Junyoung MEDICAL

Avance®
Nerve Graft

The Natural Connection

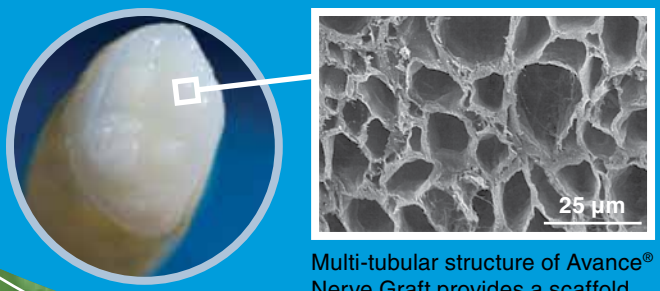
Connecting nerves.
Connecting lives.

AxoGen®
Nerve Regeneration

Bringing the science of nerve repair to life.

Avance® Nerve Graft is peripheral nerve allograft for bridging nerve discontinuities.

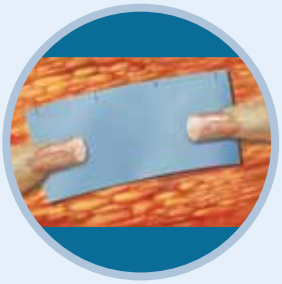
Avance® Nerve Graft is a decellularized and cleansed extracellular matrix from donated human peripheral nerve. The cleaning process preserves the inherent and relevant structural characteristics of the tissue.



Multi-tubular structure of Avance® Nerve Graft provides a scaffold for axons to grow through

Avance® Nerve Graft provides the following features:

- Decellularized and cleansed extracellular matrix.
- Structurally supports the body's own regeneration process.
- Handling similar to an autograft nerve without the loss of donor nerve function.
- Flexible and pliable.



Step 1: Prepare nerve

Expose nerve at the appropriate incision site according to standard operating procedures. Prepare the nerve bed. Examine the local tissues, resecting scar tissue as needed. The proximal and distal segments of the injured nerves should be debrided to healthy tissue by visual and tactile cues.

Note: Axoplasmic fluid will often weep out of the resected nerve ending and may be one indication of adequate debridement.

Step 2: Select appropriate size Avance® Nerve Graft

After measuring the distance between the proximal and distal nerve stumps, as well as the diameters of each nerve stump, select the appropriate size Avance® Nerve Graft.

If the diameter of Avance® Nerve Graft is smaller than the nerve diameter, cable grafting may be performed.

Individual fascicles may be isolated and used to connect to fascicles of a smaller-diameter nerve.

Step 3: Prepare and thaw Avance® Nerve Graft

Using standard aseptic technique, peel open the outer foil chevron pouch and pass the inner Tyvek® pouch to the sterile field for further handling.

Open the inner Tyvek® chevron pouch and remove the product tray. Open the tray and fill the premolded thawing reservoir with room temperature sterile saline or sterile Lactated Ringer's Solution.

The graft will thaw in approximately 5 to 10 minutes. Do NOT heat the graft or add heated saline to the graft.

Allow graft to thaw completely before use. A thawed graft is soft and pliable throughout.

NEVER IMPLANT A PARTIALLY OR FULLY FROZEN GRAFT.

Avance® Nerve Graft preserves the inherent and relevant structural characteristics of human nerve tissue.

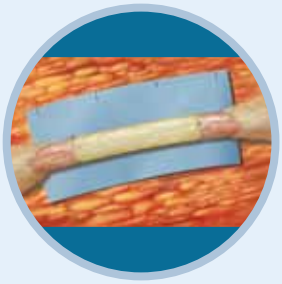
The decellularized and cleansed extracellular matrix of Avance® Nerve Graft works with the natural healing process of the body. It has intact endoneurial tubes that provide a pathway for regenerating axons from the proximal to the distal end of the transected nerve.

Similar to nerve autografts, Avance® Nerve Graft provides the surgeon with desired handling and structural characteristics: pliability of soft tissue, an intact epineurium to suture the graft in place, and intact endoneurial tubes for the axons to grow through.

