neurinnov

INNOVATION IN NEUROSTIMULATION

Introduction to Neurinnov

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Neurinnov, a game-changing technology for people suffering from SCI

- Spin-off from INRIA and the University of Montpellier
- HQ: Montpellier, France
- Founded in **2018** by David Guiraud and David Andreu
- Investors: IRDI, Crédit Agricole/Sofilaro, UI/Mérieux Equity Partners
- Raised **€7.6m** since inception, of which **57%** from non-dilutive sources

SCI: Spinal Cord Injury

Neurinnov, a game-changing technology for people suffering from SCI

OUR MISSION

Enable patients living with complete spinal cord injury to regain essential hand grasping functions and autonomy

THE PROBLEM

No solution today for restoring hand movement due to the challenges of contracting muscles in a synergistic way

OUR SOLUTION

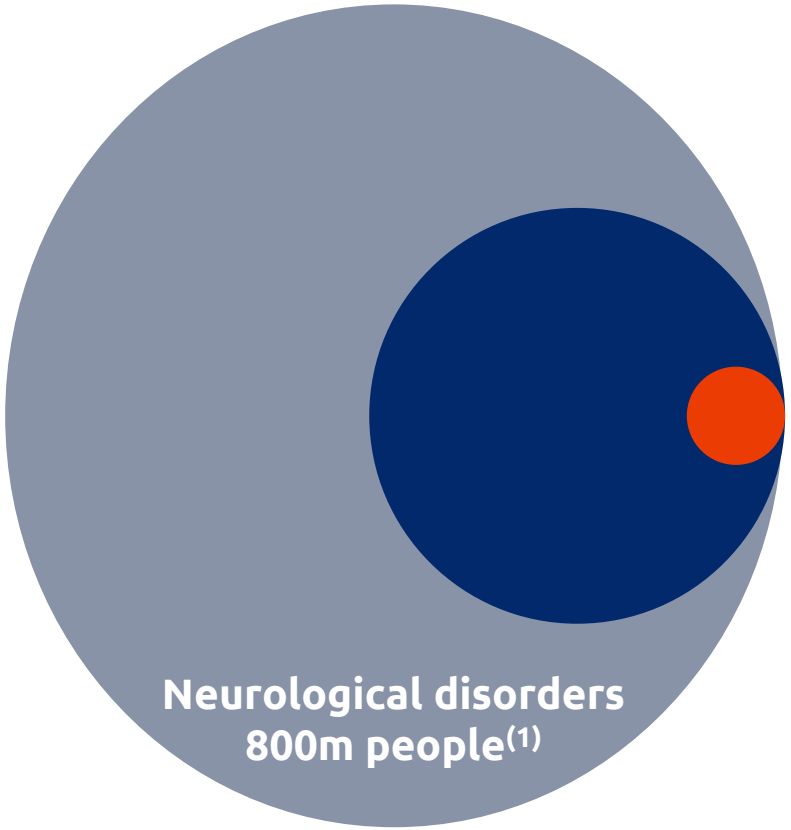
The first neural stimulation solution that generates electrical currents through a subset of nerve fibres to selectively and synergistically activate targeted muscles

CLINICAL RESULTS

Successful proof of concept; hand movements obtained with reliable and reproducible stimulation settings with only 2 epineural electrodes

SCI: Spinal Cord Injury

Why prehension?
Our approach



Disengagement from large-cap pharmas

- 50% less chance of making it to the market(1)
- 30% longer to develop vs other indications(1)

Development of new therapies, incl. neuromodulation

- Brain-stimulation, artificial intelligence, neurostimulation, etc.
- $7bn market (2019 ➡ $18bn (2030); 9% annual growth(2)

WHY PREHENSION?

