MILITARY HEALTH SYSTEM RESEARCH SYMPOSIUM (MHSRS)

Peer-Reviewed Orthopaedic Research Program • Clinical Trial

Early Outcomes of a DoW Sponsored Clinical Trial to Address Amputated Nerve Ends

Tolerability / Feasibility Study on Nerve Caps

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Funded by the U.S. Department of Defense (PRORP).
Award W81XWH-18-PRORP-CTRA • Log OR180222

Disclosures

Evan J. Hernandez, MBA – has no conflicts to report.

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Learning Objectives

1

MECHANISM

Describe how an FDA-cleared nerve termination cap reduces formation of symptomatic neuromas in transected “large diameter” nerves by containing axonal growth within bifurcated chambers of the termination cap.

2

PAIN OUTCOMES

Discuss early and sustained improvements in patient-reported residual and phantom limb pain after amputation or treatment of a symptomatic neuroma.

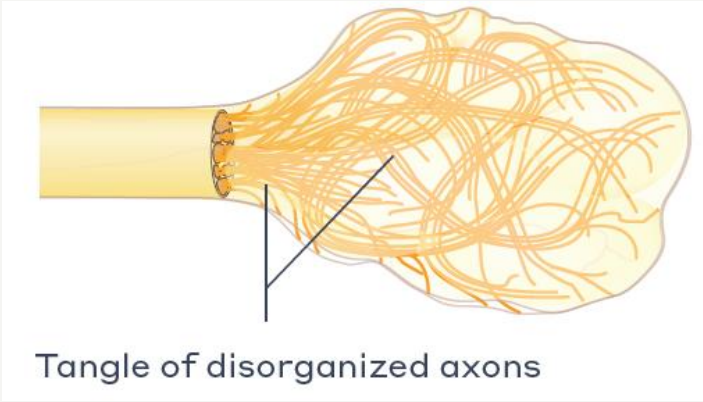
3

LARGE-DIAMETER NERVES

Discuss clinically meaningful improvements in patient-reported outcomes for “large diameter” nerves that were treated with a nerve termination cap at the time of amputation.

The Clinical Problem

- In amputation surgery, traction neurectomy has been the traditional standard.
- Some neuromas become symptomatic likely due to pathological interactions between the axons within the neuroma[1,2] as well as traction between the nerve and scar tissue.[1,3,4]
- Upwards of 42% of amputees develop symptomatic neuromas after traction neurectomy. [5]
- Neuromas contribute to higher rates of phantom and residual pain. [6]
- Neuromas reduce functional and rehabilitative capacity, inhibiting physical activity levels and capabilities. [6]



Porcine SIS Extracellular Matrix Cap

- A tubular, chambered device made from porcine SIS extracellular matrix
  - remodels into the patient's own new tissue layer
  - protects the nerve end from mechanical stimulation and neurotrophic factors
- One closed end that terminates the nerve
- Bifurcated chambers contain axonal growth
  - maintains a suitable distance for axonal outgrowth and exhaustion to reduce the potential for neuroma formation
  - reduces pathologic axon interaction
- FDA 510(k)-cleared for nerve end protection

STUDY OBJECTIVE

Evaluate the effectiveness of the FDA-cleared nerve cap at preventing symptomatic neuroma formation in patients undergoing major limb amputation.

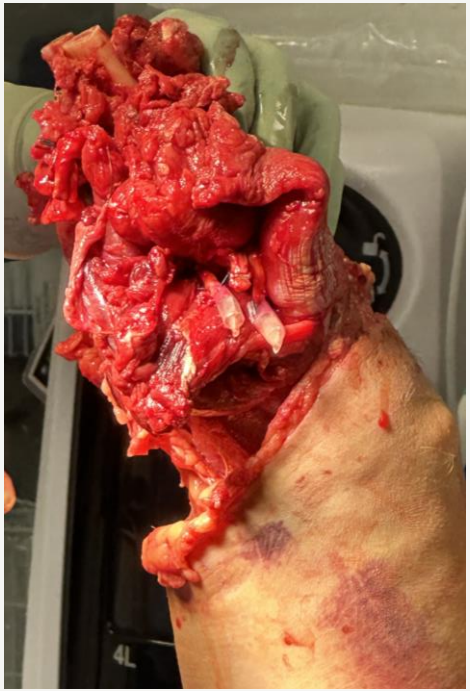
Study Design

Population
Patients undergoing traumatic limb amputation or revisional amputation procedures at University Medical Centers.

