery with Remplir... Remplir is increasing the success rate and efficiency of nerve transfer surgery.

Leading Australian orthopaedic nerve specialist and clinical trial lead,
Dr Alex O'Beirne

1. Pre-market Australian Clinical Study

Study objective

An Australian case series study was conducted to evaluate outcomes of nerve reconstruction using Remplir in patients with injuries to the spinal cord, brachial plexus or upper extremity peripheral nerves.

Study population

A total of 36 peripheral nerve reconstructions in 19 patients, aged between 18 and 50 years, were performed. Patients in the clinical trial suffered traumatic nerve injuries following motor vehicle, sporting and/or work-related incidents, resulting in partial or total loss of use of their arms and, in more severe cases, their legs and torso as well (quadriplegia). Patients experienced significant pain and were unable to perform basic activities of daily living (i.e. eating, bathing, dressing and toileting), play sport and/or work. Without surgery they would not have regained normal use of their injured arm and hand.

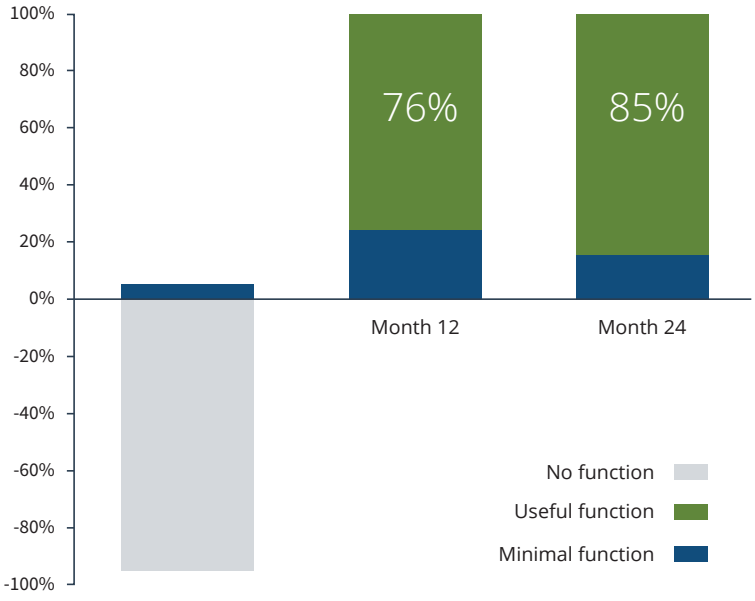
Study results

Patients received one or more nerve repairs (nerve transfer or nerve graft) augmented with Remplir. Recovery after treatment was assessed by grading[1] the strength of target muscles closest to the site of nerve repair. Outcome data at 12 months post-treatment was available for 16 of 19 patients and 33 nerve repairs *(Figure 1).*

Functional recovery of muscles controlled by the repaired nerve was observed in 76% (25 of 33) repairs at 12 months post-treatment and in 85% (23 of 27) of nerve repairs at 24 months post-treatment. The results demonstrate that functional gains were not only maintained but continued to improve between 12-and 24-months post-treatment.

Figure 1: Patients regained voluntary muscle movement within 12 months, increasing strength and range of motion at 24 months

[1] British Medical Research Council Grading System (MRC grade), with a score of 0 to 5. A score of zero (0) indicates no nerve connection to the muscle (ie., no recovery), a score of five (5) is given to muscles with normal power/strength. A score of 3 or better is clinically defined as a meaningful functional recovery.



Useful Function

Voluntary movement with improved strength and range of motion

Minimal Function

Voluntary movement restored, limited strength and range of movement

No Function

No voluntary movement

Final Results

85% **(23 of 27)** Of nerve repairs resulted in functional recovery of muscles controlled by the repaired nerve

Reconstruction of Upper Extremity Peripheral Nerve Injuries Using an Epineurial-Like Collagen Device—A Prospective Clinical Study

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Abstract

Background Epineurium acts as a barrier to protect nerves from injury and maintains its structural and functional integrity. A device was developed to mimic the native structure of epineurium. The aim of this study was to evaluate its biological characteristics and clinical performance in the reconstruction of upper extremity peripheral nerves.

Methods Scanning electron microscopy, transmission electron microscopy, and enhanced microcomputed tomography were used to examine the ultrastructural characteristics of the device. A prospective case series with 2-year follow-up was undertaken and reported. Patients who required nerve reconstruction in the upper extremities were included and underwent single or multiple nerve reconstructions in one or both upper limbs.

