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Remplir™ evidence compendium

This compendium brings together our clinical research and scientific evidence to support informed decision-making. It highlights key studies, findings, and insights, providing a clear and concise reference for healthcare professionals seeking reliable, evidence-based information.

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CONTENTS:

CLINICAL PAPER SUMMARY

Reconstruction of Upper Extremity Peripheral Nerve Injuries Using an Epineurial-Like Collagen Device - A Prospective 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 were performed in 19 patients aged between 18 and 50 years. 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 (tetraplegia). 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.

"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."

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

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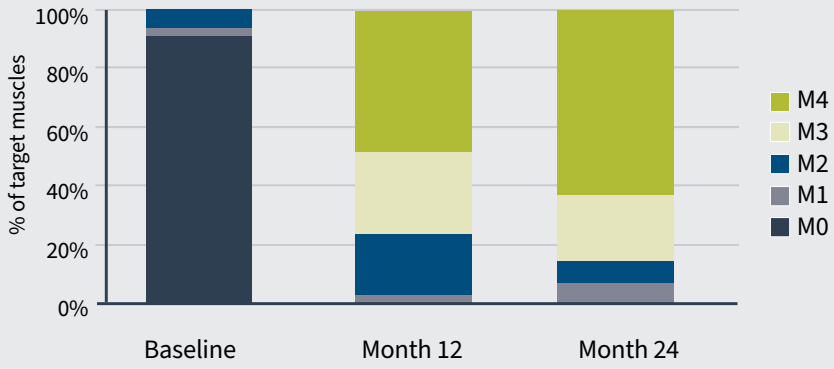
Study results:

Patients received one or more nerve repairs (nerve transfer or nerve graft) augmented with Remplir. Recovery after treatment was assessed by grading 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



Grade M3 and M4 – voluntary movement with improved strength and range of motion. Maximum level of recovery expected.

Grade M2 – voluntary movement restored, limited strength and range of movement.

Grade M0 or M1 – no voluntary movement.

Final Results:

85%

(23 of 27)

of nerve repairs resulted in functional recovery of muscles controlled by the repaired nerve at the 24-month post-treatment assessment

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WHITE PAPER

A Comparative Study of Collagen Nerve Wraps in Peripheral Nerve Repair – Preclinical Rat Sciatic Nerve Transection Model

Data presented at the 2025 IFSSH and IFSHT Triennial Congress in Washington, D.C.
M.H. Zheng, E. Landao-Bassonga, C. Lee, T.S Cheng, R. Oliver, M. Lloyd, D. Wills, W.R. Walsh

Introduction:

Surgical repair of transected nerve is essential to restore continuity, however the outcomes from suture only repair are often suboptimal.[1] Nerve wrap devices are commonly used to prevent connective tissue invasion and provide a protective environment for optimal nerve healing and regeneration.

This study evaluated the safety and biological performance of Orthocell's Remplir™ Nerve Wrap (porcine collagen) in comparison to a similar marketed nerve repair device (crosslinked bovine collagen nerve wrap comparator) in a rat sciatic nerve transection model.

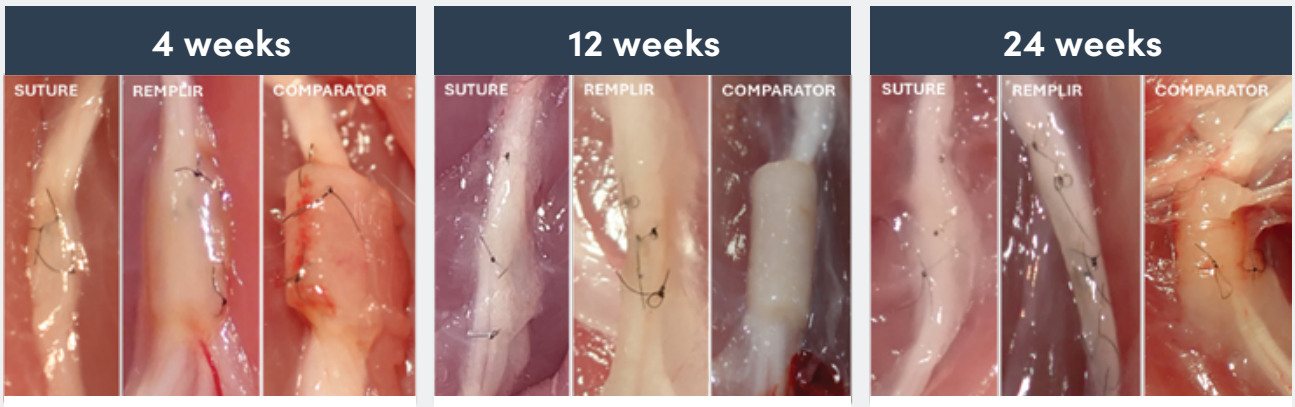
Methods:

Rat sciatic nerves were transected and immediately repaired with two epineural sutures reconnecting the proximal and distal ends. A collagen device (Remplir or Comparator) was wrapped around the repair site and fixed in place with an epineurial suture at each end, or the repair site was left unwrapped (Suture only control). Gross anatomical, histological and immunohistochemical assessment of biocompatibility and nerve regeneration was performed at 4-, 12- and 24-weeks post-treatment.

Key Results:

1. No adverse tissue reactions

No evidence of systemic or local toxicity, nor abnormal inflammation or scarring was observed after implantation of Remplir. Macroscopic observation of the implant site showed significant resorption and integration of Remplir at 12 weeks with complete host tissue integration by 24 weeks post-repair (Figure 1). No chronic inflammation, foreign body reaction or fibrosis, and minimal adhesions to surrounding soft tissue, were observed with the use of Remplir. In contrast, the Comparator device was largely intact at 4- and 12-weeks with only microscopic signs of resorption evident at 24 weeks post-repair. The use of the Comparator device was associated with noticeable and progressive increase in adhesions to surrounding tissues over the study period (Figure 1). Localized hematomas, and perineurial fibrosis and encapsulation leading to nerve constriction indicative of foreign body response were often observed in Comparator-assisted repairs (Figure 2). Axonal escape and neuroma formation were noted in Suture-only controls.



Remplir conforms to host tissue to protect transected nerve with no adverse reactions and minimal soft tissue adhesion. Device resorption and integration with host epineural tissue observed.

Comparator device largely intact with noticeable adhesion and tethering to surrounding soft tissue and no observable resorption or host tissue integration.

Remplir visibly resorbed and integrated into host epineurial tissue. Tissue appearance similar to Suture-only controls.

Comparator device remains largely intact with minimal resorption and adhering to surrounding soft tissuesurrounding soft tissue.

Remplir completely resorbed and integrated into host epineurial tissue with near native-like tissue appearance.

Comparator device still intact with partial resorption but significant adhesion to surrounding soft tissue.

Figure 1: Remplir resorbs and integrates into host epineurial tissue with no adverse reactions. Representative examples of gross observations of Suture only, Remplir-assisted, and Comparator-assisted repairs at 4-, 12-, and 24-weeks post-repair.

Hematoma, signs of hemorrhage, and nerve compression were often observed in Comparator-assisted repairs indicative of local irritation and inflammation.

Figure 2: Comparator-assisted repairs exhibited adverse tissue responses consistent with foreign body reactions including formation of local hematoma and progressive fibrotic encapsulation leading to nerve constriction across the repair site.

2. Resorption and integration into host tissue

Early resorption and integration of Remplir into host epineurial tissue, which could facilitate axon regeneration during early healing, was observed after 4 weeks (Figure 3). By 12 weeks post-repair, Remplir had substantially resorbed and integrated into epineurial-like tissue, with complete resorption and integration into host epineurial tissue observed at 24 weeks. Normal physiological inflammation, consistent with healing processes was observed across the observation period. No multinucleated giant cells or other signs of foreign body response to Remplir were observed. In contrast, the Comparator device appeared to remain intact throughout the observation period, encapsulating the nerve with minimal evidence of resorption or integration with host epineurial tissue (Figure 3). Significant inflammation with presence of multinucleated giant cells was observed within the device's collagen matrix and at the device-nerve interface.