Avance® Nerve Graft is supplied in a variety of lengths and diameters.

Step 4: Handle Avance® Nerve Graft

Avance® Nerve Graft should be handled like an autograft nerve. The grafts should be held by the epineurium. The graft can be trimmed using a scalpel.



Step 5: Suture Avance® Nerve Graft to nerve stumps

Avance® Nerve Graft can be transplanted using the same micro-surgical technique used when implanting a nerve autograft. Either end of the graft can be coapted to the proximal stump of the host nerve.

Typically, nerve repair is performed with nylon micro-sutures placed in the epineurium. Usually, a simple suture technique is used to coapt the nerve stumps. Gently draw the nerve stump flush with Avance® Nerve Graft prior to tying the knot, making sure the graft endings are aligned with the nerve stumps.

Destroy any thawed tissue not used in the surgical procedure in accordance with local, state, and federal regulations for human tissue.

Note: Avoid tension on the peripheral nerve to be repaired during the entire procedure.

Step 6: Complete and mail the Tissue Utilization Report back to AxoGen, Inc.

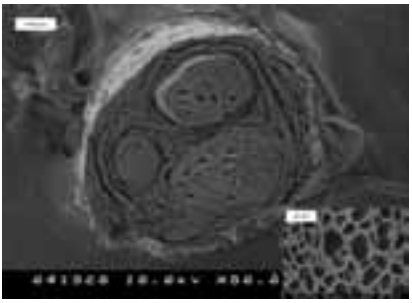
Each graft package has a Tissue Utilization Report (TUR) and a set of product identification labels. In accordance with FDA and JCAHO requirements, a TUR should be completed for each nerve graft.

Record the distinct HCT/P identification code in hospital or facility records and in the patient's file. Complete all information on the card, affix ONE (1) product identification label of each graft used, seal, and return to AxoGen Inc. It is the responsibility of the healthcare institution to maintain recipient records for the purpose of tracking tissue post-implantation.

The Tissue Utilization Report is NOT intended to be a substitute for a facility's internal tissue transplantation tracking system.

PROCESSED NERVE ALLOGRAFTS

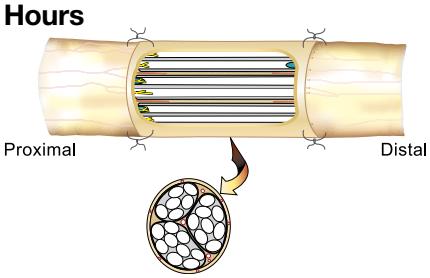
Processed Nerve Allograft—Decellularized, cleansed and sterilized extracellular matrix from human peripheral nerves.



SEM Photo of Processed Nerve Allograft

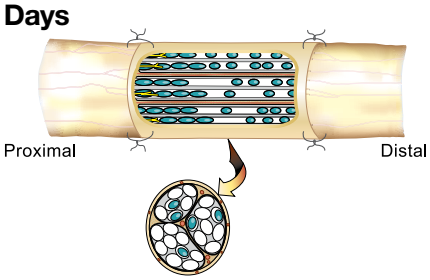
HOW PROCESSED NERVE ALLOGRAFTS WORK

Hours



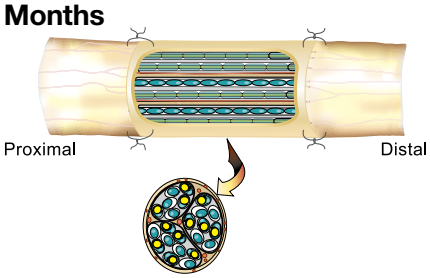
When implanted, the body begins to revascularize and repopulate the extracelluar matrix (ECM) of the processed nerve allograft with cells.

Days



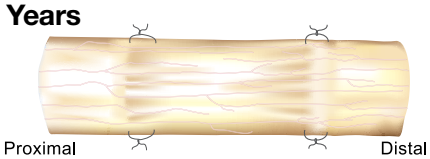
Axons begin to cross the ECM scaffold of the processed nerve allograft toward the distal nerve stump. The advancing axons become remyelinated by the Schwann cells.

