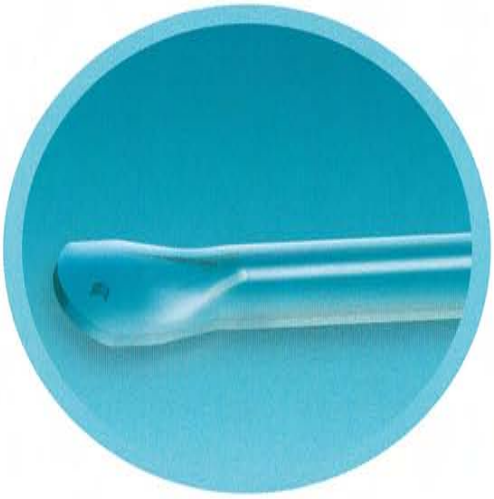
NEUROCAP®

Peripheral Nerve Capping Device



Evidence Based Performance

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NEUROCAP®

A UNIQUE DEDICATED DEVICE FOR THE MANAGEMENT OF END-NEUROMAS

Neuromas are a highly disabling pathology

Symptomatic neuroma may develop after a nerve dissection following any trauma to a peripheral nerve, whether accidental or planned (i.e. surgery). Neuroma-induced neuropathic pain and morbidity seriously affect the patient's daily life and socioeconomic functioning. The incidence of symptomatic neuromas after peripheral nerve injury is estimated to be 3-5%, however certain surgeries (e.g. autograft procedures, amputations) may have up to a 30% incidence rate. On average, patients are undergoing 2.8 re-interventions after the initial treatment of a neuroma. Following treatment of a neuroma, 86% of patients experience none to minimal improvement

NEUROCAP® design is straightforward, simple and effective

NEUROCAP® is intended to protect a peripheral nerve end and to separate the nerve from surrounding environment to reduce the development of a symptomatic end-neuroma. NEUROCAP® is a transparent tubular device with one open end and one closed end. Dislocation of the nerve stump is prevented by suturing the nerve end into the cap. A hole at the sealed end of the tube allows easy fixation of the nerve stump with a suture to the surrounding tissue. This allows an effective capping technique without the necessity of excessive manipulation or sacrificing other tissue. Currently, there is no gold standard for neuroma treatment; burying of the nerve stump is the most common procedure

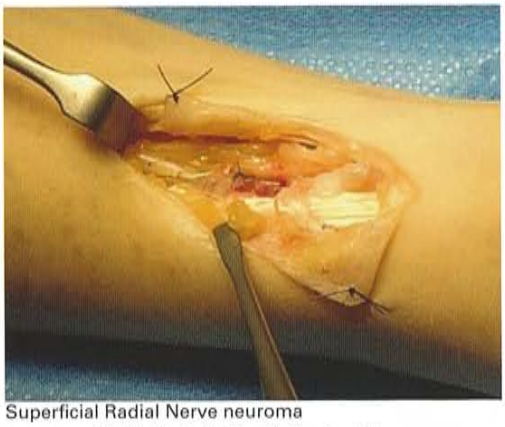
NEUROCAP®'s unique features support important (clinical) needs:

- Made of inert and biodegradable lactide and caprolactone copolymers with an excellent safety track record of implementation in other medical devices
- Transparent and simple design for easy handling and optimal nerve positioning during the procedure
- Controlled mechanical strength and flexibility prevent (a) axonal sprouting (b) adhesion of the nerve-ends into muscle and scar tissue
- Predictable bioresorbability to support a sustainable encapsulation of the nerve stump
- Long-term pre- and clinical follow-up data (12 months) indicate an effective barrier function and considerable and lasting pain reduction in treated patients

NEUROCAP® is the only clinically proven nerve capping device

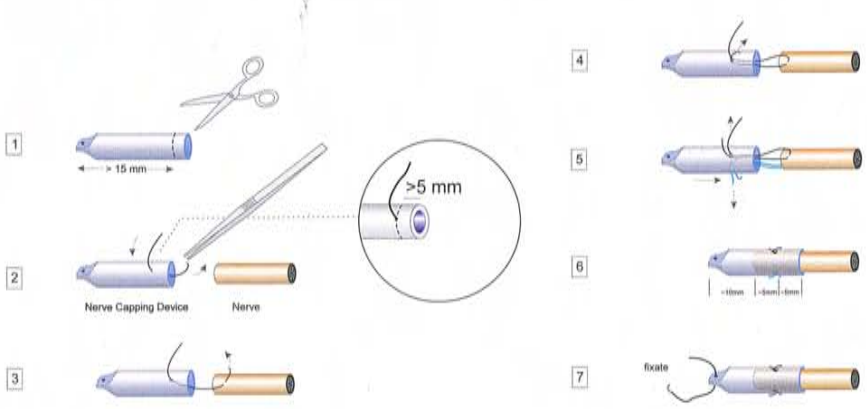
A strong body of evidence supports the effectiveness of NEUROCAP®.