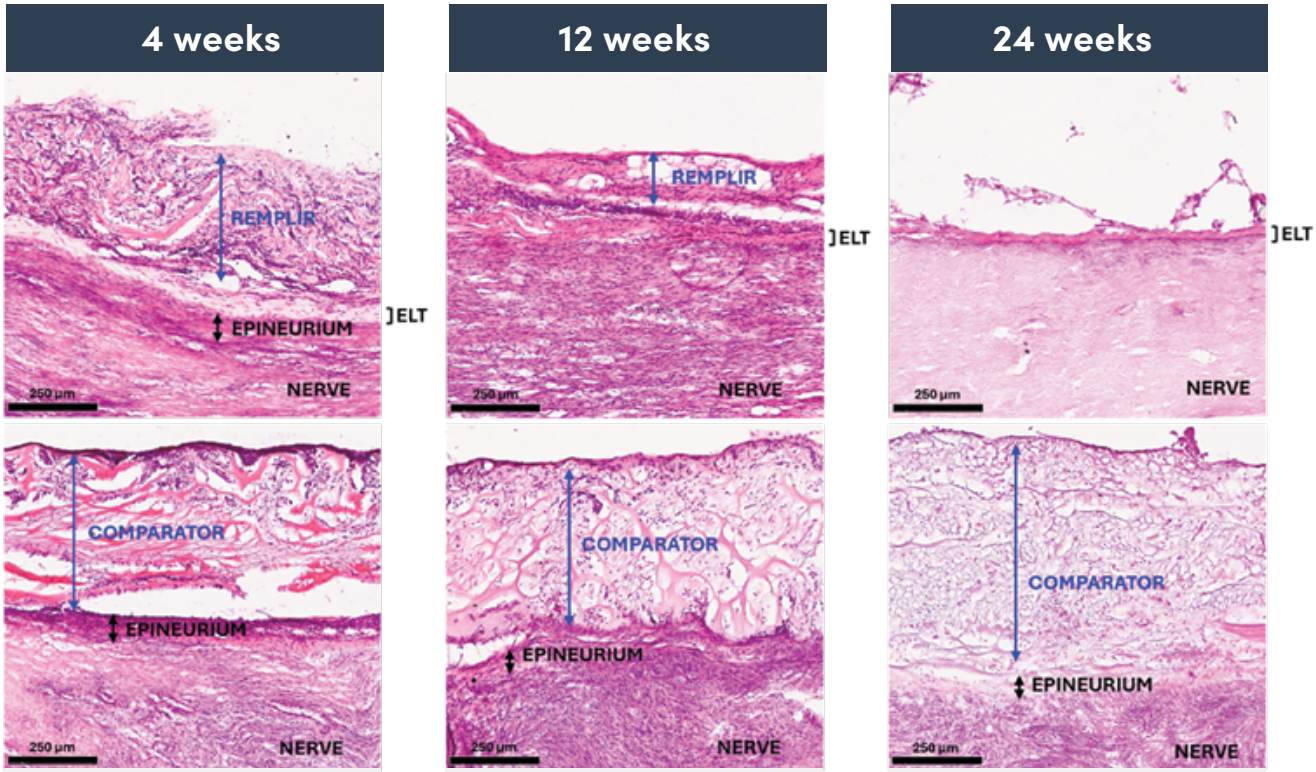


Figure 3: Resorption and integration of Remplir into host epineurial tissue. Representative H&E-stained longitudinal sections of device resorption and host tissue integration at 4-, 12-, and 24-weeks post-repair.

3. Regeneration of high-quality nerve tissue

Neurofilaments are parallel bundles of dense fibres that act as internal scaffolding, providing mechanical stability and maintaining optimal axonal calibre for signal conduction. After peripheral nerve injury, neurofilaments are broken down and cleared during the process of Wallerian degeneration in the distal nerve stump. Neurofilament staining 12 weeks post-treatment revealed Remplir-assisted repairs had the most continuous and longitudinally

aligned axonal regeneration across the transection site, closely approximating the organization seen in normal nerve (Figure 4). In contrast, both Suture-only and Comparator-assisted repairs exhibited marked disorganization at the transection site, including misalignment and fragmentation of neurofilament bundles, indicative of axonal misdirection and potential neuroma formation (Figure 4 and Figure 5).

The use of Remplir facilitates superior axonal continuity from proximal to distal segments with robust axonal bridging across the transection site that can lead to faster restoration of electrophysiological signaling and a higher likelihood of functional recovery.

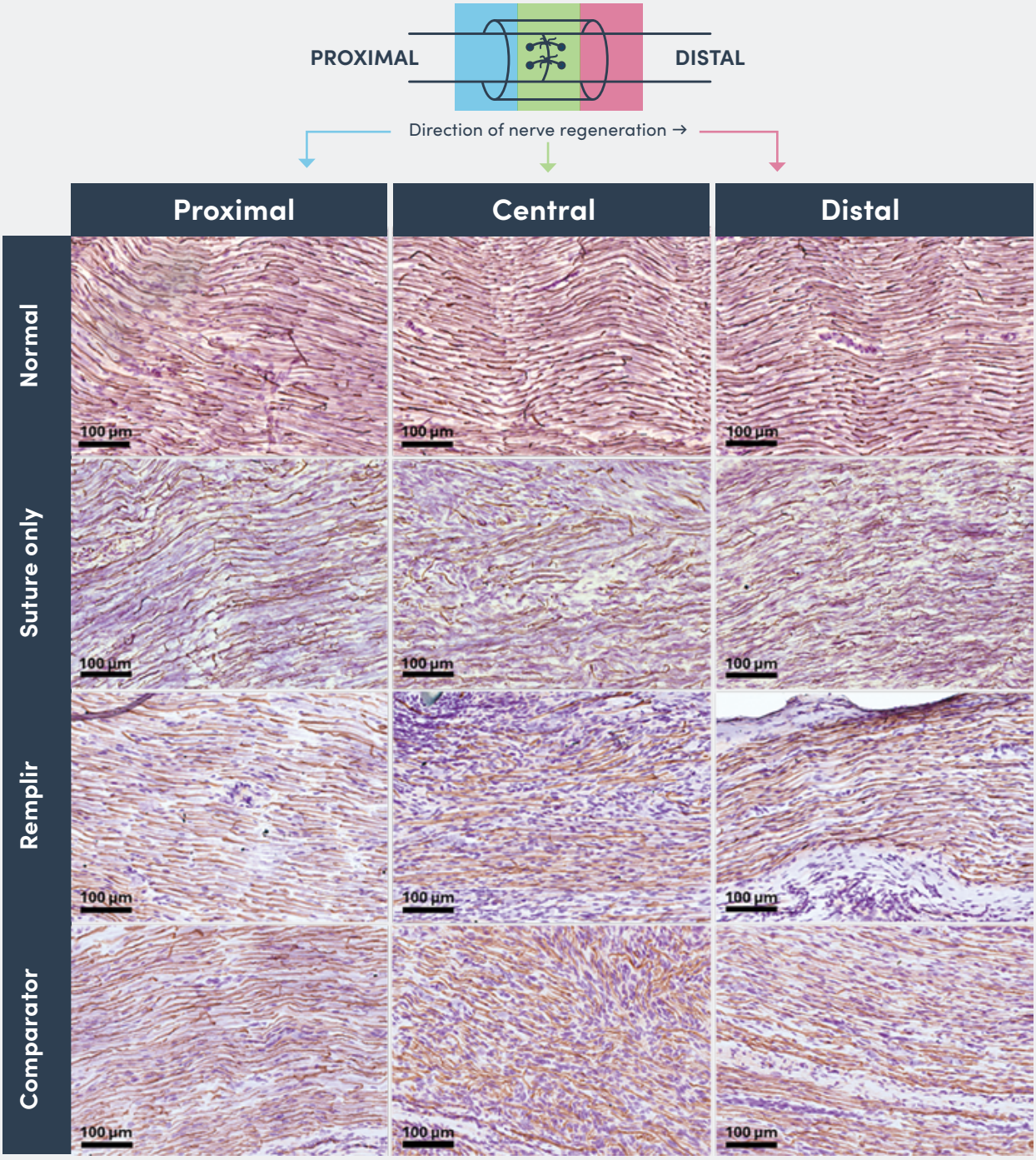


Figure 4: Remplir-assisted repairs facilitate superior axonal continuity from proximal to distal segments with robust axonal bridging across the transection site. Representative neurofilament-stained longitudinal nerve sections showing the proximal, central repair, and distal region of regenerated nerve tissue from Suture-only, Remplir-assisted, and Comparator-assisted repairs at 12-weeks post-repair.

