axoguard®

the right biomaterial for the right application

a proven difference with consistent host tissue response

revolutionizing the
science of nerve repair™

axogen®

a head-to-head comparative study

An animal study of the two most prevalent biomaterials used for nerve conduits examined host tissue response and axon regeneration in a 5 mm sciatic nerve gap model. The biomaterials' properties are well understood, but the effects on nerve regeneration have not been previously well characterized, which is the purpose of this research.

porcine small intestine submucosa (SIS, Axoguard® Nerve Connector) vs. cross-linked bovine collagen type I (CLC, Integra NeuraGen®)

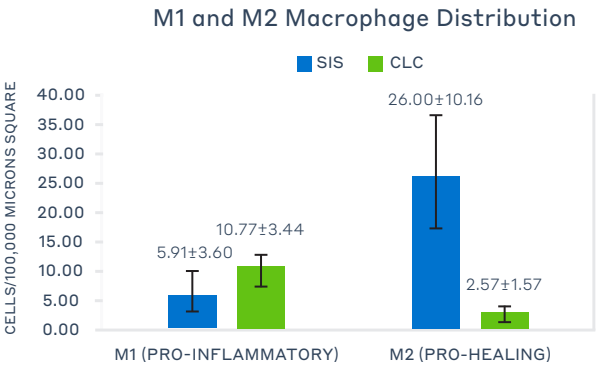
- N=9 male Lewis rats per group
- Four-week time point from initial repair
- Conduit dimensions: 10 mm length, 1.5 mm diameter

biomaterials at a glance

	SIS	CLC
processing	minimally processed to preserve native extracellular matrix	denatured and cross-linked
appearance	semitranslucent	opaque
flexibility	pliable	rigid
material fate	remodels (6 months)	resorbs (3–6 months)

SIS performed significantly better than CLC in all outcomes and categories[1]

macrophage phenotype differentiation



M1: p=0.013 and M2: p<0.001, Mann-Whitney U Test.

host inflammatory response

	M2/M1[a]
SIS	6.15±3.01
CLC	0.23±0.10

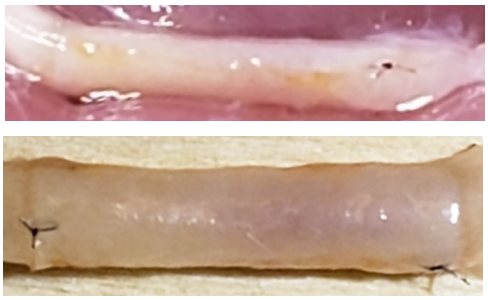
[a]p<0.001, Mann-Whitney U Test.

clinical relevance

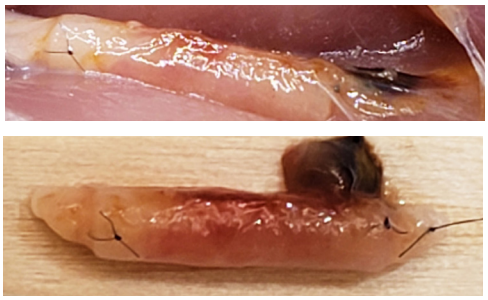
Increased levels of M2 macrophages are indicative of a remodeling response, while M1 macrophages are indicative of a chronic inflammatory response.[2]

adverse events

SIS



CLC



Representative examples at four-week time point

No adverse events with minimal soft tissue attachment.

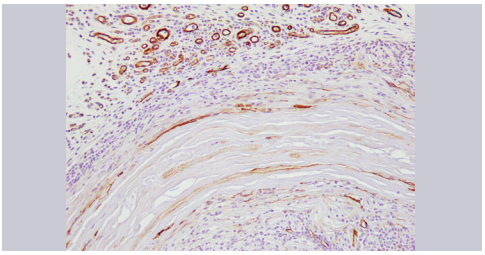
Adverse events included soft tissue attachment and tethering (n=2), small hematoma formation (n=2) and hemorrhages (n=9) indicative of local irritation by the conduit.

clinical relevance

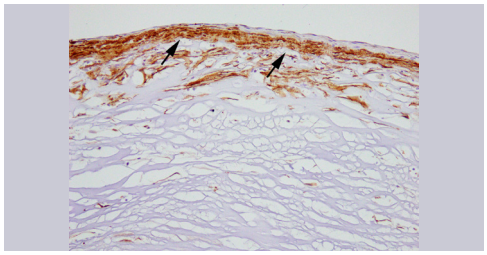
Local irritation and tethering have the potential to cause chronic inflammation and may lead to product extrusion and poor outcomes.[3]

encapsulation

SIS



CLC



Alpha smooth muscle actin (α-SMA) staining at four-week time point

No sign of encapsulation.