Nerve inclusion
Amputated nerve endings measuring > 4 mm to < 7 mm in diameter.

Intervention
Nerve endings “capped” with the nerve cap at the time of surgery.

Follow-up
Prospective follow-up over 12 months.



Outcomes Assessed

1

Pain

Phantom & residual limb pain (Visual Analog Scale, 0–100 mm)

2

Neuroma formation

Diagnosis of symptomatic neuromas

3

Quality of life

Patient-reported outcomes (6 pain-related PROMIS® measures)

4

Safety

Adverse events, including device-related events

Patient Cohort

15
Patients enrolled

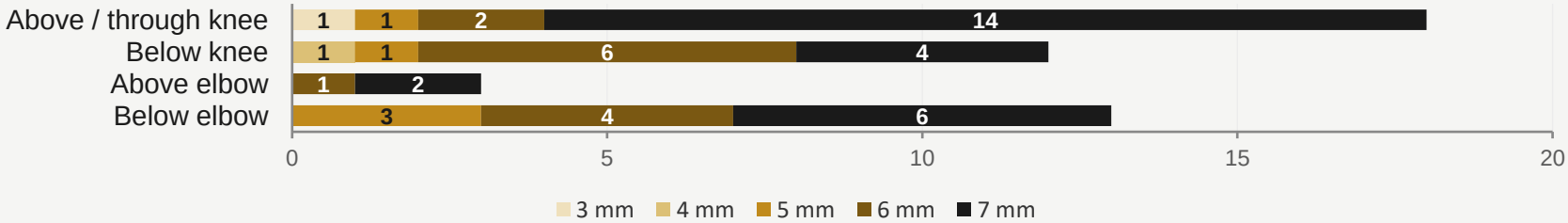
13
Male patients

20–63
Age range (years)

44
Nerve caps implanted*

12 mo
Follow-up duration

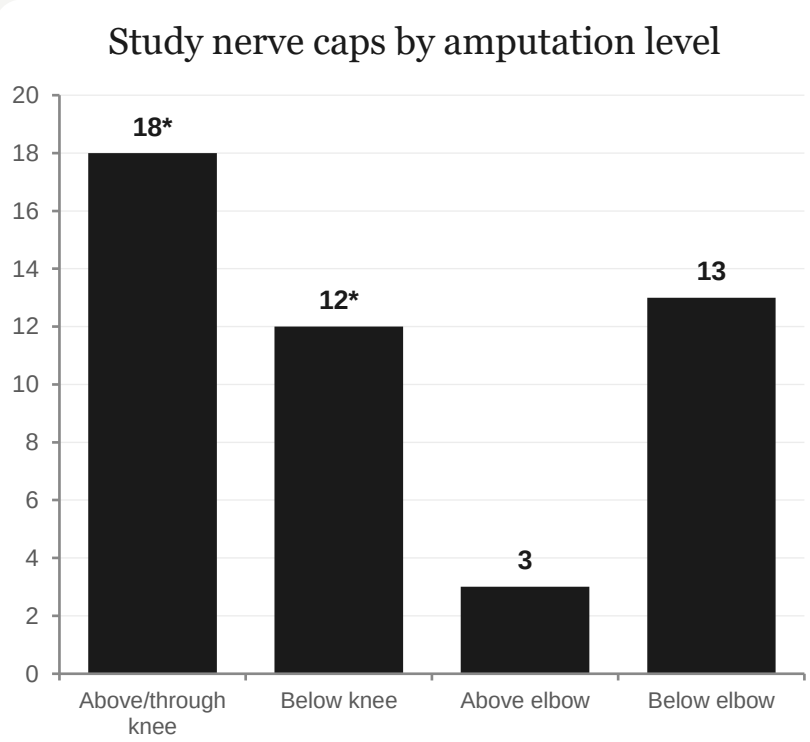
Nerve cap diameters by amputation level



**Two additional implanted nerve caps were 3-4mm in diameter, however those two participants received nerve caps of eligible sizes.*

