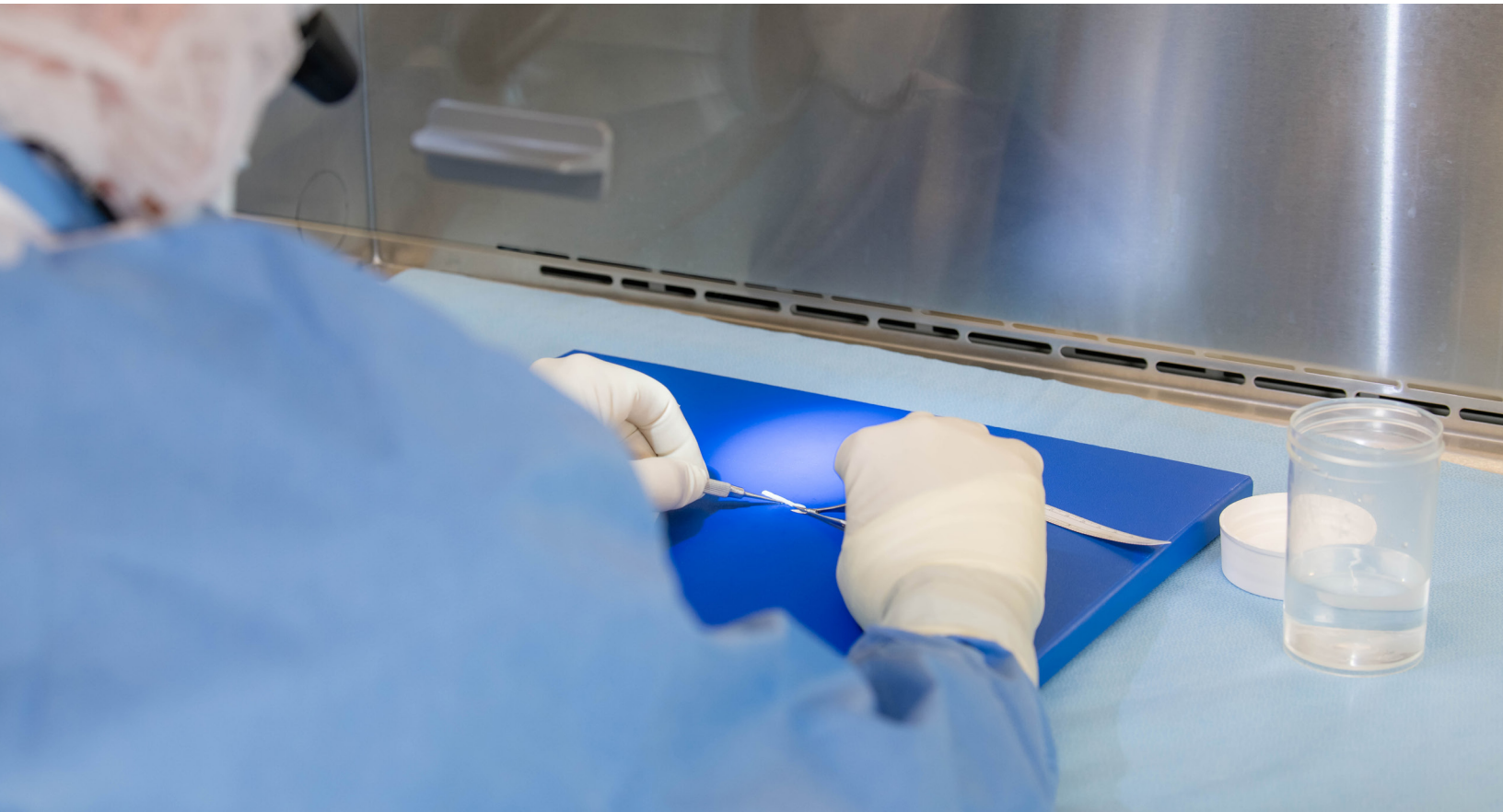




the avance method™



Axogen Processing Center. Dayton, Ohio

delivering positive outcomes and efficiency to your practice

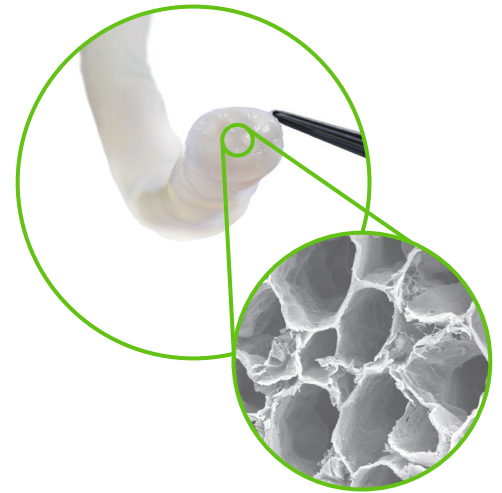
The Avance Method™ is Axogen's proprietary methodology for recovering, cleansing, sterilizing and ensuring quality of the Avance® Nerve Graft. Studies have demonstrated Avance Nerve Graft is the most effective alternative to a patient's own tissue.¹⁻⁶

revolutionizing the
science of nerve repair™

proprietary methodology ensuring regenerative potential

The Avance Method is a unique methodology specifically designed to maintain both the natural nerve structure and biological activity of human nerve tissue. As a result, Avance Nerve Grafts deliver overall meaningful recovery comparable to autograft, without the cost, time and comorbidities associated with autograft harvest.³

- 14+ years of unrivaled expertise in nerve tissue recovery
- Designed to mimic aspects of the body's natural Wallerian degeneration process
- Preserves the delicate architecture of native nerve which provides structural support for the regenerating axons