Neurinnov has designed a selective neurostimulation solution for a sub-set of nerve fibres

Targeting prehension as a first indication

- Unmet need
- Technology validation enhanced by the complexity of dealing with prehension; shorter time-to-market

"The hand is one of the most complex and beautiful pieces of natural engineering in the human body. Whether the issue lies in the median nerve of the hand or an injury of the shoulder, each part of the system must work harmoniously to allow for painless"

Dr Keith Santiago

Why prehension?
Unmet medical need with no solution

POOR QUALITY OF LIFE REQUIRING AN EXPENSIVE 24/24h & 7/7d DEPENDENCE

302,000 and 18,000
people in the US with tSCI[3] and new people in the US with tSCI p.a.[3]

352,000 and 32,000
people in the EU with tSCI[4] and new people in the EU with tSCI p.a.[5]

48%
reduction of life expectancy for people living with SCI[6]

25%
risk of depression[7]

$230,000
yearly expenses for a person with high tetraplegia[8]

$5.8m
lifetime cost for a 25-yr-old person with high tetraplegia[9]

77%
% of people with SCI who indicate regaining arm and hand function would most improve their quality of life[10]

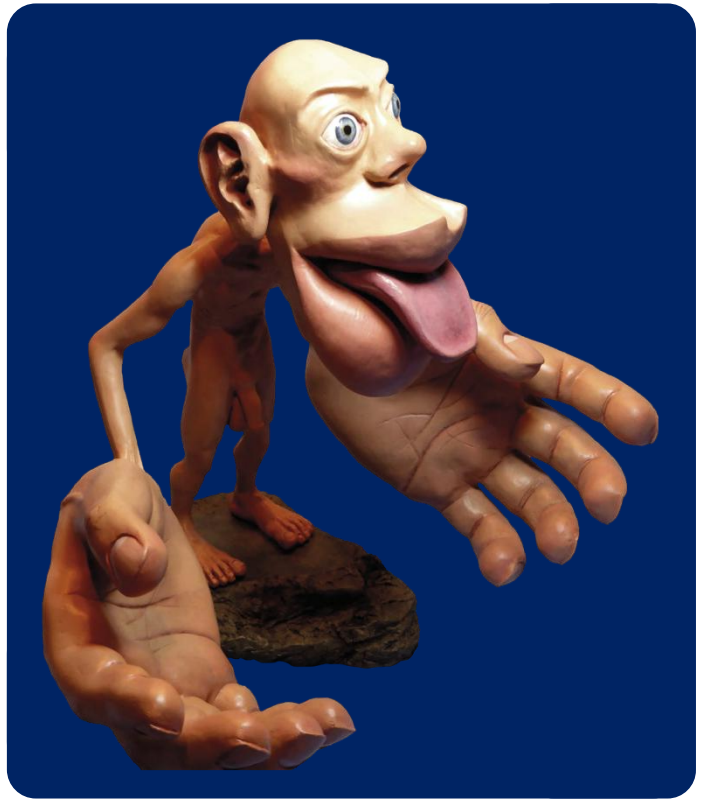
Hand function, our initial focus

tSCI: Traumatic Spinal Cord Injury
SCI: Spinal Cord Injury

Why prehension?

A beautifully complex challenge validating the technology

HOMUNCULUS(a)



- **Complex mechanical system**
  - 27 bones in each hand (26% of the total number of bones)[11]
  - 38 muscles and over 100 ligaments[11]
- **Complex command**
  - 3 nerves running down the arm and hand[11]
  - Each muscle serviced by 50/200+ neurones[12]
  - About 60,000/70,000 myelinated fibres in the radial and median nerves[13]
- **An area with a very high density of sensory receptors/neurons**