Nerve Cap Utilization by Amputation Level

Amputation level	Nerve caps implanted	Number of subjects	Nerve caps / patient	Range
Above/through knee	18*	5	3.6	2–5
Below knee	12*	4	3.0	2–5
Above elbow	3	1	3.0	3
Below elbow	13	5	2.6	1–3
Total	**46***	**15**	**3.1**	**1-5**



**46 nerve caps were placed across 15 patients.*

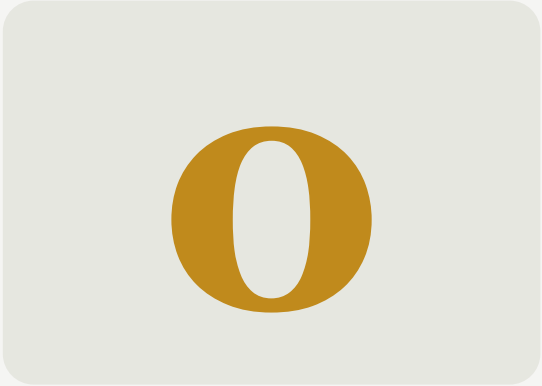
**Includes the two smaller diameter nerve caps implanted; one above/through knee and one below knee.*

Key Findings at a Glance

0	−65.4 mm	−63.2 mm	6 / 6	0
symptomatic neuromas diagnosed	phantom limb pain (VAS, 12 mos.)	residual limb pain (VAS, 12 mos.)	PROMIS pain measures improved	Nerve cap-related adverse events

No formation of symptomatic neuromas and no nerve cap-related adverse events were observed across the 12-month pilot study.

Symptomatic Neuroma Formation



No formation of symptomatic neuromas

were diagnosed during the 12-month follow-up.

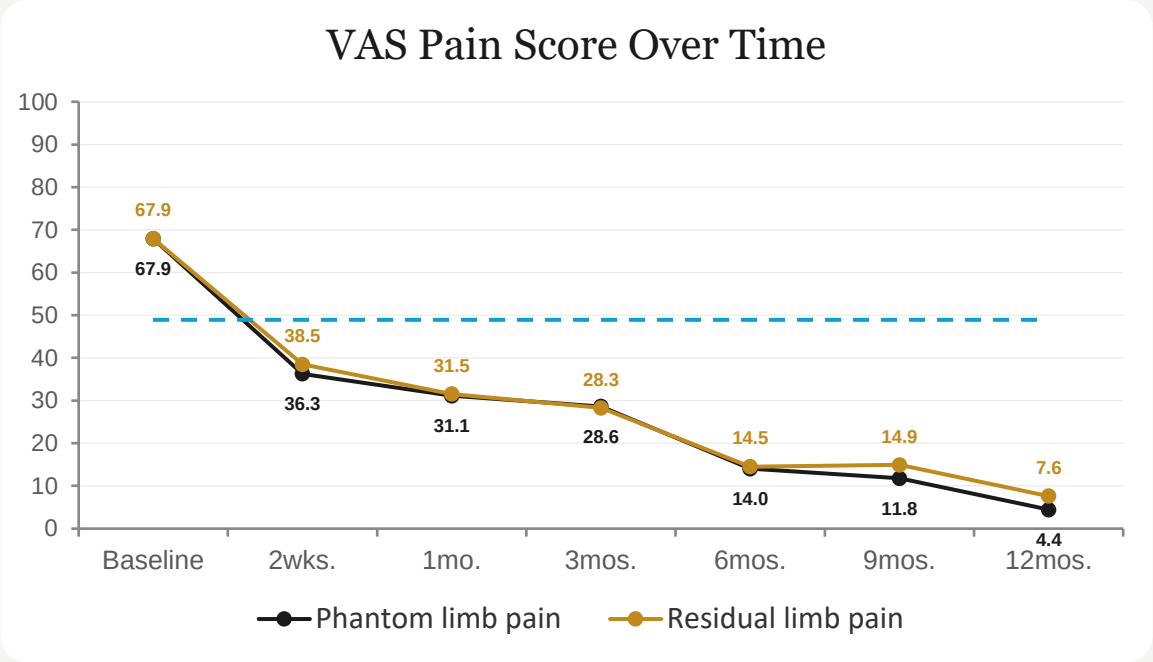
Visual Analog Scale (VAS) Pain Reduction

Change from pre-operative baseline (mm) on the 0–100 mm VAS.
Minimal clinically important difference (MCID) = 19 mm.