- Pivotal clinical data of the STOP Neuroma trial (one-year clinical patient follow-up) confirms safety and performance of NEUROCAP® application in the treatment of symptomatic end neuroma in peripheral nerves (publication in progress).
- The PROTECT Neuro study, a multicenter post-market clinical follow-up study in both the US and Europe, is designed to strengthen and expand the clinical value of NEUROCAP® in the upper and lower extremities over a 2-year period of patient monitoring. Patient enrollment of this PMS study successfully concluded in summer 2018.
- The modes of action of the device, creating a full barrier with the surrounding tissues, preventing axonal sprouting and avoiding the formation of end-neuromas, is clearly demonstrated in a rat sciatic nerve model and is currently prepared for publication.



Superficial Radial Nerve neuroma
(courtesy: Dr M. Bertleff, The Netherlands)

NEUROCAP® Product Application



NEUROCAP®

SAFE AND EFFECTIVE MANAGEMENT OF SYMPTOMATIC NERVE-END NEUROMA

STOP Neuroma Trial: this pivotal study reveals reduction of symptomatic pain over a year clinical follow up

Objective	A cohort study with a 12-month clinical follow up (N=10) to assess safety and performance of NEUROCAP® for the treatment of symptomatic end-neuroma
Participating centers	• Medical center Lelystad / MC Groep (NL); M. Bertleff, MD, PhD • University Medical Center Groningen (NL); T. Middelberg, MD, PhD • Maastricht University Medical Center (NL); T. van Mulken, MD
Endpoints	**Primary endpoint safety (6 wk FU)** • Demonstrate device safety, defined as < 8.3% serious adverse device effects **Primary endpoints effectiveness (6 wk FU)** • Reduction of pain caused by symptomatic neuroma (VAS; Elliot; DN4) • Improvement of quality of life • Reduction or stabilization of quantity/class of pain medication used to treat neuroma pain **Secondary endpoints (3, 6, 12 mo FU)** • < 8.3% serious adverse device effects • Reduction of pain caused by symptomatic neuroma (VAS; Elliot; DN4) • Improvement of quality of life • ≤ 20% recurrence of symptomatic neuroma • Reduction of quantity/class of pain medication • Ease of use and placement of the device
Timelines	• Enrollment concluded: March-2017 • Last patient, last visit (12-month follow up): March-2018 • Final data: May/June-2018 (presented during FESSH-2018)

Patient (gender-age)	Neuroma	NEUROCAP® size	Pre-op VAS (0-100 mm)	+ 6 wks VAS (0-100 mm)	+ 3 mths VAS (0-100 mm)	+ 6 mths VAS (0-100 mm)	+ 12 mths VAS (0-100 mm)
F27	SRN neuroma	2,5 mm	81	1	1	1	1
F66	SRN neuroma	3,0 mm	93	9	25	30	8
F42	Dorsal branch ulnar nerve and SRN	2,5 mm	79	6	1	3	6
F25*	Dorsal branch ulnar nerve	2,0 mm	64	1	1	72	60
F21	SRN neuroma	2,5 mm	80	26	27	27	30
M59**	SRN neuroma	3,0 mm	9	30	30	14	62
F41***	Radial nerve	3,0 mm	78	13	12	72	21
F33	SRN neuroma	1,5 mm	80	1	9	1	1
F37	Median nerve	1,5 mm	78	1	0	1	1
M41****	Sens. branch median nerve	1,5 mm	91	85	72	NA	NA
MEDIAN (range)	-	-	79 (9-93)	8 (1-85)	11 (0-72)	14 (1-72)	8 (1-62)

* *Non-device related AE at 6 months after external trauma (hit on operational site). Surgically treated between 6- and 12-month follow-up.*

** *Uncertainty on first measurement, validation needed. However recurrent neuroma*

*** *Patient indicates variable pain rates, sometimes spontaneous and sometimes when carrying heavy load. Pain is much less frequent than before surgery*

**** *SAE after external trauma (bumped on table corner); severe seroma formation at operational site. Re-operated and Neurocap® removed; study exit after removal*

NEUROCAP®

EVIDENCE BASED DATA TO STRENGHTEN AND BROADEN THE CLINICAL VALUE

PROTECT NEURO post-market study: first preliminary results confirm the pivotal STOP Neuroma outcomes