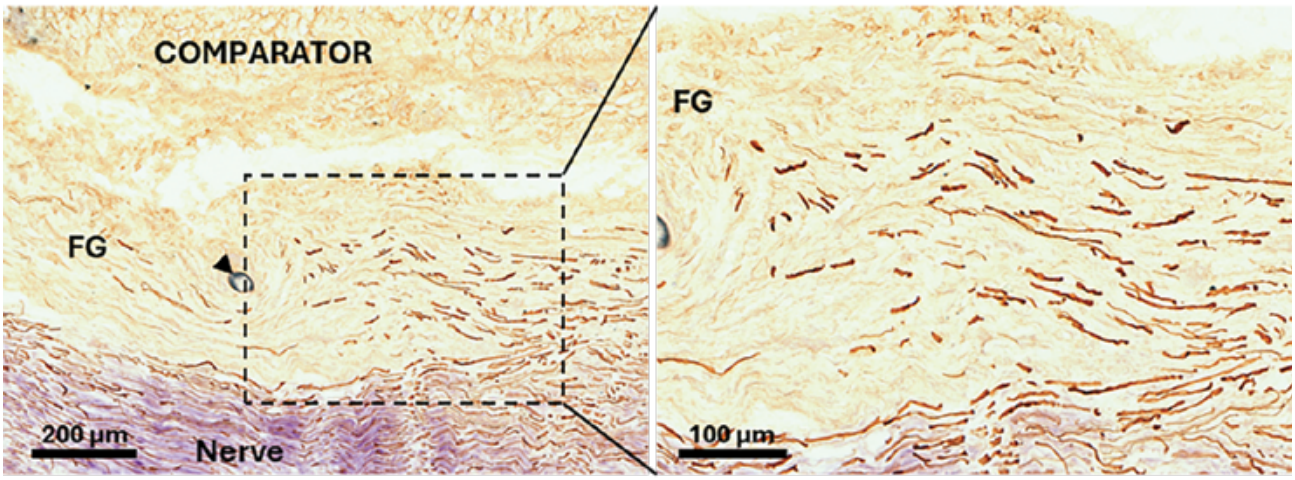


Figure 5: Neurofilament ingrowth and axonal misdirection into fibrogranulation tissue (FG) adjacent to nerve and implanted Comparator device indicating potential neuroma formation. Arrow head indicates suture material.

Toluidine-stained cross-sections of the distal nerve segment at 4-weeks post-repair showed that Remplir-assisted repairs supports earlier axonal regeneration and remyelination compared with Suture-only and Comparator-assisted repairs. The distal nerve segments of Remplir-assisted repairs exhibited greater density of small myelinated axonal profiles indicating earlier axonal sprouting and onset of remyelination (Figure 6). This early regenerative trend in Remplir-assisted repair is inline with the superior neurofilament organization observed in Remplir-assisted repairs at 12-weeks. In contrast, both Suture-only and Comparator-assisted repairs shows irregular and fewer myelinated axons.

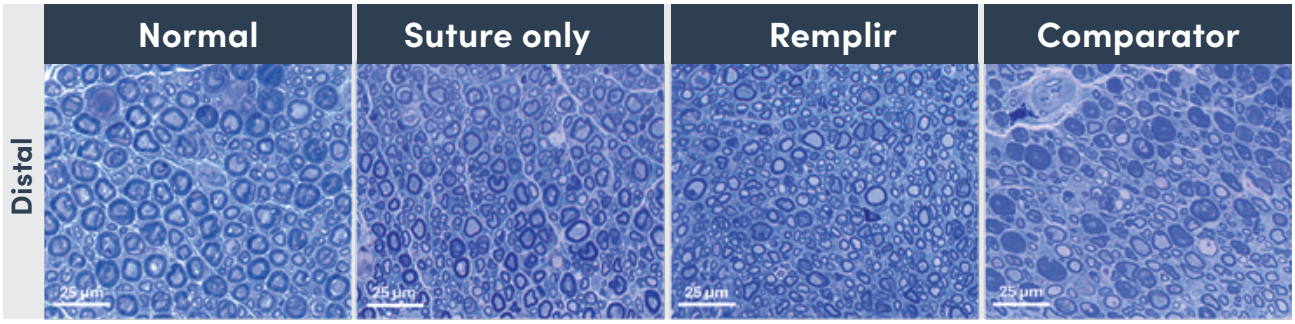


Figure 6: Remplir-assisted repairs facilitates early distal axonal sprouting and axon remyelination. Representative images of toluidine blue-stained cross-sections showing the distal nerve segment of regenerated nerve tissue from Suture-only, Remplir-assisted, and Comparator-assisted repairs at 4-weeks post-repair.

Quantitative morphometric analysis of distal nerve segments from 4-24 weeks showed that Remplir-assisted repairs showed favourable regenerative features, with trends towards increased distal axon density and myelinated axon density, and comparatively improved distal:proximal myelination profile (Figure 7).

Together, these findings reinforce Remplir's ability to support effective axonal bridging, regeneration and maturation. Repairs using the comparator device showed poor distal regeneration due to axonal misalignment and misdirection, while Suture-only repair achieved intermediate but suboptimal results.

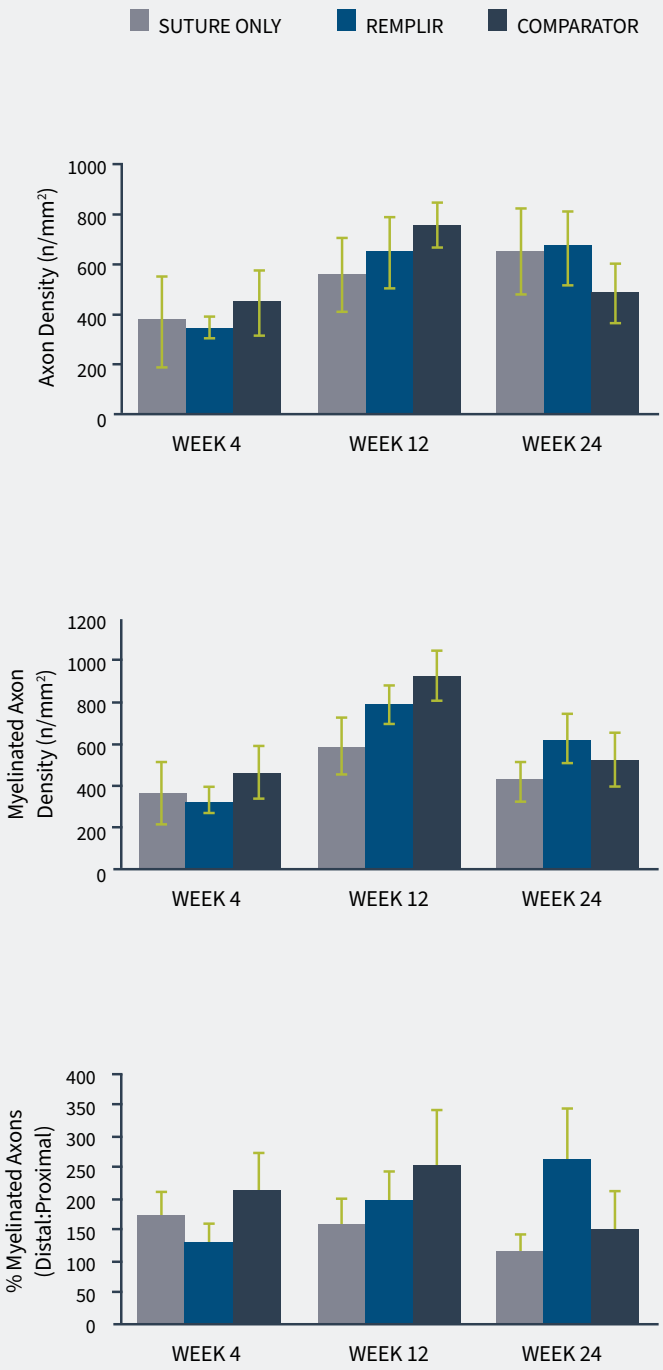


Figure 7: Remplir-assisted repairs support a more favourable regenerative profile. Quantitative morphometric assessment of distal axon density, myelinated axon density, and % myelinated axons (distal:proximal) at 4-, 12-, and 24-week post-repair.