- Enzyme treatment exposes bioactive laminin known to promote nerve regeneration
- Extensive quality assays verify quality and consistency



 **avance**[®]
nerve graft

The Avance Method results in consistent, reliable nerve grafts that are well studied and well established in clinical practice.

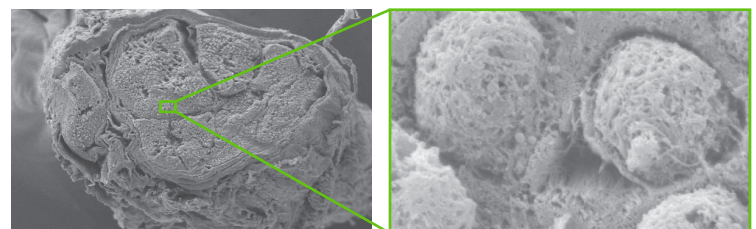
optimal tissue preparation is essential for regeneration

Tissue cleansing plays a critical role in preparing the allograft to be effectively utilized by the body during nerve regeneration. The Avance Method systematically cleanses the Avance Nerve Graft for *the precise amount of time and rate of agitation, at the optimal temperature.*⁶

donor nerve recovery

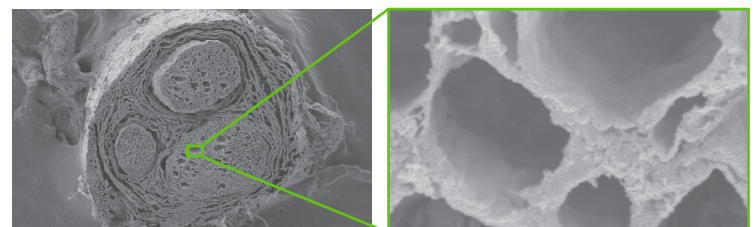
When a donor nerve is recovered:

- Cell and axon remnants fill the endoneurial tubes.
This physically blocks the supporting structures vital to axon regeneration.
- Chondroitin sulfate proteoglycans (CSPGs) are bound to the extracellular matrix (ECM) lining the endoneurial tubes.
CSPGs inhibit axon regeneration by blocking axon access to the bioactive laminin.