Results The device mimics the structural and biological properties of epineurium. During surgical use, it can form compression-free and self-engaged wrapping around the repaired nerves. A total of 36 peripheral nerve reconstructions were performed using either nerve transfer or nerve grafting in 19 patients. Of these, 14 patients had upper limb nerve injuries and 5 had C5 to C8 spinal cord injuries resulting in tetraplegia. Nerve reconstruction using the device restored peripheral nerve function, with functional motor recovery (FMR) observed in 76% of the most proximal target muscle at 12 months and 85% of most proximal muscles at 24 months post-treatment. FMR was observed in 61% of all target muscles at 12 months and 75% at 24 months post-treatment.

Keywords
- nerve reconstruction
- epineurium
- nerve transfer
- upper extremity

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2. Post-market Australian Clinical Experience

Remplir was first approved for sale in Australia in 2022 and has subsequently received regulatory approval in New Zealand, Singapore and the USA. Around 3,000 patients have received Remplir for a range of surgical procedures with no adverse events/serious incidents, no usability complaints, no field safety actions or recalls, and no new safety signals reported.[2] Remplir applications have included:

- Nerve transfer for reconstruction of upper limb function in high peripheral nerve, brachial plexus and cervical spinal cord injury
- Free functioning muscle transfer after brachial plexus injury
- Revision carpal and cubital tunnel procedures
- Schwannoma and neuroma resection (terminal and in-continuity)
- Nerve capping concomitant with upper limb amputation
- Digital nerve repair with autograft

See case examples below

User Feedback

Cadaver workshops have been conducted with plastic and orthopedic surgeons from across Australia for product familiarization and surgeon training. Feedback from workshops was that the device is easy to manipulate around the nerve, and it conformed around the nerve without compression. The flat sheet format of Remplir was reported to be easier to use than the standard tube format of other devices. The majority (80%) of surgeons surveyed reported that the device was easy to suture and 65% of surgeons agreed that use of Remplir is likely to reduce operative time.

Post-market Clinical Follow-up Study

Orthocell is sponsoring a multi-center post-market clinical follow-up study conducted at selected sites in Australia. The study, which commenced recruitment in January 2025, will collect both retrospective and prospective data on the safety and performance of Remplir in peripheral nerve surgery. Preliminary outcomes from this study are expected in Q3 2025.

ANZCTR Australian New Zealand Clinical Trials Registry

// Read More here

[2] As at 15 April 2025

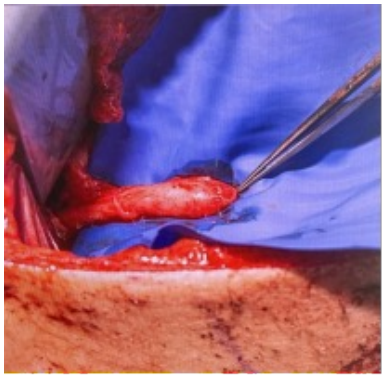
3. Case Examples

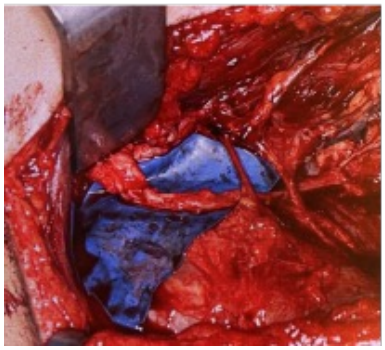
CONNECT with Remplir™

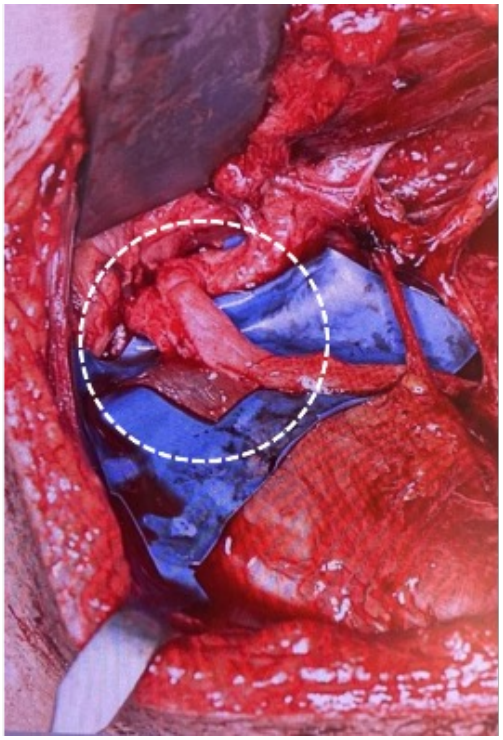
Trauma: motor vehicle, power tool, surgical injuries, sports and military related accidents