4. Supports a more favourable M2 macrophage regenerative environment

Macrophages play important and well-orchestrated roles in peripheral nerve repair. Early pro-inflammatory M1 macrophage presence is necessary for debris clearance and activation of repair programs. Timely switch (polarization) from M1 to pro-regenerative M2 macrophage supports angiogenesis, Schwann cell activity and axonal guidance, and extracellular matrix remodeling. Prolonged M1 macrophage activity or delayed switch to the M2 macrophage response leads to chronic inflammation and fibrosis that can hinder axonal regeneration[2].

Remplir supports the most effective M1 (pro-inflammatory) to M2 (pro-regenerative) transition, with early pro-regenerative M2 macrophage activity sustained through the critical regeneration window (weeks 4 to week 12) (Figure 8). The Comparator device shows persistent pro-inflammatory M1 macrophage dominance and weak pro-regenerative M2 response, consistent with its inferior histological and morphometric outcomes (Figure 8).

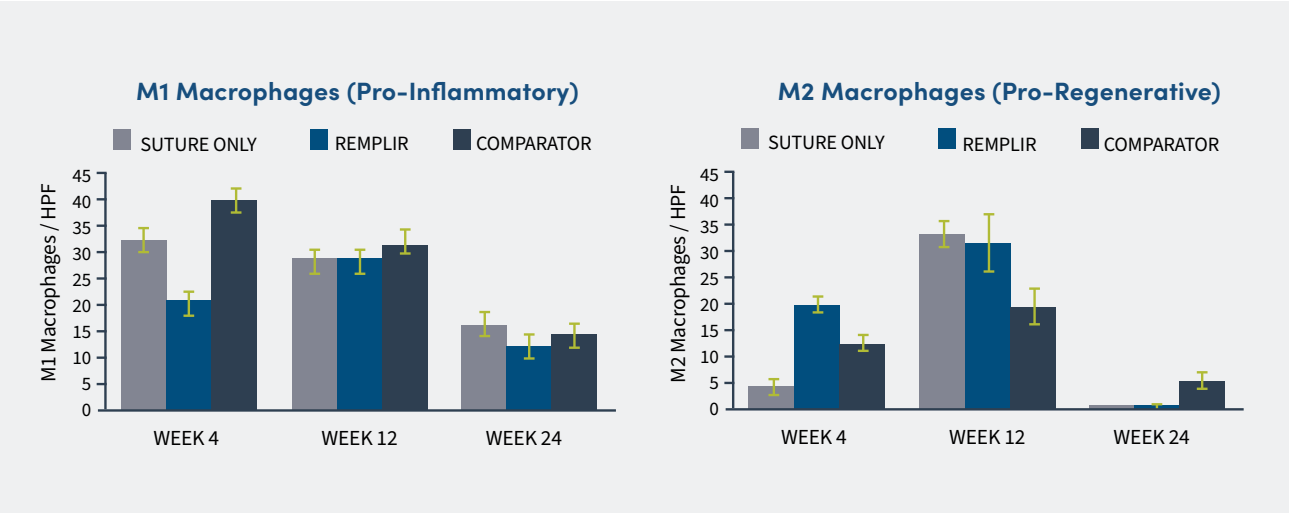


Figure 8: Remplir-assisted repairs demonstrated a trend towards an accelerated shift from pro-inflammatory M1 to pro-regenerative M2 macrophage profile indicating a comparatively more favourable immune environment for regeneration than Suture-only and Comparator-assisted repairs. Bar charts of M1 and M2 macrophage counts at 4-, 12-, and 24-weeks following surgical repair with Suture-only, Remplir-assisted repair, or Comparator-assisted repair.

5. Return of motor and mechanosensory function

Over the 24-week sensorimotor testing period, Remplir-assisted repairs were associated with earlier and greater restoration of motor function (Extensor Postural Thrust Force) and a generally more favourable trajectory of mechanosensory recovery (von Frey test) compared with Suture-only repairs (Figure 9).

These functional improvements are consistent with Remplir's ability to support high quality nerve regeneration (superior central axonal alignment and improved distal axon myelination) and more favourable macrophage-mediated repair kinetics, which together promote more effective reinnervation.

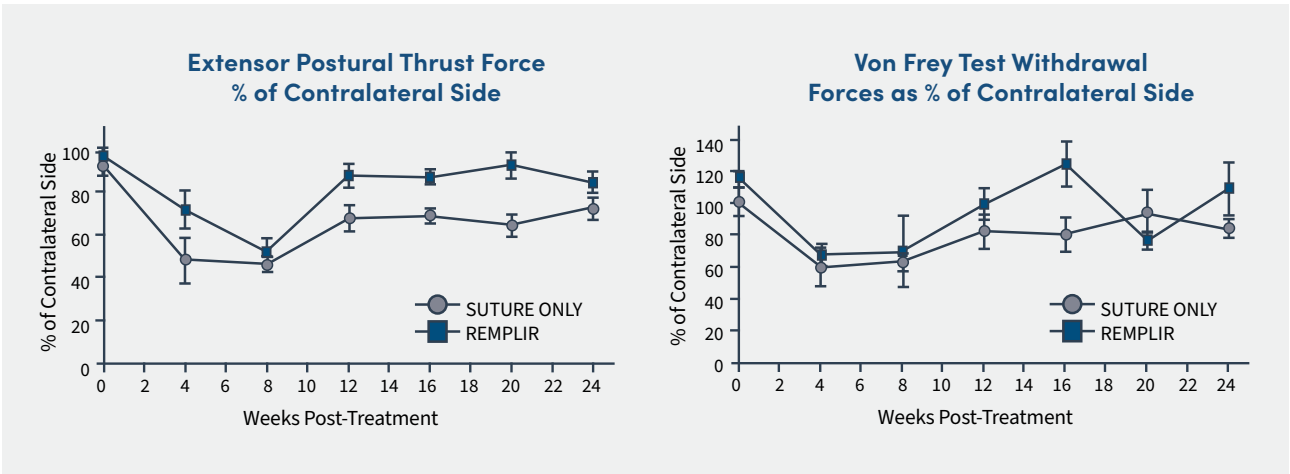


Figure 9: Over the 24-week period, Remplir-assisted repairs consistently show comparatively greater motor recovery (Extensory Postural Thrust Force) and mechanosensory recovery (von Frey test) relative to Suture-only repairs, aligning with structural evidence of enhanced axonal regeneration and reinnervation.

Conclusion:

Across structural, morphometric, and immunological assessments, Remplir demonstrated a comparatively more favourable regenerative profile than both Suture-only and Comparator-assisted repairs. The use of Remplir supports high quality nerve regeneration with improved axonal organization distal nerve maturation (axon remyelination), a more timely transition from pro-inflammatory to pro-regenerative macrophage states, and earlier recovery of motor and sensory function. Together, Remplir provides a more supportive immune and regenerative microenvironment that delivers superior conditions and guidance for consistent nerve regeneration and clinical outcomes.