Objective	A cohort study (N=73) to collect long-term performance data (24 months clinical follow-up) and the ease of use of NEUROCAP® for reduction of peripheral symptomatic end-neuroma formation in both upper and lower extremities
Participating centers	• University of Pennsylvania (US), PA - Prof. dr. Levin, Principal Investigator • Buncke Clinic (US) - Dr. Buncke • VCU Richmond (US) - Dr. Isaacs • Geisinger Institute Danville (US) - Dr. Klena • Thomas Jefferson Philadelphia (US) - Dr. Culp • Peachtree Clinic Atlanta (US) - Dr. McClelland • Stanford University (US) - Dr. Curtin • VA Portland (US) - Dr. Layman • Arizona Hand Center (US) - Dr. Champagne • University Lund (SV) - Prof. Dr. Dahlin • Birmingham Hand Center (UK) - Dr. Power • Centro di Mano Milano (IT) - Prof. Dr. Pajardi • CFCM Paris (FR) - Dr. Houvet • University Linköping (SV) - Dr. Nyman • University Göteburg (SV) - Dr. Sassu • Parc Sanitari de Joan de Deu (ES) – Dr. Aparicio • BG Trauma Center Frankfurt am Main (GR) – Prof. Dr. Sauerbier • Institut de la main de la Clinique Jeanne d'Arc (FR) – Dr. Loubersac / Dr. Gaisne
Endpoints	**Primary endpoint (3, 6, 12, 24 mo FU)** • Reduction of pain caused by symptomatic neuroma (VAS) **Secondary endpoints (3,6,12 mo FU)** • Elliot Neuroma score • Rate of recurrence of painful neuroma • Pain medication use • Level of disability (QuickDASH/Goals) • Ease of use and physician satisfaction
Timelines	• Patient enrollment concluded in July-2018 • Last patient, last follow up: expected July-2020 • Final data: available during Q3-2020

Variable	Screening Mean ± SD (N = 73)	+3 mo FU Mean ± SD (N = 49)	+6 mo FU Mean ± SD (N = 34)	+12 mo FU Mean ± SD (N = 10)
VAS	70.6 ± 17.8	18.1 ± 21.7	26.5 ± 27.7	25.7 ± 23.0
Quick DASH*	56.0 ± 20.8	30.0 ± 23.7	26.7 ± 24.7	39.8 ± 31.0
Goals**	10.6 ± 2.7	4.9 ± 3.9	4.3 ± 3.9	6.5 ± 5.4
Elliot	12.5 ± 3.7	5.2 ± 4.3	6.2 ± 5.4	6.6 ± 5.1

* *QuickDASH Screening: n = 48; 3-months: n = 33; 6-months: n = 22; 12-months: n = 4*

** *Goals Screening: n = 63; 3-months: n = 44; 6-months: n = 33; 12-months: n = 10*

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The ANIMAL study strongly underlines its effective mode of action in creating a full barrier with the surrounding tissues, preventing axonal sprouting and avoiding the formation of end-neuroma. 3, 6 and 12 months post implantation histology underlines NEUROCAP®'s action as effective barrier for unwanted nerve outgrowth.

Objective	A randomized controlled study (N=42 animals) to assess the implantation effects of the NEUROCAP® device in a rat sciatic nerve model after 12 weeks, 6 months, and 12 months
Participating centers	• VA Portland (US) - Dr. Peterson
Endpoints	• **Procedural data, Adverse events, Clinical observations, Histopathology**
Observations and final conclusions	• No adverse procedural observations, clinical observations, or other adverse events that attributed to the use of NEUROCAP® throughout the duration of the study. • Chaotic fascicles score increased in controls and decreased in the NEUROCAP® group over 12-mo • Inflammation score remained low in controls and decreased in NEUROCAP® group to 0.0 at 12-mo • Nerve outgrowth score significantly higher in control group compared to NEUROCAP® group • No neuromas in NEUROCAP® group at any time point (wrt control group: 20% at 3-mo; 38% at 6-mo; 100% at 12-mo) • NEUROCAP® treated nerves seem to become more organized with absence of neuroma formation (in contrast to the control nerves) • Publication in preparation

NEUROCAP®
Histological evaluation at 3, 6 and 12 months after implantation
(10x total magnification)

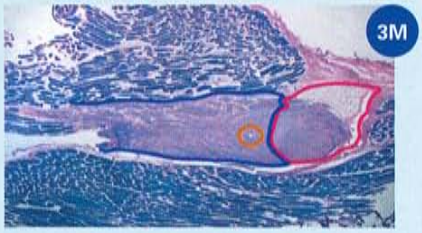
At 3 months, the device blocks sprouting by acting as physical and mechanical barrier

At 6 months, NEUROCAP treated nerve-end stump shows organized fibers

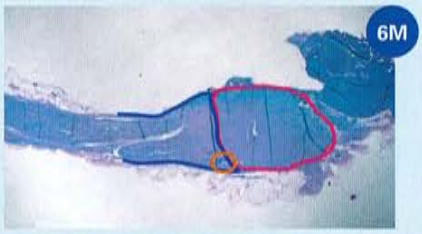
At 12 months, NEUROCAP treated nerve-end is organized and atrophied without neuroma

CONTROL GROUP

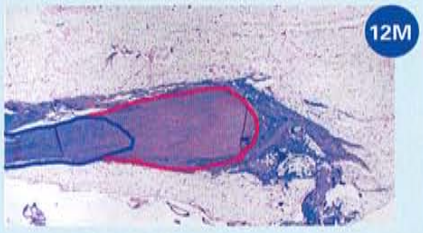
Histological evaluation at 3, 6 and 12 months after implantation
(10x total magnification)



Control with formation of a neuroma



Control with well-formed neuroma



Control with well-formed neuroma

NEUROCAP® is available in a diameter range of 1,5 - 8 mm.

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