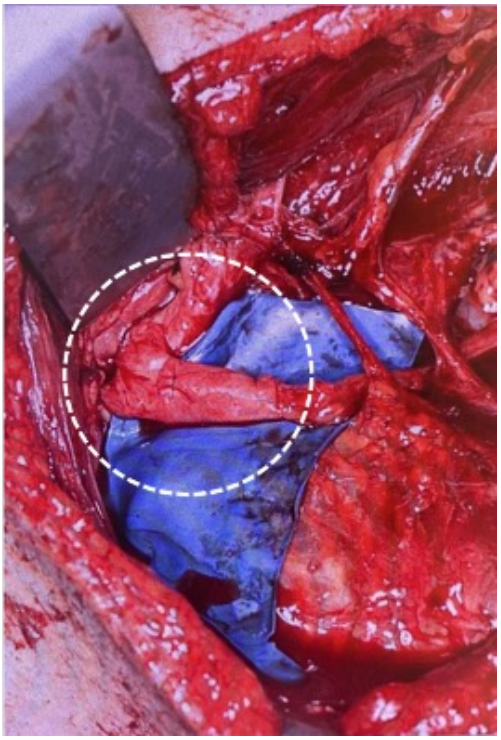
Male patient (21 years of age) with axillary nerve injury caused by GHJ dislocation four months prior to treatment. Patient presented with a dense axillary nerve palsy with avulsion just distal to the circumflex branch of the axillary artery with scarring +++ and 2cm adhesions on either side. Nerve transfer performed using radial nerve to medial head of triceps as donor. Remplir used to assist coaptation with significant size mismatch.

Case Courtesy of Dr Alex O'Beirne







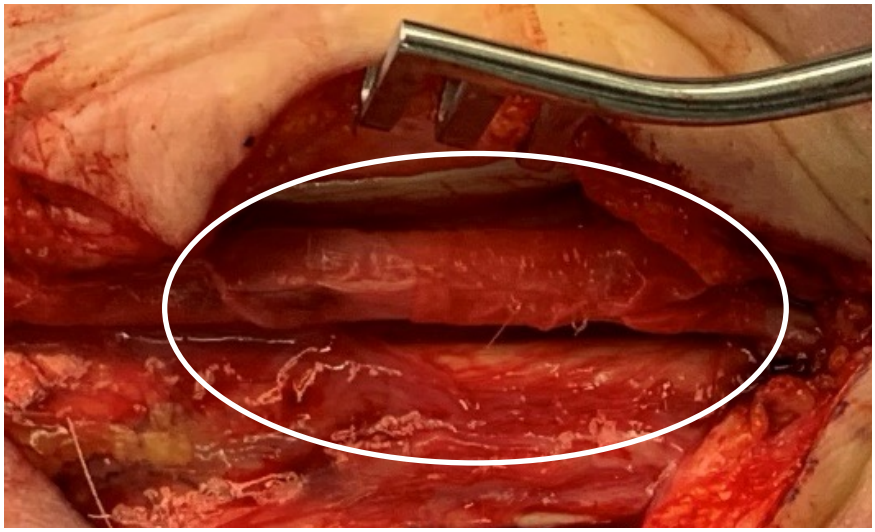


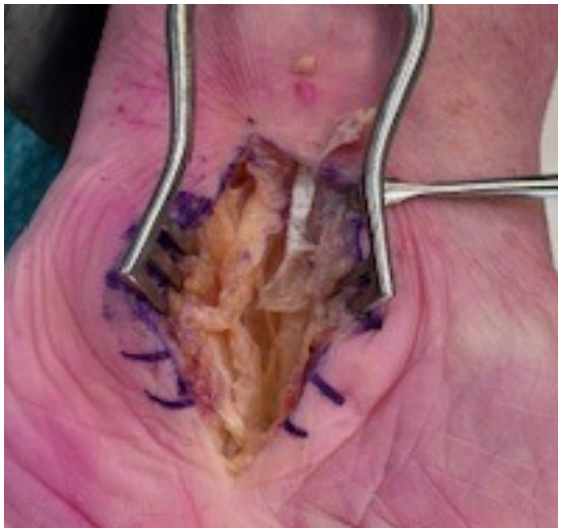
PROTECT with Remplir™

Compression: blunt trauma, compression neuropathy (e.g. carpal/cubital tunnel)