Disclaimer

All animal procedures were performed in compliance with the Australian Code for the Care and Use of Animals for Scientific Purposes 8th Edition (2013), NSW Animal Research Act 1985 No 123, NSW Animal Research Regulation 2021, to the principles of Good Laboratory Practice for Nonclinical Laboratory Studies (FDA, OECD), and approved by the University of New South Wales (UNSW) Animal Care and Ethics Committee (ACEC Approval #22/127A).

References: 1. Leis A, Smetana BS, Strohl AB, Styron JF. Comparative Effectiveness Systematic Review and Meta-analysis of Peripheral Nerve Repair Using Direct Repair and Connector-assisted Repair. Plast Reconstr Surg Glob Open. 2024;12(7):e5927 **2.** Badylak SF, Valentin JE, et al. Macrophage phenotype as a determinant of biologic scaffold remodeling. Tissue Eng Part A. 2008;14(11):1835-1842

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WHITE PAPER

Interim results: Post-Market Clinical Follow-up Study to Evaluate the Safety and Performance of Remplir™ Collagen Membrane in Peripheral Nerve Surgery

1 Background

This document summarises the interim results from an Australian post-market clinical follow-up study, designed to collect data on the real-world safety and performance of Remplir when used in a range of different peripheral nerve surgical procedures.

The study was prospectively registered on the Australian New Zealand Clinical Trials Registry (ACTRN12624001213538).

2 Methods

2.1 Study design

This is a multi-center, prospective and retrospective observational study. The patient cohort included individuals who received Remplir as part of normal clinical practice in the post-approval phase, as well as patients who received a peripheral nerve procedure with Remplir prior to regulatory approval, via the TGA's Special Access Scheme. Patients who participated in the pre-market clinical study of Remplir were excluded from this cohort. Patients were followed for up to 24 months after receiving Remplir, or in accordance with the standard clinical practice at the site for the relevant procedure.

2.2 Eligibility criteria

Inclusion Criteria:

- Underwent a peripheral nerve procedure using Remplir
- If still in clinical follow-up, able to sign informed consent in accordance with ICH-GCP

Exclusion Criteria:

- Participated in the pre-market clinical study of Remplir

2.3 Outcome measures

The primary safety outcome is the incidence of post-treatment complications considered related to use of Remplir. The primary performance outcome is treatment success, assessed in accordance with the type and intended purpose of the nerve procedure:

- For motor nerve reconstruction procedures, treatment success is defined as functional motor recovery, assessed using the British Medical Research Council scale with an MRC grade ≥3.
- For sensory nerves reconstruction procedures, sensory recovery was assessed using Semmes-Weinstein monofilament testing (SWMT) or Static two-point discrimination (S2PD). Functional sensory recovery was defined as SWMT filament ≤ 3.61 or S2PD ≤ 15 mm.
- For procedures not involving nerve transection or reconstruction such as nerve decompression, and procedures for carpal/cubital tunnel syndromes, treatment success was assessed using a published grading scale.1 For analysis, both (i) improvement, where most pre-operative symptoms were completely relieved, and (ii) complete relief of pre-operative symptoms were classified as treatment success.
- For management of neuromas, treatment success was assessed as either, improvement (most symptoms completely relieved) or complete relief of pre-operative symptoms (if there is a pre-existing neuroma), and no symptomatic neuroma formation. For analysis, treatment success was defined as the absence of symptomatic neuroma formation or recurrence, together with an outcome classified as either: (i) improvement, where most pre-operative symptoms were completely relieved; or (ii) complete relief of pre-operative symptoms.

3 Results

3.1 Participant demographics and baseline characteristics

A total of 80 participants were included in the interim analysis, with a mean age of 50.1 years (range 14 to 82). Across the cohort, 104 peripheral nerve procedures were performed, with the majority of procedures localized to the upper limb (86.5%). The majority (49.0%) were nerve decompression procedures using Remplir as a protective wrap in participants with chronic nerve injuries such as carpal and cubital tunnel syndromes. Nerve reconstruction procedures (including nerve transfer and nerve grafting) for acute injury were the next most common (46.2%). In the participants with acute injury, 45.5% had an injury at the peripheral nerve level, 30.3% had a brachial plexus injury, and 24.2% had a cervical spinal cord injury. There were 2 procedures in which Remplir was used as a nerve cap for neuroma prophylaxis.

3.2 Safety

In this cohort, no adverse device effects, serious adverse device effects, or device deficiencies were reported. The device was well tolerated when used in routine clinical practice. No cases of symptomatic neuroma formation were reported in any participant following treatment with the device.

3.3 Performance (treatment success)

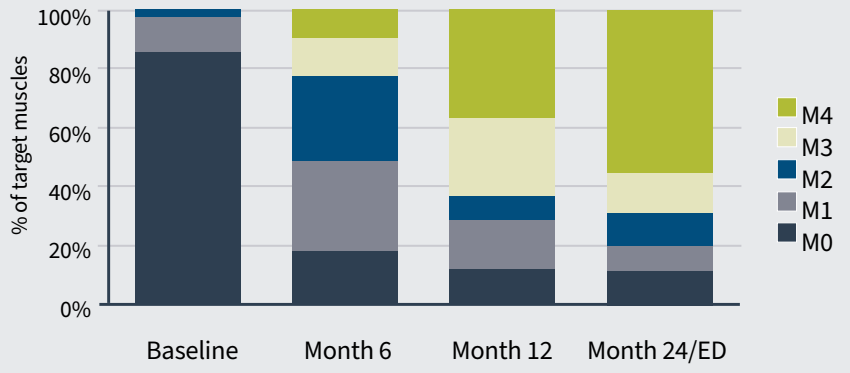
A total of 71 participants, corresponding 83 nerve procedures, had sufficient follow-up data for inclusion in the performance dataset. Performance data is analyzed relative to nerve procedure type (as per section 2.3). Some participants had multiple nerve procedures during the same operation that were assessed for performance outcomes. For example, some participants with brachial plexus or cervical spinal cord injuries underwent multiple nerve transfer procedures targeting different muscles or sensory regions.

The overall treatment success rate, according to the pre-specified protocol criteria, was 88.0% (73/83 nerves).

Motor nerve reconstruction

A total of 19 participants underwent procedures to restore motor function in 31 nerves. Motor recovery was assessed by grading the strength of target muscles controlled by the repaired nerve in accordance with the British Medical Research Council grading system (MRC score). Results showed that 90.3% (28/31 nerves) reached functional recovery (MRC ≥3) in at least one muscle target at an average of 10.8 months after surgical treatment with Remplir. Figure 1 summarises the full dataset[2] by percentage of target muscles in each MRC grade at each time point.

Figure 1 - Recovery of Muscle Power in Participants undergoing motor nerve reconstruct[3]



Grade M3 and M4 – voluntary movement with improved strength and range of motion. Maximum level of recovery expected.

Grade M2 – voluntary movement restored, limited strength and range of movement.

Grade M0 or M1 – no voluntary movement.

Nerve decompression/neurolysis

47 participants provided performance data on nerve decompression or neurolysis procedures using Remplir. This included 18 carpal tunnel revision procedures, and 15 cubital tunnel procedures (13 primary, 2 revision). Results showed that 89.4% (42/47 nerves) of nerve decompression procedures resulted in significant improvement (most symptoms resolved) or complete relief of symptoms after treatment. No participants who received nerve decompression with Remplir required additional revision surgery during the follow-up period.

Other nerve reconstruction procedures

In addition, one participant, corresponding to one nerve procedure, underwent nerve reconstruction with Remplir for the management of pain and paraesthesia, with the procedure meeting the criteria for treatment success.