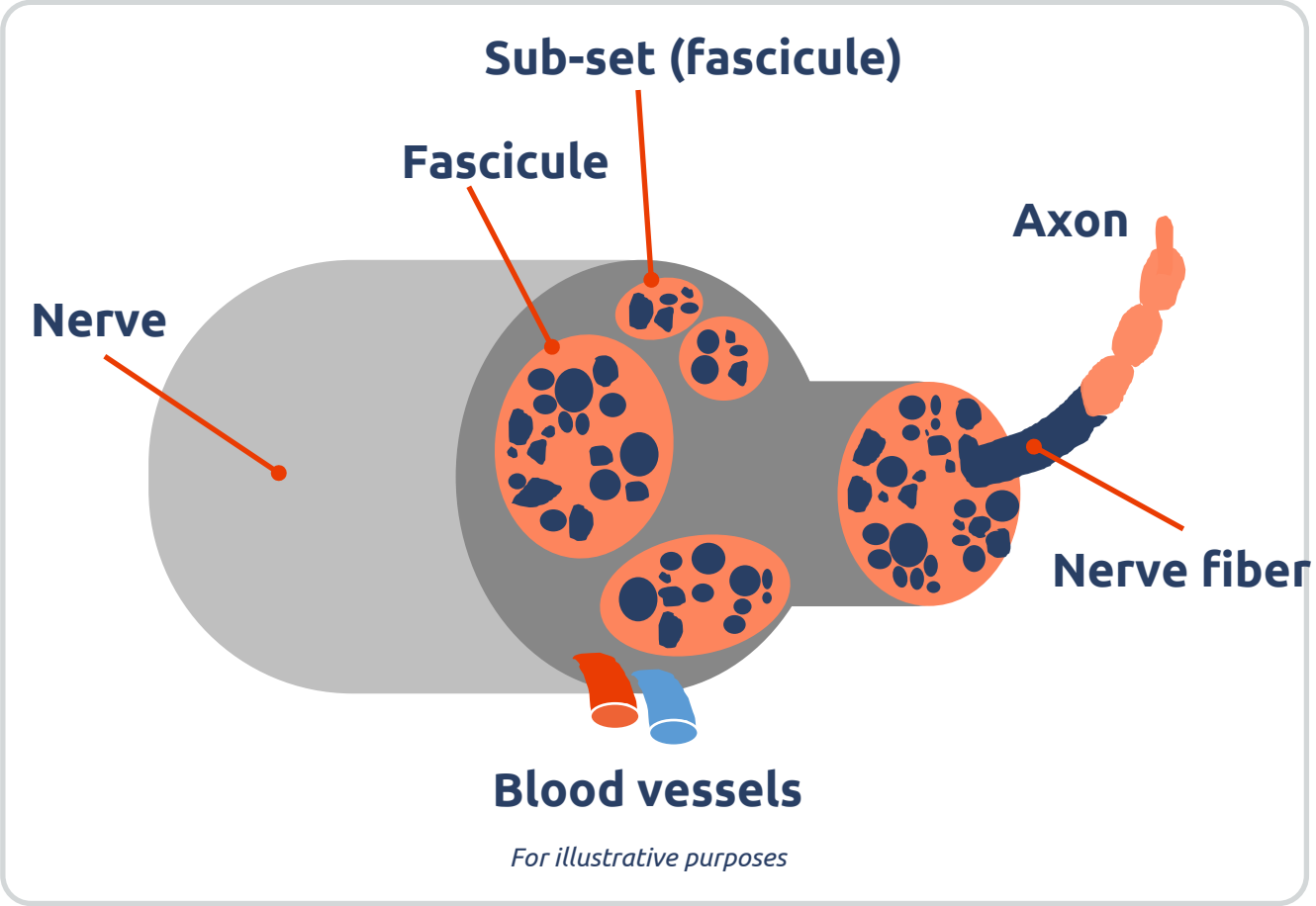
- **Coordinated activation of muscles (timing, force, angles…) required to shape the hand in relation to the physical properties of the object**
- **Selecting a set of muscle synergies is key vs isolating each muscle's contraction**

(a) Distorted representation of the human body, based on the neurological map of the areas and proportions of the human brain dedicated to processing motor functions and/or sensory function, for different parts of the body

Strong potential of electrophysiology

Why? How?