Months



The processed nerve allograft remodels into the patient's own tissue as the axons continue to move toward their distal end targets.

Years



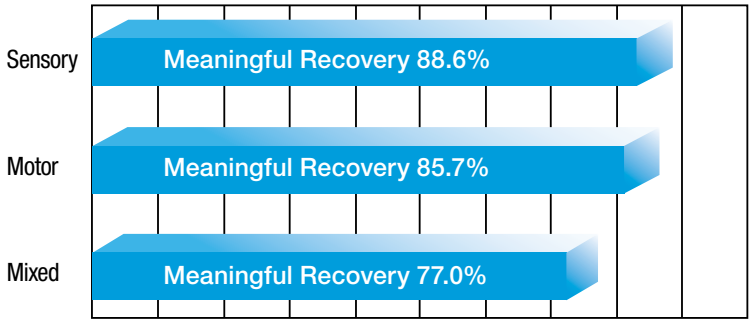
Within the remodeled scaffold, the axons finish their maturation process.

CLINICAL STUDIES OF PROCESSED NERVE ALLOGRAFTS

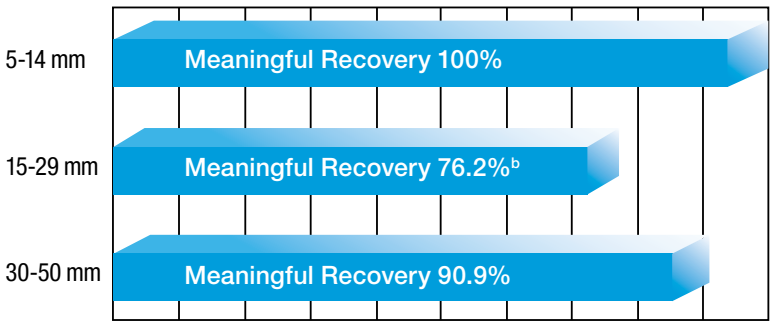
Brooks et al. Study[1]

- 12 sites; 25 surgeons; 132 nerve injuries in adult patients
- Largest multicenter study for nerve allograft and peripheral nerve repairs
- Assessed sensory, mixed and motor nerves in gaps between 5 and 50 mm

Repairs Reporting Recovery[a] by Nerve Type



Repairs Reporting Recovery[a] by Gap Length



[a] Mackinnon modification of the Medical Research Council grading system used for evaluation of sensory and motor recovery. Meaningful recovery was defined as S3 / M3 – S4 / M5.

[b] Value includes revisions deemed unrelated to nerve graft. When excluded, Meaningful Recovery was reached in 85% of repairs.[1]

Karabekmez et al. Study[2]

- 10 nerve injuries
- Static and moving two-point discrimination tests were used to evaluate functional recovery

Graft Length	Average Static 2PD	Average Moving 2PD
5-10 mm (N=4)	5.3 mm	4.3 mm
30 mm (N=6)	5.8 mm	4.5 mm
All Graft Lengths (N=10)	5.5 mm	4.4 mm

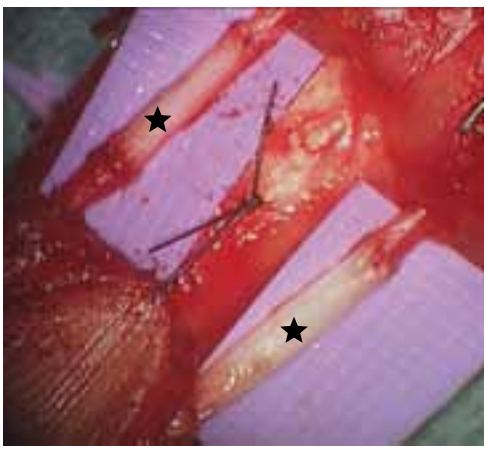
CLINICAL STUDIES SUMMARY

Clinical Studies Conducted with Processed Nerve Allograft						
Study	**Year Published**	**No. of Repairs**	**Nerve Injury Types**	**Test Article**	**Gap Length (mm)**	**Meaningful Recovery[a]**
Brooks et al.[1]	2011	132	Sensory Mixed Motor	Avance® Nerve Graft	5-50 (avg. 22)	87%
Karabekmez et al.[2]	2009	10	Sensory	Avance® Nerve Graft	5-30 (avg. 22)	100%
Shanti et al.[3]	2011	1	Sensory	Avance® Nerve Graft	—	100%

[a] Mackinnon modification of the Medical Research Council grading system used for evaluation of sensory and motor recovery. Meaningful recovery was defined as S3 / M3 - S4 / M5.