Sensory nerve reconstruction

Two sensory nerve reconstruction procedures were included in the analysis. Although neither procedure met the pre-specified protocol criteria for treatment success, both participants demonstrated post-operative improvement in sensory function. One participant underwent a medial plantar nerve graft with Remplir and improved from having no sensation in the hallux and foot, to an SWMT filament result of 6.65. The second participant underwent sensory nerve transfer from the superficial radial nerve to median nerve with Remplir for restoration of finger and thumb sensation. This participant reported an improvement from of 4.56 pre-surgery to 4.31 post-treatment SWMT result.

Neuroma management

Two participants corresponding to two nerve procedures underwent procedures for treatment neuromas in continuity, i.e. pre-existing symptomatic neuromas. Both procedures achieved treatment success, with no symptomatic neuroma formation or recurrence reported during the follow-up period.

4 Summary

This interim analysis demonstrates the clinical utility of Remplir across a range of peripheral nerve surgical procedures, including nerve transfer procedures for restoration of upper limb function following cervical spinal cord or brachial plexus injury, as well as nerve decompression procedures for carpal and cubital tunnel syndromes. The safety and performance findings observed in this interim cohort align with the published clinical evidence for Remplir, including the clinical study reported in Journal of Reconstructive Microsurgery Open.[3] Collectively, these findings support a positive risk-benefit profile for the use of Remplir in peripheral nerve surgery. The clinical study is ongoing and remains in the recruitment phase, proactively collecting clinical performance and safety data. Continued data collection will further strengthen the evidence base by enabling evaluation in a larger cohort and supporting further evaluation of outcomes across peripheral nerve procedure types.

References: 1. 1. Jariwala A et al (2015). Outcome analysis of cubital tunnel decompression. Scott Med J. 2015;60(3):136-40. https://doi org/10.1177/0036933015589487 **2.** Includes all data available at each time point. N=65 at baseline, N=45 at month 6, N=52 at month 12, N=36 at month 24/early discontinuation **3.** O'Beirne, A et al (2024). Reconstruction of upper-extremity peripheral nerve injuries using an epineurial-like collagen device: A prospective clinical study. Journal of Reconstructive Microsurgery Open, 9(1). https://doi.org/10.1055/s-0044-1785213

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WHITE PAPER

Biomechanical Comparison of Nerve Wrap Elasticity: Remplir™ vs Porcine Small Intestine Submucosa (SIS)

Introduction:

Elasticity is an essential property of nerve tissue. During everyday limb movements, peripheral nerves experience mechanical stresses such as strain and stretch, which they accommodate through their natural ability to glide and elongate.[1]

When a nerve is repaired with a nerve wrap product, it is beneficial for the wrap material to have similar elasticity to the nerve tissue to avoid creating a mechanical mismatch that restricts nerve swelling and glide. Wraps that are too stiff can compress the healing nerve, reducing blood perfusion[2] that can impair regeneration[3] and function.[4]

Moreover, elasticity of nerve wraps can influence the rate of axonal regeneration and myelination after surgical repair of transected nerves.[5]

These findings suggest that nerve wraps with similar elasticity to nerve support natural nerve mechanics and optimize recovery.

Methods:

Percent elongation and Young's modulus are two variables that describe how elastic a material is. Percent elongation reveals how much a material can stretch before it breaks; more stretch means the material is more flexible. Young's modulus measures how hard it is to stretch the material; a higher value means it is stiffer.

An independent laboratory performed elasticity testing on samples of Remplir (n=67) and Axoguard Nerve Protector® (porcine SIS), Axogen® Corporation (n=11). The nerve wraps were trimmed to the same size (30x10mm) and hydrated before testing to mimic in vivo conditions. Each wrap was then loaded onto a tensile testing device that stretched the wrap at a rate of 25mm per minute. Data recorded from the tensile testing were used to calculate percent elongation and Young's modulus.

Young's modulus values for native nerve tissue were obtained from a published study.[6] Median nerve specimens from nine cadavers were stored at −20°C and later tested at room temperature using a tensile testing device similar to that employed for the nerve wraps.

Results:

The average percent elongation of Remplir is over two times that of porcine SIS (Figure 1), a statistically significant difference ($p<0.0001$). Test results also show that Remplir can stretch by over 200%, which will accommodate nerve swelling after nerve repair.

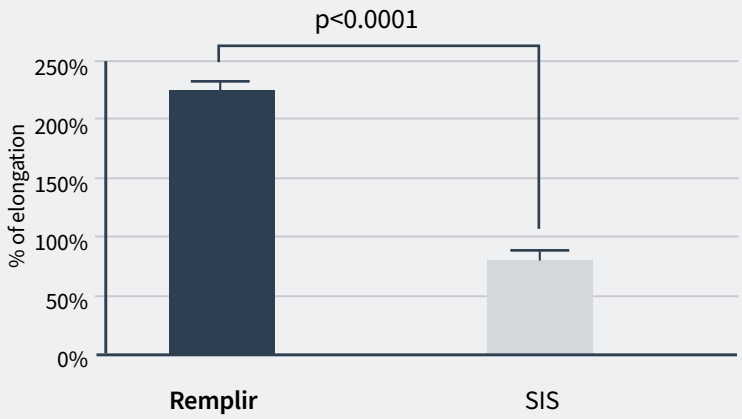

Figure 1: Tensile testing shows Remplir can elongate significantly more than porcine SIS before failure. Data are mean ± SEM.

Test results also show that the porcine SIS nerve wrap is significantly stiffer than Remplir (p<0.0001). The average Young's modulus values were 17.9 for Remplir, 14.6 for human nerve, and 92.7 for porcine SIS (Figure 2). When the Young's modulus results are compared to human nerve,[6] Remplir closely resembles human nerve (no significant difference) whereas porcine SIS does not.

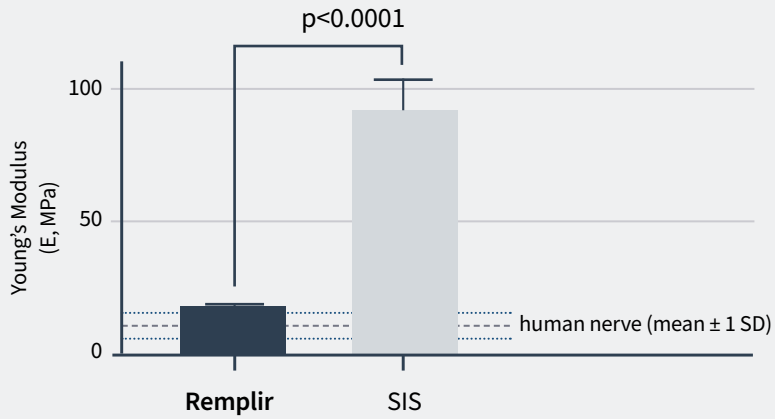

Figure 2: Tensile testing shows the Young's modulus value for Remplir is similar to human nerve[6] and significantly lower than porcine SIS. Data are mean ± SEM unless otherwise stated.

Conclusion:

Elasticity of a material can be studied by measuring elongation and stiffness. These bench top data, produced by an independent laboratory, show that the elasticity of Remplir is comparable to human nerve and that Remplir can stretch to over 200% to accommodate nerve swelling after surgical repair. On both measures of elasticity, elongation and stiffness, results from Remplir were more physiologically relevant than the porcine SIS nerve wrap.