Nerve wrapping with Remplir after surgical treatment for compression neuropathy can potentially improve patient outcomes. The smooth outer surface of Remplir consists of collagen bundles that are tightly packed, acting as a barrier between the epineurium and surrounding soft tissue. This feature of Remplir promotes nerve gliding and reduces the risk of adhesion formation after primary or revision surgery for compression neuropathy. As Remplir consists of collagen fibres that are similar in size and arrangement to normal human epineurium, it is an ideal scaffold for regeneration of healthy nerve tissue. Images below are of Remplir being used as a wrap in conjunction with carpal tunnel revision surgery

Pictures courtesy of Dr Matt Lawson Smith





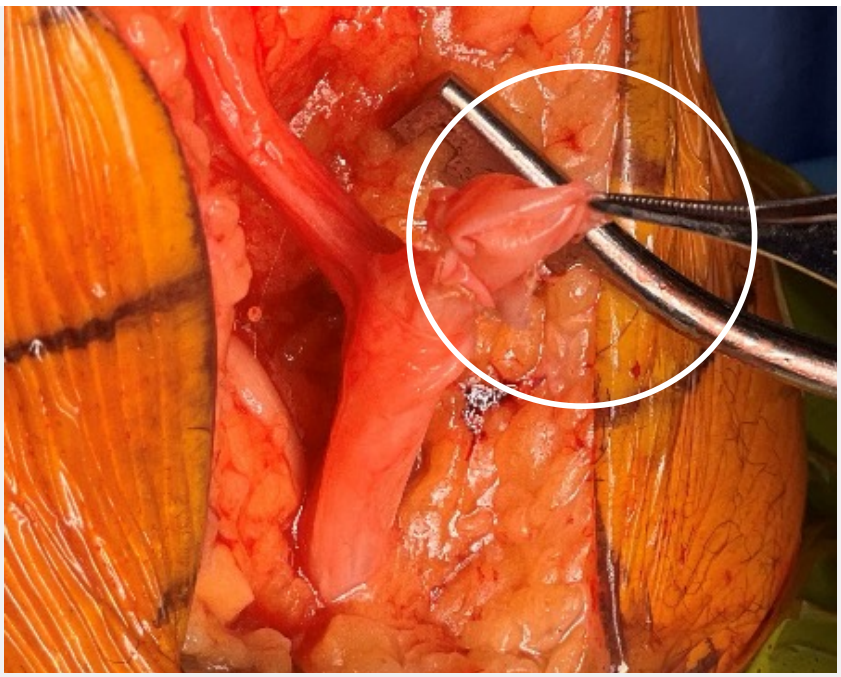
CAP with Remplir™

Iatrogenic: amputation, stump neuroma, mastectomy, schwannoma

Outcomes from three cases of peripheral nerve capping with reinnervation into adipose tissue for prophylaxis and management of neuroma were presented at the 2024 Combined Meeting of the American Society for Surgery of the Hand and the Australian Hand Surgery Society. After neurolysis and mobilization of the transected nerve, subcutaneous adipose tissue was harvested and placed around the nerve stump.

Remplir was wrapped around the encased nerve end and sutured into a cap. The construct was then secured without tension in an adipose tissue pocket.

Cases courtesy of Dr David Gamble and Dr Richard Carey Smith



4. Pre-clinical Data

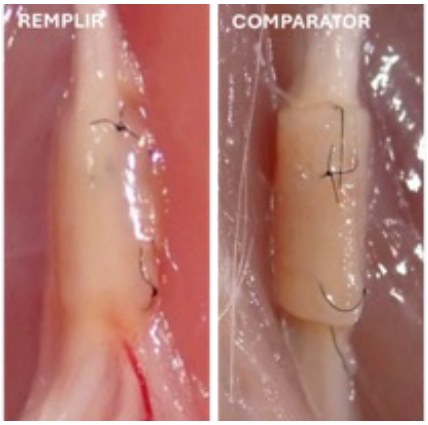
Comparative study in rat sciatic nerve transection

This study aimed to demonstrate safety and performance outcomes of Remplir compared to a similar nerve repair device in a rat sciatic nerve injury model. Repair of surgically transected nerves (n=72) was evaluated in three treatment groups: repair using sutures (control group), repair with sutures and Remplir, and repair with sutures and the comparator. Assessment of biocompatibility and nerve regeneration was performed at 4-, 12- and 24-weeks post-treatment. Functional testing for motor and sensory recovery was also performed.