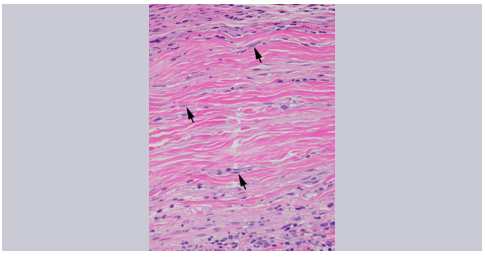
Clear signs of encapsulation.

clinical relevance

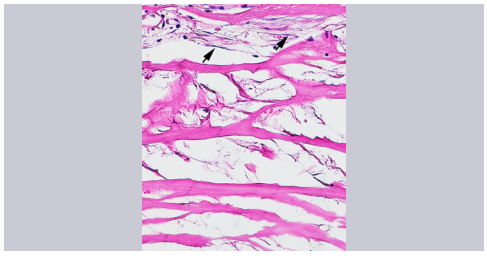
Encapsulation can lead to product extrusion, compromised vascular structures, constriction and poor outcomes due to excess scar formation.[3,4]

cellular ingrowth and remodeling

SIS



CLC



H&E staining

Deeper cellular ingrowth (arrows), attributed to the retained extracellular matrix structure, allows the host to remodel the material.

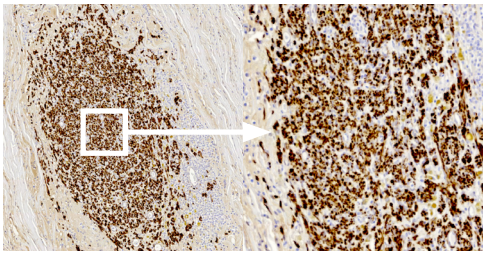
Superficial cellular ingrowth (arrows) as material resorbs.

clinical relevance

Host tissue remodeling of the SIS material provides a permanent protective tissue layer that provides a barrier to soft tissue attachment and axonal escape.[5-7]

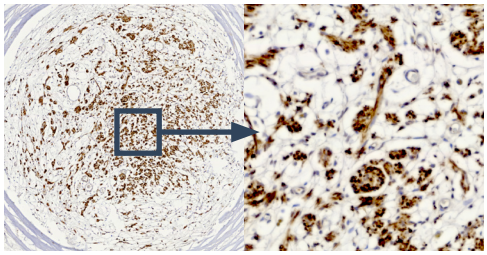
axonal organization

SIS



Significantly increased axonal density in the central lumen with more organized axonal growth.

CLC



Significantly less axonal density in the central lumen and disorganized axonal growth.

Neurofilament staining

clinical relevance

Organized axonal growth can result in more consistent outcomes; disorganized growth may lead to compromised regeneration and poor outcomes.[8]

why SIS is the preferred biomaterial

- Dominant host M2 macrophage response following SIS implantation indicates constructive remodeling[1]
- Combines strength, pliability and semi-translucency with significantly more beneficial cellular ingrowth compared to CLC as seen in an animal study
- Gradually remodels while not encapsulating
- Repairs with SIS in this study show significantly increased axon density and organization compared to CLC, which may result in more consistent outcomes

Disclaimer

This experimental protocol adhered to the guidelines of the Animal Welfare Act (CFR 9) and was approved before testing by the Institution Animal Care and Use Committee at the University of Florida (Protocol # 201910721).

References

1. Data on file. **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. **3.** Liodaki E, Bos I, et al. Removal of collagen nerve conduits (NeuraGen) after unsuccessful implantation: focus on histological findings. *J Reconstr Microsurg.* 2013;29(8):517-522. **4.** Chamberlain LJ, Yannas IV, Hsu HP, Spector M. Connective tissue response to tubular implants for peripheral nerve regeneration: the role of myofibroblasts. *J Comp Neurol.* 2000;417(4):415-430. **5.** Kokkalis ZT, Pu C, et al. Assessment of processed porcine extracellular matrix as a protective barrier in a rabbit nerve wrap model. *J Reconstr Microsurg.* 2011 Jan;27(1):19-28. **6.** Ko Y, Park JH, et al. Growth behavior of endothelial cells according to electrospun poly(D,L-lactic-co-glycolic acid) fiberdiameter as a tissue engineering scaffold. *Tissue Eng Regen Med.* 2016;13(4):343-351. **7.** Hodde JP, Record RD, et al. Vascular endothelial growth factor in porcine-derived extracellular matrix. *Endothelium.* 2004;8(1):11-24. **8.** Tork S, Faleris J, et al. Application of a porcine small intestine submucosa nerve cap for prevention of neuromas and associated pain. *Tissue Eng Part A.* 2020;26(9-10):503-511.

Axoguard Nerve Connector

INDICATIONS FOR USE: Axoguard Nerve Connector is intended for the repair of peripheral nerve discontinuities where gap closure can be achieved by flexion of the extremity. The device is supplied sterile and is intended for one-time use.

CONTRAINDICATIONS: This device is derived from a porcine source and should not be used for patients with known sensitivity to porcine material.

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