References: 1. Topp KS, Boyd BS. Structure and biomechanics of peripheral nerves: nerve responses to physical stresses and implications for physical therapist practice. Phys Ther. 2006;86(1):92-109. doi:10.1093/ptj/86.1.92 **2.** Ju MS, Lin CC, Fan JL, Chen RJ. Transverse elasticity and blood perfusion of sciatic nerves under in situ circular compression. J Biomech. 2006;39(1):97-102. doi:10.1016/j.jbiomech.2004.10.026 **3.** Malekzadeh H, Otto-Moudry R, Moore AM. The role of vascularization in nerve regeneration: mechanistic and therapeutic perspectives. Int J Mol Sci. 2025;26(17):8395. doi:10.3390/ijms26178395 **4.** Wall EJ, Massie JB, Kwan MK, Rydevik BL, Myers RR, Garfin SR. Experimental stretch neuropathy. Changes in nerve conduction under tension. J Bone Joint Surg Br. 1992;74(1):126-129. doi:10.1302/0301-620X.74B1.1732240 **5.** Liu F, Xu J, Liu A, et al. Development of a polyacrylamide/chitosan composite hydrogel conduit containing synergistic cues of elasticity and topographies for promoting peripheral nerve regeneration. Biomater Sci. 2022;10(17):4915-4932. Published 2022 Aug 24. doi:10.1039/d2bm00327a **6.** Stouthandel MEJ, Vanhove C, Devriendt W, et al. Biomechanical comparison of Thiel embalmed and fresh frozen nerve tissue. Anat Sci Int. 2020;95(3):399-407. doi:10.1007/s12565-020-00535-1

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WHITE PAPER

Safety Data Summary: Remplir™

1. Introduction & Product Overview

This document summarises the safety profile of Remplir, with supporting evidence from Orthocell's collagen medical device family.

Orthocell's collagen medical device family consists of implantable collagen membranes of various thicknesses and sizes, designed for different clinical indications (nerve, bone, tendon and cartilage). The collagen membranes have been approved by global regulatory authorities (for use in both peripheral nerve repair and dental guided bone and tissue regeneration) and have been marketed/used in patients since 2017.

Remplir (peripheral nerve repair) is currently approved/cleared for use in Australia, New Zealand, Canada, United States, Singapore, Thailand and Hong Kong, and Striate+™ (guided bone and tissue regeneration) is currently approved/cleared in Australia, New Zealand, Europe, United Kingdom, United States, Switzerland, Singapore and Albania.

This white paper details the safety data summary of approved devices Remplir and Striate+, by reviewing data from inputs such as complaints, regulatory databases, literature, clinical data (inclusive of post-market clinical follow up studies), manufacturing data, scientific literature and market and customer feedback up until July 2025.

2. Safety Data Sources

Pre-clinical Testing:

- ISO 10993 biocompatibility series (cytotoxicity, sensitisation, irritation and sensitisation, local and systemic toxicity, pyrogenicity, genotoxicity).
- Animal testing (rat sciatic nerve and canine dental guided bone regeneration (GBR).

Clinical Data:

- Published clinical studies.
- Manufacturer-sponsored post-market clinical follow up studies.

Post-market Surveillance:

- Over 70,000 units sold globally.
- Vigilance reports, customer feedback, and regulatory databases.

Scientific Literature:

- Published studies on implantable collagen medical devices in the relevant therapeutic area.

3. Safety Data Summary

Pre-clinical:

- No evidence of inflammation or foreign body reactions were observed in animal testing.
- All ISO 10993 endpoints passed; no cytotoxicity, sensitisation, or irritation observed.

Clinical:

- No device related adverse events.

Post-market:

- No reportable adverse events of units sold worldwide.

Scientific Literature:

- Literature is consistent with established safety profile of collagen medical devices.

4. Conclusion

The data gathered from safety data continues to support the following conclusions:

- Orthocell's collagen medical devices (Remplir & Striate+) are safe, and no new safety signals have been detected from post-market experience of over 70,000 device sales.
- The benefits of the use of the collagen medical device in its approved clinical indication (peripheral nerve repair or dental guided bone and tissue regeneration), outweigh any risks.
- The benefit-risk profile of the collagen medical device is favourable.

References : 1. Regulatory Databases: Manufacturer and User Facility Device Experience (MAUDE); Recalls and Safety Alerts for Health Products (Canada); Medicines and Healthcare products Regulatory Agency (MHRA); Swissmedic (Switzerland); Device Adverse Event Notifications (DAEN) (Australia); Database of Recalls, Product Alerts and Product Corrections (DRAC) (Australia). **2.** O'Beirne, A., Cullen, J., Landao-Bassonga, E., Zheng, M., Lee, C., Kaluskar, P., Tai, A., & Zheng, M. (2024). Reconstruction of upper-extremity peripheral nerve injuries using an epineurial-like collagen device: A prospective clinical study. Journal of Reconstructive Microsurgery Open, 9(1). https://doi.org/10.1055/s-0044-1785213. **3.** Allan, B., Ruan, R., Landao-Bassonga, E., Gillman, N., Wang, T., Gao, J., Ruan, Y., Xu, Y., Lee, C., Goonewardene, M., & Zheng, M.-H. (2021). Collagen membrane for guided bone regeneration in dental and orthopedic applications. Tissue Engineering Part A, 27(5–6), 372–381. https://doi.org/10.1089/ten.tea.2020.0140

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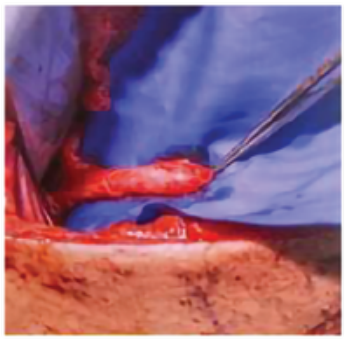
CASE STUDY

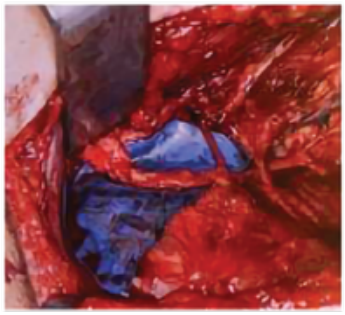
CONNECT with Remplir™

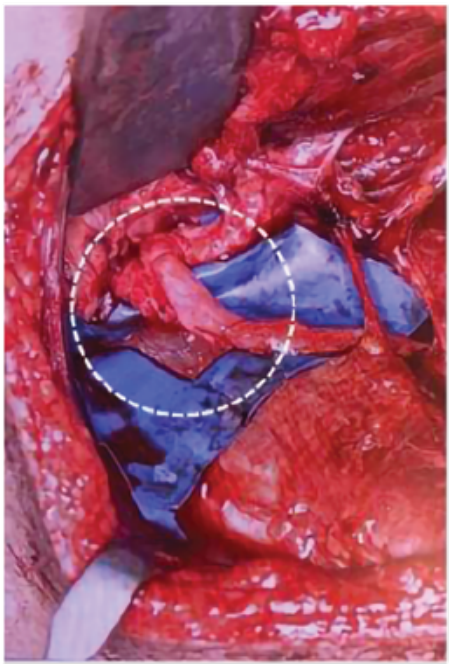
Trauma:

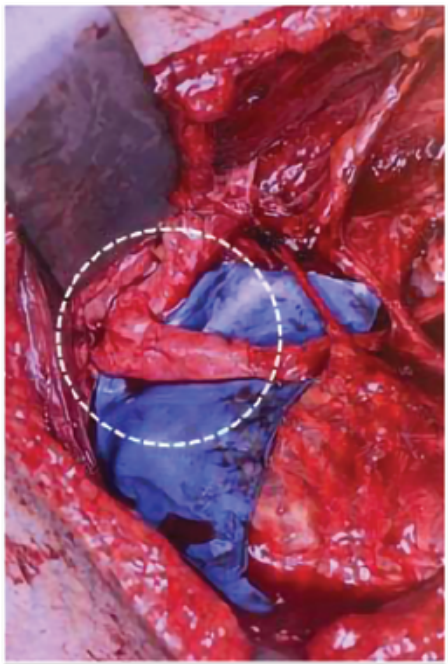
Motor vehicle, power tool, surgical injuries, sports and military related accidents

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

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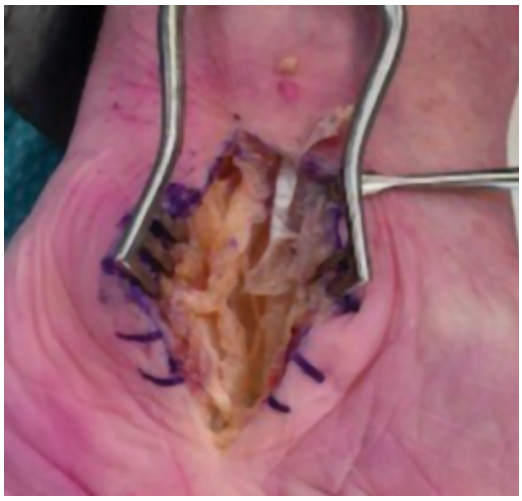
CASE STUDY