Unprocessed nerve (SEM)

Unprocessed nerve
(SEM - magnified)



Avance Method nerve (SEM)

Avance Method nerve
(SEM - magnified)

donor nerve preparation

Avance Method preparation steps include:

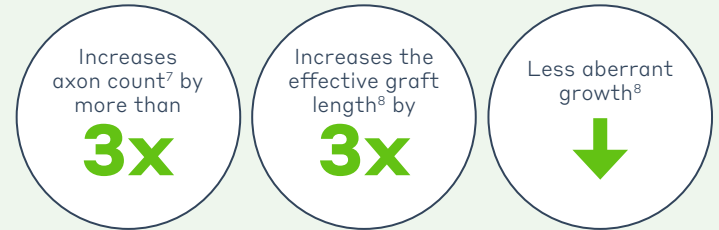
- Detergent washes to clear the axon remnants and other cellular debris from the endoneurial tubes, while preserving the delicate 3D macro- and micro-architecture of the native nerve.

This clears a path for Schwann cell migration and axon regeneration.

- Enzyme treatment cleaves the glycosaminoglycan (GAG) side chains of the CSPGs.

This inactivates their inhibitory effects and exposes bioactive laminin known to promote nerve regeneration.

Benefits of inactivating CSPGs in nerve allografts:



Allografts treated to inactivate the inhibitory aspects of the CSPGs have shown an increased number of axons growing through the graft, increased effective length of the graft, and decreased aberrant growth.⁸



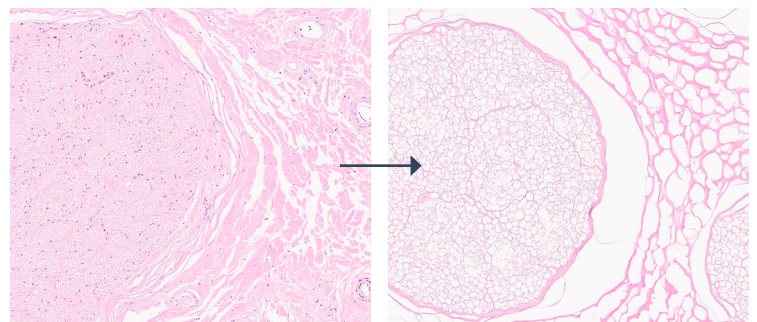
The Avance Method **maintains** endoneurial tubes, which act as the road to physically support axons, **exposes** bioactive laminin acting as the navigation system to promote axon regeneration, and **inactivates** CSPGs, which act as stop signs and inhibit axon regeneration.

quality assays ensure presence and preservation of essential nerve characteristics

The Avance Method's proprietary quality assays ensure bioactivity and endoneurial tube quality and consistency. This extensive testing verifies the identity, purity and safety of each Avance Nerve Graft lot.

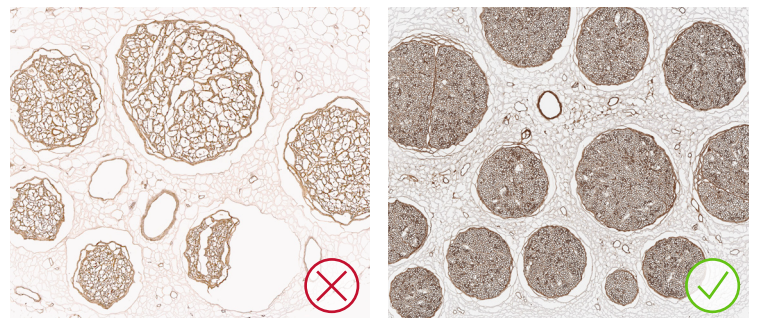
Histological safeguards:

- H&E Stain: demonstrates cellular debris has been removed
- Laminin Stain: identifies the presence of laminin, and highlights endoneurial tube structure
- Endoneurial Tube Assessment (ETA): certifies endoneurial tube quality by assessing size and circularity of the laminin surface
- CSPG Stain: confirms inactivation of inhibitory CSPGs



Unprocessed nerve (H&E stain)

Avance Method nerve (H&E stain)



Rejected graft (laminin stain)

Accepted graft (laminin stain)

the avance method: unparalleled expertise and safety

Over 50,000 nerve repairs worldwide since 2007, with no reported implant-related reportable adverse events

Overall, **82% meaningful recovery rates** across sensory, mixed and motor nerve repairs in gaps up to 70 mm³

12+ years of evidence with more than **135 clinical peer-reviewed publications** on Avance Nerve Graft

#1 choice for hand surgeons in digital nerve gaps of 2 cm⁹

Subject of the world's largest peripheral nerve repair registry study, the 31-center **RANGER® Registry**

Avance received a **Regenerative Medicine Advanced Therapy (RMAT)** designation from the FDA highlighting the strength of clinical evidence and the unmet need for improved nerve injury treatments



Axogen Processing Center. Dayton, Ohio

talk to your sales rep today or visit axogeninc.com to learn more

citations

1. Rinker B, et al. Use of processed nerve allografts to repair nerve injuries greater than 25 mm in the hand. *Ann Plast Surg.* Jun 2017;78(6S suppl 5):S292-S295. 2. Leversedge F, et al. A multicenter matched cohort study of processed nerve allograft and conduit in digital nerve reconstruction. *J Hand Surg Am.* Sep 30, 2020;S0363-5023(20)30413-30415. 3. Safa B, et al. Peripheral nerve repair throughout the body with processed nerve allografts: results from a large multicenter study. *Microsurgery.* Jul 2020;40(5):527-537. 4. Means KR, et al. A multicenter, prospective, randomized, pilot study of outcomes for digital nerve repair in the hand using hollow conduit compared with processed allograft nerve. *Hand (NY).* 2016 Jun;11(2):144-51. 5. Mauch JT, et al. A systematic review of sensory outcomes of digital nerve gap reconstruction with autograft, allograft, and conduit. *Ann Plast Surg.* 2019 Apr;82(4S Suppl 3):S247-S255. 6. Axogen data on file. 7. Krekoski CA, et al. Axonal regeneration into acellular nerve grafts is enhanced by degradation of chondroitin sulfate proteoglycan. *J Neurosci.* Aug 15, 2001;21(16):6206-6213. 8. Neubauer D, et al. Chondroitinase treatment increases the effective length of acellular nerve grafts. *Experimental neurology.* 2007;207(1):163-170. 9. Azouz SM, et al. A survey of the prevalence and practice patterns of human acellular nerve allograft use. *Plast Reconstr Surg Glob Open.* Aug 6, 2018;6(8):e1803.

indications and trademark disclaimers

Avance® Nerve Graft

REGULATORY CLASSIFICATION: Avance Nerve Graft is processed and distributed in accordance with US FDA requirements for Human Cellular and Tissue-based Products (HCT/P) under 21 CFR Part 1271 regulations, US State regulations and the guidelines of the American Association of Tissue Banks (AATB). Additionally, international regulations are followed as appropriate. Avance Nerve Graft is to be dispensed only by or on the order of a licensed physician.

INDICATIONS FOR USE: Avance Nerve Graft is processed nerve allograft (human) intended for the surgical repair of peripheral nerve discontinuities to support regeneration across the defect.

CONTRAINDICATIONS: Avance Nerve Graft is contraindicated for use in any patient in whom soft tissue implants are contraindicated. This includes any pathology that would limit the blood supply and compromise healing or evidence of a current infection.

*Each patient outcome is dependent upon the nature and extent of nerve loss or damage, the timing between nerve loss and repair, and the natural course of the patient's recovery.

visit our
website
for more
information



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