Pathway to stimulate a subset of nerve fibres within a nerve

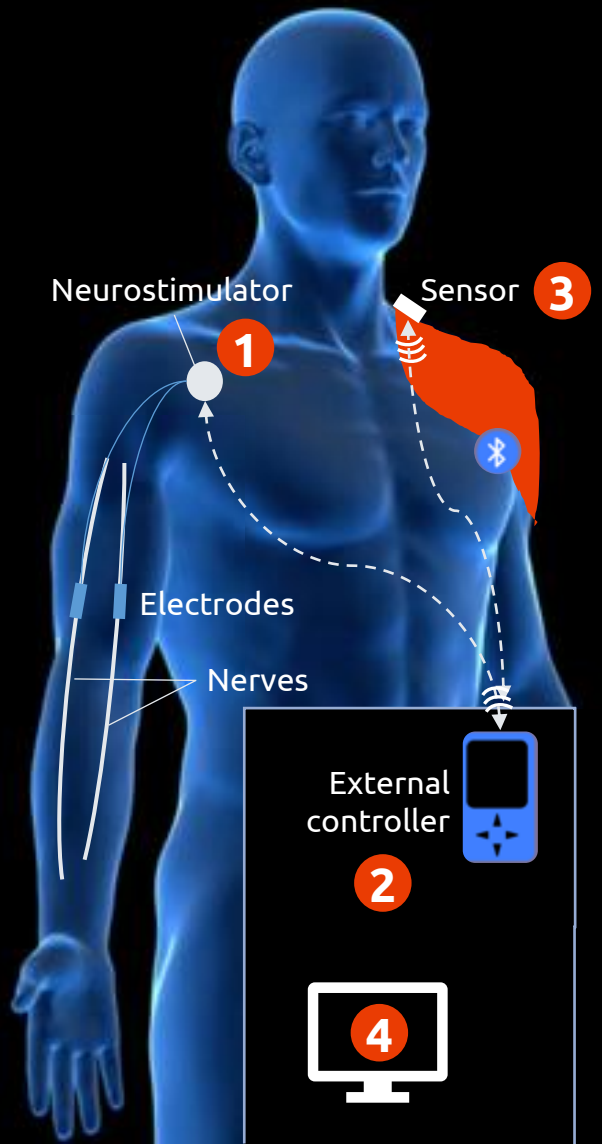


For illustrative purposes

- Activation of a nerve fibres must be selective
- Preliminary studies showing outstanding results in the number and complexity of movements that could be induced through different stimulation patterns and configurations

neurinnov INNOVATION IN NEUROSTIMULATION

Our breakthrough and highly differentiated solution



A PRODUCT DESIGNED TO OFFER A BREAKTHROUGH SOLUTION

1. **Neurostimulator, the core of our technology**
   ➔ **Groundbreaking, differentiated and versatile**
   Connected to two cuff electrodes
2. **Controller, the external part directly associated with the targeted defficiency (e.g. prehension)**
   Sends data and energy to the neurostimulator
3. **A wide range of sensors[(a)] to ensure greater market uptake**
   Allows the patient to pilot the device
4. **Easy and quick set-up through connected hardware and software**
   Powerful algorithms and highly intuitive interface

(a) Including IMU (Inertial Measurement Unit (device measuring the body's movements); EMG (Electromyography recording of the electrical activity produced by muscles), voice, joystick

Free Hand® led the way for Neurinnov

FREE HAND® = SAME FUNCTIONALITY AS NEURINNOV, BUT…

- c. 300 patients implanted; discontinued in 2001
- Unique insights gathered by our scientific and medical advisors (e.g. Dr. Fattal and Teissier)

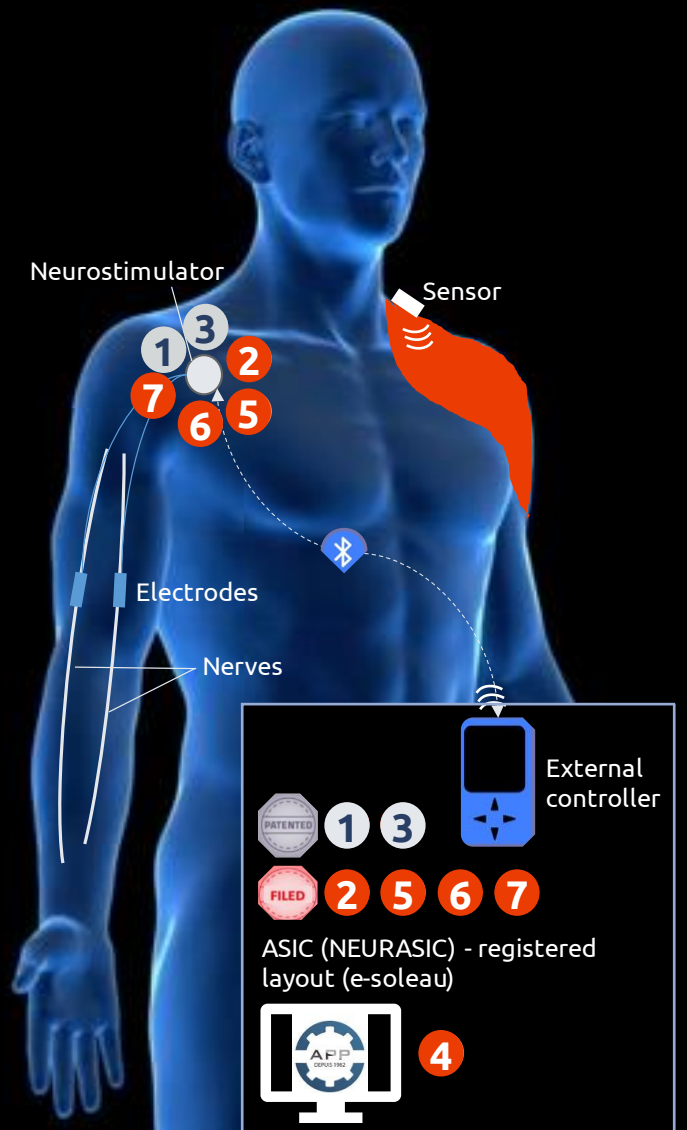
… TWO SEPARATE APPROACHES TO STIMULATION