Study Findings

- Processed nerve allografts have been shown to be a safe and effective option for nerve reconstruction.[1,2,3]
- No graft related rejection or infection have been reported in multiple studies.[1,2,3,4,5]
- *"The outcomes…compare favorably with those reported in the literature for nerve autograft and the processed nerve allograft returned a higher rate of meaningful functional recovery than those reported in the literature for nerve conduits." –from Brooks et al. 2011[1]*



CLINICAL EXAMPLE

Reconstruction of the ulnar and radial digital nerves with processed nerve allografts (stars).

Image courtesy of Darrell N. Brooks, M.D.
The Buncke Clinic

SUMMARY

Processed nerve allografts have shown clinical benefit in studies for peripheral nerve reconstruction. There are several benefits of this nerve repair option.

- The 3-dimensional structure inherent to the nerve is maintained to provide structural support for regenerating axons.
- The extracellular matrix becomes revascularized and remodeled into the patient's own tissue.
- Flexibility to choose the appropriate diameter and length to allow for customized peripheral nerve repairs.
- Commercially available, without the complication, expense, and morbidity of nerve autograft.

The benefits and limitations of processed nerve allograft should be carefully evaluated when selecting treatment options for peripheral nerve injuries. Ultimately, clinical judgment should be used to select the method with which a nerve is repaired.

Historical Literature Reference

Study	Year Published	No. of Repairs	Nerve Injury Types	Test Article	Gap Length (mm)	Positive Outcomes
Wangensteen and Kalliainen[6]	2009	126	Sensory Mixed Motor	NeuraGen® Type1 Bovine Collagen Tube	2.5-20 (avg. 12.8)	43%
Kim et al.[7-11]	2001-06	52	Sensory Mixed	Autograft Direct Suture	—	67-86%
Frykman and Gramyk[12]	1991	90	Mixed	Autograft Direct Suture	<50	75-78%
Frykman and Gramyk[12]	1991	107	Sensory	Autograft for Digital Nerve Injury	<50	80%
Weber et al.[13]	2000	62	Sensory	Neurotube® PGA Tube	0-30 (avg. 7.0)	74%
Weber et al.[13]	2000	74	Sensory	Autograft Direct Repair	0-30 (avg. 4.3)	86%
Kallio et al.[14,15]	1993	254	Sensory	Autograft Direct Repair	10-70	70%
Lohmeyer et al.[16]	2009	12	Sensory	NeuraGen® Type1 Bovine Collagen Tube	6-18 (avg. 12.5)	75%

References

[1] Brooks DN, Weber RV, Chao J, et al. Processed nerve allografts for peripheral nerve reconstruction: A multicenter study of utilization and outcomes in sensory, mixed, and motor nerve reconstructions. *Microsurgery.* Published online 2011 November.

[2] Karabekmez FE, Duymaz A, Moran S. Early Clinical Outcomes with the Use of Decellularized Nerve Allograft for Repair of Sensory Defects Within the Hand. *Hand (NY)* 2009 September;4(3):245–249.

[3] Shanti RM, Ziccardi VB. Use of Decellularized Nerve Allograft for Inferior Alveolar Nerve Reconstruction: A Case Report. *Journal of Oral and Maxillofacial Surgery* 2011;69(2):550-553.

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[9] Kim DH, Kam A, Chandika P, Tiel RL, Kline DG. Surgical management and outcome in patients with radial nerve lesions. *J Neurosurg* 2001;95:573–583.

[10] Kim DH, Murovic JA, Kim YY, Kline DG. Surgical treatment and outcomes in 45 cases of posterior interosseous nerve entrapments and injuries. *J Neurosurg* 2006;104:766–777.