Pain type	2 weeks	12 months
Phantom limb pain	**−31.5 mm**	**−65.4 mm**
Residual limb pain	**−27.3 mm**	**−63.2 mm**

Rapid and sustained improvement: both pain types dropped below the MCID threshold by 2 weeks and continued to fall through 12 months.

VAS Pain Reduction Over Time



Lower VAS score = less limb pain

VAS pain scores at study timepoints (0-100 mm scale).

Both pain types show reductions in VAS that exceed the 19 mm MCID (dashed line).

Improvement was evident by 2 weeks and deepened through 12 months.

PROMIS Patient-Reported Outcomes

6

pain-related PROMIS® measures improved

Pain Intensity·v1.0·Form 3a
Pain Interference·v1.0·Form 8a
Pain Behavior·v2.0 (Bank)·Form 20a
Fatigue·v1.0·Form 8a
Sleep Disturbance·v1.0·Form 8a
Physical Function·v2.0·Form 6b

Early response

Reductions seen as early as 2 weeks post-operatively for both phantom and residual pain.

Sustained benefit

Improvements were maintained through the full 12-month follow-up.

Clinically meaningful

Changes generally exceeded the 10-point PROMIS MCID.

Adverse Events

0

No nerve cap-related adverse events

The nerve cap was well tolerated throughout the 12-month study period.

Tolerability & feasibility supported. Combined with zero symptomatic neuromas, this supports continued clinical evaluation of the nerve cap and possible greater adoption across different patient cohorts.

Conclusions

- High levels of pain and the potential for symptomatic neuroma formation are unfortunate common sequelae of patients undergoing amputation.
- The use of a nerve cap was associated with significant, sustained improvements with regard to phantom and residual VAS limb pain up to 1 year post-cap placement.
- All 6 PROMIS measures evaluated improved, generally exceeding the MCIDs throughout the 12-month study duration.
- The nerve cap is a viable solution to treat and/or prevent the formation of symptomatic neuromas in certain amputated nerves that measure ≤ 7 mm in diameter.

Funding & Disclosures

Funding

This study is being funded by the Department of Defense via the Peer Reviewed Orthopaedic Research Program Award.

Funding Number: W81XWH-18-PRORP-CTRA **Log Number:** OR180222

Learning objectives addressed: (1) nerve cap mechanism of neuroma prevention; (2) early and sustained pain improvement; (3) meaningful outcomes for large-diameter nerves.

References

1. Nashold B.S. Jr., Goldner J.L., Mullen J.B., and Bright D.S.. Long-term pain control by direct peripheral-nerve stimulation. J Bone Joint Surg Am 64, 1, 1982

2. Provost N., Bonaldi V.M., Sarazin L., Cho K.H., and Chhem R.K.. Amputation stump neuroma: ultrasound features. J Clin Ultrasound 25, 85, 1997

3. Fisher G.T., and Boswick J.A.. Neuroma formation following digital amputations. J Trauma 23, 136, 1983

4. Mathews G.J., and Osterholm J.L.. Painful traumatic neuromas. Surg Clin North Am 52, 1313, 1972

5. Pet MA, Ko JH, Friedly JL, Smith DG. Traction neurectomy for treatment of painful residual limb neuroma in lower extremity amputees. *J Orthop Trauma.* 2015

6. Valerio IL, Dumanian GA, Jordan SW, et al. Preemptive treatment of phantom and residual limb pain with targeted muscle reinnervation at the time of major limb amputation. *J Am Coll Surg.* 2019

Thank you!

Questions and discussion

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