	FREE HAND® (epimysial/intramuscular stimulation)	NEURINNOV (selective neurostimulation)

Surgery	• **Two surgeries**
	  • One major (c. 6h) to place the 12 electrodes on all key muscles
	  • Another one to position the implant/ do the setting
		• **One short (c. 2h) surgery to place two neural electrodes**

Setting	• **2 months**	• **2 weeks**

Protected innovation



- **Initial filings in France and scope expansion through PCT in Europe, USA, Canada, China, Australia**
- **7 families of patented and filed applications, incl. protections with APP (Agence pour la Protection des Programmes)**
- **Continued expansion to further enhance the versatility of the platform, e.g. stimulation of deep fibers**

1. Selectivity of stimulation / Power distribution between cathodes of the multipolar electrode
2. Balanced/synchronous selectivity of stimulation / Power distribution between cathodes of the multipolar electrode
3. Decentralised intelligence
4. Configuration software and training simulator
5. Bus
6. Inductive transcutaneous link
7. Fast sequencing of stimulations

What the Team has Delivered

Between 2017 and now

Why? How?

- **Positive results in all clinical studies**
  - **15 patients** in 2017[(a)]
  - **9 patients** in 2017/18 **(1h)**[(b)]
  - **4 patients** in 2022/23 **(28d)**[(c)] **(First in Human validation of the approach)**
- Data published in Nature and Neurotrauma
- Completion of the electronic stimulator circuit (digital and analog)
- Development of a larger range of sensors
- Finalisation of the encapsulation of the medical device
- **4 patents** filed
- Raised **€7.6m**, of which more than half through non-dilutive means and debt and **€3m** in a seed investment in 2021
- Investment in the team and preparation of the medical documentation

(a) Study aimed at evaluating the ability of tetraplegic individuals to utilise either voluntary contractions of supra-lesioned muscles recorded by surface electromyography or voluntary shoulder movements recorded via an inertial unit

(b) Feasibility study to observe the effects of selective electrical stimulation in terms of muscle's activation, force produced, and movement induced in tetraplegic patients undergoing surgery

(c) Clinical study to investigate the activation of effective functional hand movements in individuals with complete tetraplegia through neurostimulation; electrodes implanted and maintained for 28 days to comply with European Medical Device Regulation 17/745

Way forward
Series of well-defined value-enhancing drivers

Why? **How?**

Between 2017 and now

- See previous slide

2024

Cadaver experiment

- Surgical procedure validation
- Implant design freezing (fixation)
- Ancillaries validation

Large animal trial (>30d)

- Functional validation
- Biological risk assessment (till 2025)

Sensors clinical trial (targeted patient population)

- Clinical performance

2025/27

4 patients | 30 patients

- Reference centres identified
- Endpoints: safety, usability and clinical performance
- Notified Body: BSI

Industrialisation

2028

- Europe - Class III device under the new Medical Devices Regulation (2017/745) ("MDR")
- US to follow / post 2028