[11] Kim DH, Murovic JA, Kim YY, Kline DG. Surgical treatment and outcomes in 15 patients with anterior interosseous nerve entrapments and injuries. *J Neurosurg* 2006;104:757–765.

[12] Frykman GK, Gramyk KG. Results of nerve grafting. In:Gelberman R, editor. *Operative Nerve Repair and Reconstruction.* Philadelphia: JB Lippincott; 1991.

[13] Weber RA, Breidenbach WC, Brown RE, Jabaley ME, Mass DP. A randomized prospective study of PGA conduits for digital nerve reconstruction in humans. *Plast Recon Surgery* 2000;106:1036–1045.

[14] Kallio PK. The results of secondary repair of 254 digital nerves. *J Hand Surg* 1993;18B:327–330.

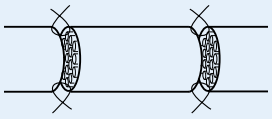
[15] Kallio PK, Vastamaki M. An analysis of the results of late reconstruction of 132 median nerves. *J Hand Surg Br* 1993 Feb;18:97–105.

[16] Lohmeyer JA, Simers F, Machens HG, Mailänder, P. The clinical use of artificial nerve conduits for digital nerve repair: A prospective cohort study and literature review. *J Reconstr Microsurg* 2009;25:55–61.

Length of Nerve Injury

0 mm | 5 mm | 10 mm | 15 mm | 20 mm | 25 mm | 30 mm | 35 mm | 40 mm | 45 mm | 50 mm | 55 mm | 60 mm | 65 mm | 70 mm

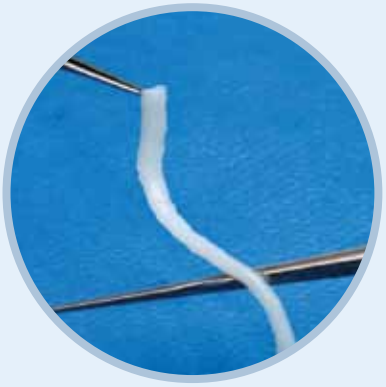
Avance® Nerve Graft



- Bridge gaps up to 70 mm
- Cable grafting (alone or in combination with autograft)
- Bridge a partially severed nerve

Material Features	Avance® Nerve Graft	Collagen or Synthetic
Remodeled into patient's own tissue	✓	
Body revascularizes the tissue during natural healing process	✓	
Easy to suture	✓	○
Flexible, pliable	✓	○
Variety of sizes available	✓	✓
Off-the-shelf option available	✓	✓

○ not representative of all materials



Avance® Nerve Graft
The Natural Connection

Code	Dimensions	Approximate Size
112215	1 – 2 mm x 15 mm	
212215	2 – 3 mm x 15 mm	
312215	3 – 4 mm x 15 mm	
412215	4 – 5 mm x 15 mm	
112230	1 – 2 mm x 30 mm	
212230	2 – 3 mm x 30 mm	
312230	3 – 4 mm x 30 mm	
412230	4 – 5 mm x 30 mm	
112250	1 – 2 mm x 50 mm	
212250	2 – 3 mm x 50 mm	
312250	3 – 4 mm x 50 mm	
412250	4 – 5 mm x 50 mm	
112270	1 – 2 mm x 70 mm	
212270	2 – 3 mm x 70 mm	
312270	3 – 4 mm x 70 mm	
412270	4 – 5 mm x 70 mm	

Actual sizes may vary

Regulatory classification: Avance® Nerve Graft is a human tissue for transplantation. It is processed and distributed in accordance with FDA requirements for Human Cellular and Tissue-based Products (21 CFR Part 1271), State regulations and the guidelines of the American Association of Tissue Banks (AATB). This graft is to be dispensed only by or on the order of a licensed physician.

Applications for use: Avance® Nerve Graft is allograft tissue for bridging peripheral nerve discontinuities.

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.

U.S. Patents: 6, 972, 168; 7, 402, 319; 7, 732, 200 and other patents pending.

AxoGen® Nerve Regeneration
Bringing the science of nerve repair to life.

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