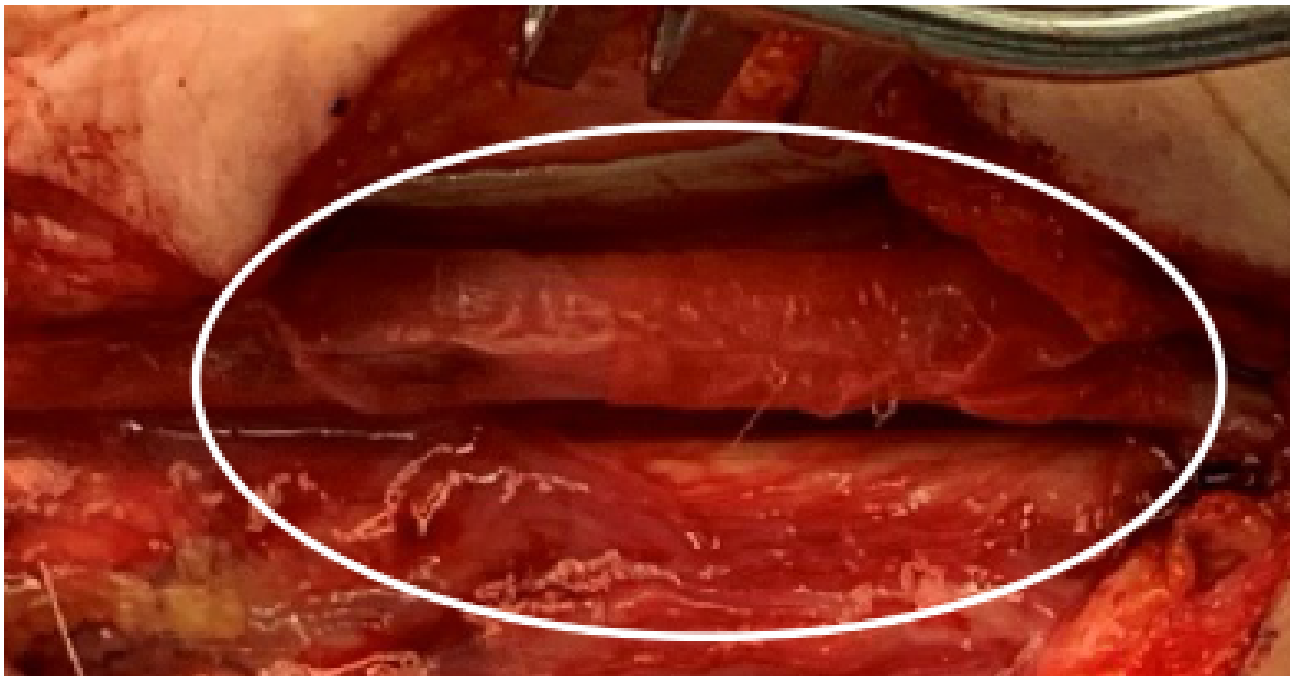
PROTECT with Remplir™

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.





Case Courtesy of Dr Alex O'Beirne

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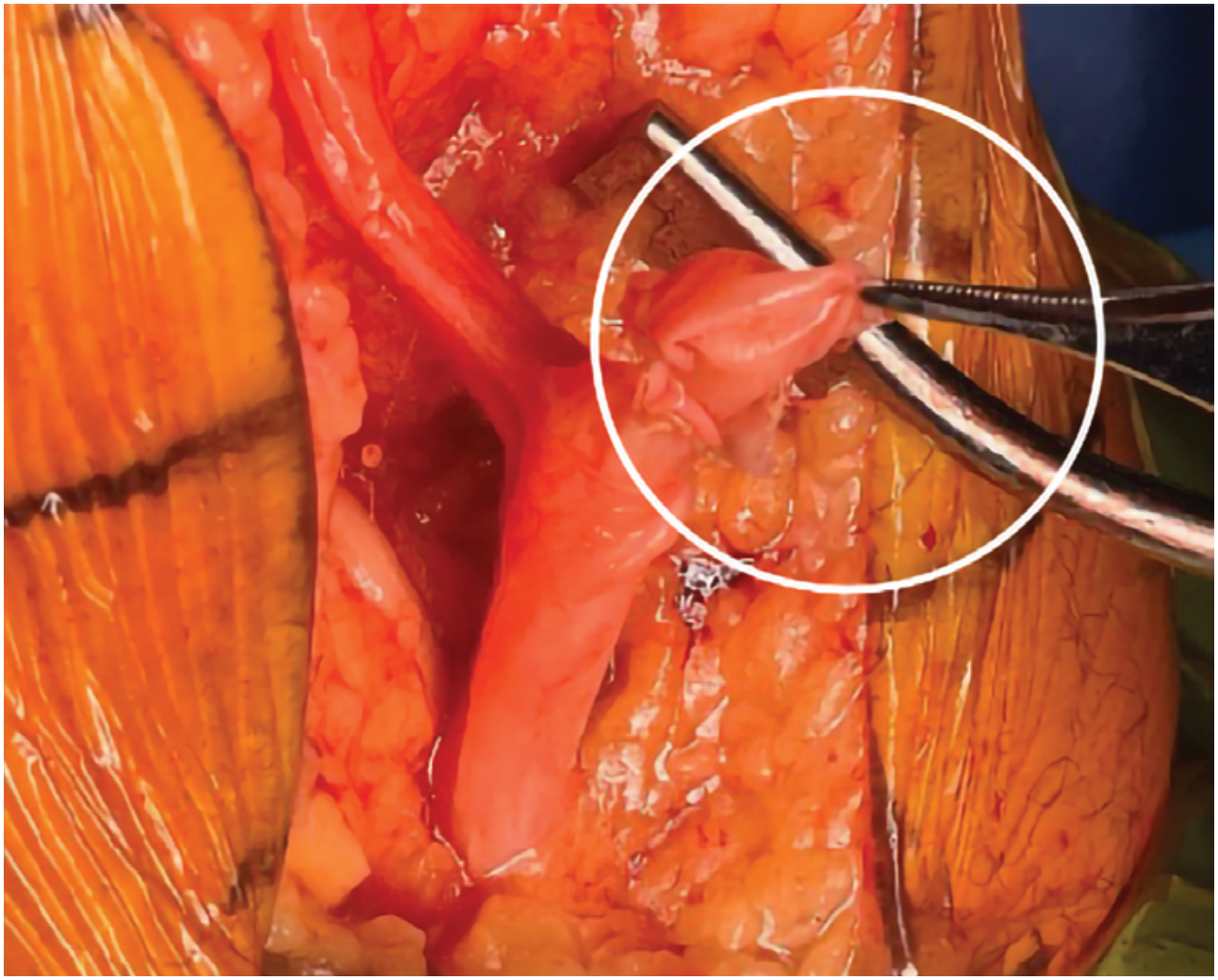
CASE STUDY

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 Prof Richard Carey Smith

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About us

Orthocell Ltd, headquartered in Perth, Australia, is the home of Remplir.

Since 2010, we've been developing and exporting innovative regenerative medicine products worldwide. As of February 2026, more than 75,000 patients have benefited from an Orthocell collagen medical device, with no reportable adverse events. Every product reflects our mission: improving mobility, function, and quality of life. We collaborate with leading surgeons and centers of excellence to translate research into practical solutions that raise the standard of care. Our deep understanding of tissue engineering, particularly the interaction between cells and scaffolds, allows us to enhance the body's natural healing and regeneration processes. Orthocell products are designed to simplify procedures, save operative time, and deliver consistent, predictable outcomes, supporting surgeons in providing the best care for their patients.

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