Results
No adverse tissue reaction

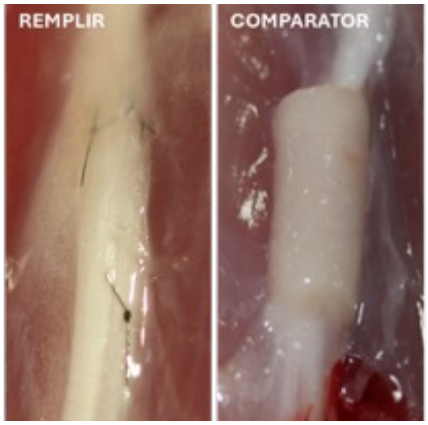
No abnormal inflammation or scarring occurred after implantation of Remplir. Macroscopic observation of the implant site showed Remplir had been remodeled into native tissue by 24 weeks post-implantation *(Figure 1)*. No chronic inflammation, foreign body reaction or fibrosis, and minimal adhesions to surrounding soft tissue, were observed.
In contrast, the comparator device was largely still intact at 24 weeks post-implantation and implantation was associated with noticeable progression of adhesions to surrounding tissues *(Figure 1).*

4 weeks



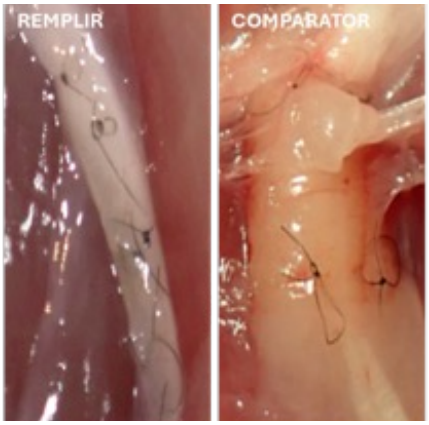
Remplir conforms to host tissue to protect transected nerve

12 weeks



Remplir largely degraded and integrated into host epineurial tissue

24 weeks



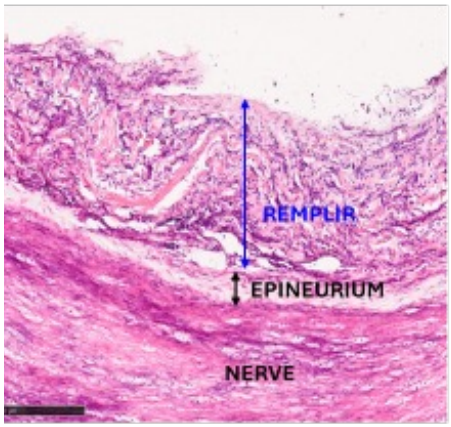
Remplir completely degraded and integrated into host epineurial tissue

Figure 1: Gross macroscopic observations of repair site at 4-, 12-, and 24-weeks post-treatment with Remplir and a comparator device.

Remodeling and integration into host nerve tissue

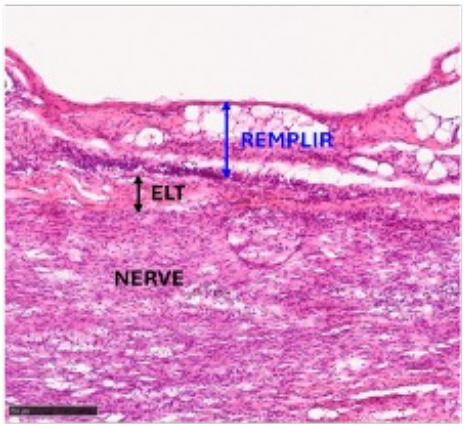
Early integration of Remplir, crucial for maintaining the structural integrity of the repaired nerve during early healing, was observed after 4 weeks *(Figure 2).* Remplir had substantially remodeled into epineurial-like tissue by 12 weeks post-implantation, with complete degradation and remodeling observed by 24 weeks. Physiological inflammation, consistent with normal healing processes and with no foreign body response, was observed across the observation period.

4 weeks



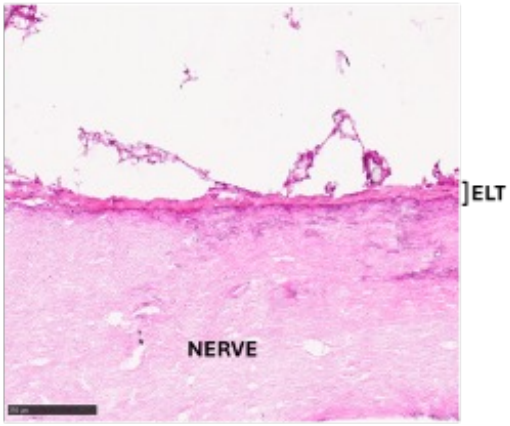
Remplir integrates with host tissue to protect transected nerve

12 weeks



Remplir largely degraded and remodeled into epineurial-like tissue (ELT)

24 weeks



Remplir completely degraded and remodeled into host epineurial tissue

Figure 2: Histological H&E-stained longitudinal sections of Remplir-repaired nerves at 4-, 12-, and 24-weeks post-treatment.

Regeneration of high-quality nerve tissue

The regeneration of high-quality nerve tissue was demonstrated by the number of myelinated (mature) axons that were detected downstream of the repair site.

Neurofilament staining at 12-weeks post-implantation shows that the axonal architecture across the transection site as a continuous and well-aligned orientation akin to normal nerve tissue *(Figure 3).* Robust axonal bridging with minimal misdirection across the transection site correlated the restoration of electrophysiological signaling.

- Longitudinal nerve sections stained for neurofilaments.
- Neurofilaments support axon structure and function

Normal nerve

Neurofilaments are thick, continuous structures with longitudinal axonal alignment.

12-weeks repair with Remplir™

Restoration of neurofilament continuity and axon alignment across the repair zone.

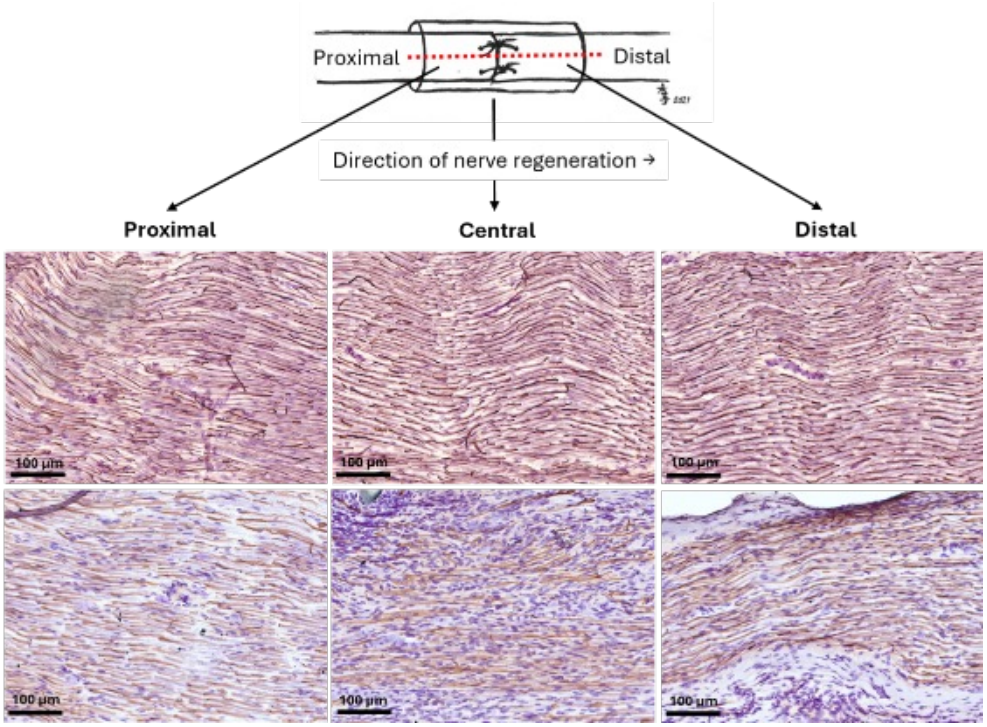


Figure 3: Immunohistochemical staining for neurofilament at the proximal, central repair, and distal nerve segments following repair with Remplir.

Return of sensory and motor function

Return of motor function demonstrated by the return of extensor muscle contraction comparable to the opposite untreated leg by 12 weeks post-treatment.

Return of sensory function was demonstrated by return of a withdrawal response to mechanical stimulus in the treated leg comparable to the opposite untreated leg by 12 weeks post-treatment.

Remplir™

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