Way forward
Our go-to-market strategy

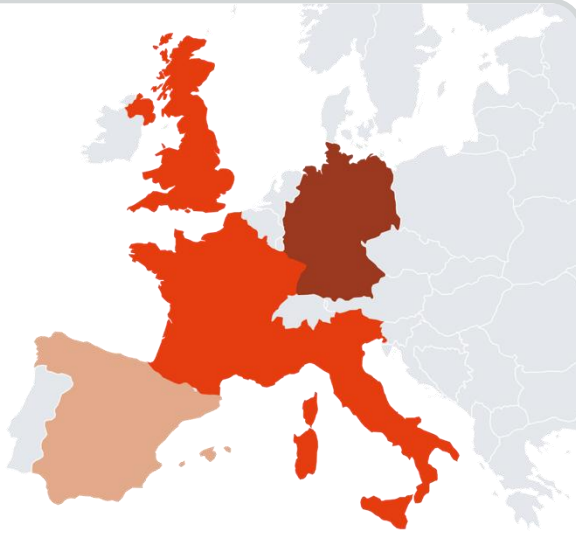
PRIMARILY TARGETING SPECIALTY REHABILITATION CLINICS

WHO?

- Focus on US and European countries with a favourable reimbursement environment and well-developed SCI rehabilitation infrastructure
- Pursuing a highly concentrated customer base with:
  - **direct field organisation in key countries in Europe (low number of rehabilitation centers)**
  - **distributors in other areas (e.g. RoW)**
- Reference centers already identified: USSAP, Clinique Saint-Jean, CHU Rennes, Rehazenter (Luxembourg)

HOW?

- Sequential approach
- Close collaboration with surgeons and therapists during and after surgery
- Education, training, publications



Enormous range of opportunites beyond prehension

- **22 million** people suffering from SCI, of which **2.5 million** with paralysis[14]
- Between **250,000 to 500,000** new SCI cases every year[15]
- **70-84%** of SCI patients develop neurogenic bladder dysfunction[16]

  Incontinence, renal impairment, urinary tract infection, stones, etc.
- **39%** of patients with SCI patients have neurogenic bowel disorders[17]

  Constipation and faecal incontinence
- **74%** of acute and chronic SCI patients have orthostatic hypotension[18]
  - **When standing after sitting or lying down**
  - **Increased risk of developing blood clots**

Highly talented and experienced team

TEAM LEADERS

Nicolas Sérandour, President
Led a radiation company (CEO and CFO) for 10 years; raised £200m+; previous experiences in Healthcare Investment banks at JPMorgan, Lehman and Lazard

David Andreu, co-founder, CTO & General Manager
HDR PhD in Industrial Informatics; lecturer-researcher at the University of Montpellier (UM); led numerous AIMD; winner of the FIEEC 2012 Prize and the MUSE 2019 Innovation Prize

David Guiraud, co-founder & CSO
HDR PhD of Biomedical Engineering; Director of research at INRIA; specialist in electrophysiology; awarded the CNRS Bronze Medal in 2005 and the Grand Prix of the French Academy of Sciences in 2010 in Biological Sciences / Information Sciences

CONSEIL DE SURVEILLANCE

- **Lucie Ayala,** Sofilaro
- **Geneviève Blanc,** IRDIEquity Partners
- **Cédric Briand,** Cochlear/Oticon
- **Jonathan Dupont,** Merieux Equity Partners

SELECTED SCIENTIFIC ADVISORS

- **Charles Fattal,** PhD, MD Physical and Rehabilitation Medicine, USSAP, France
- **Jacques Teissier,** orthopaedic and trauma surgeon, Saint-Jean Clinic, Montpellier, France
- **Christine Azevedo Coste,** INRIA Research Director

Highly talented and experienced team

VISIBILITY AND SUPPORT

OCCITANIE INNOV

La FRENCH TECH SEED

GÉNÉRATION DEEP TECH

bpifrance

GOUVERNEMENT
Liberté
Égalité
Fraternité
Ministère de l'Enseignement Supérieur et de la Recherche

LAURÉAT BOOST INVEST
MEDVALLÉE MONTPELLIER

eit Health

Co-funded by the European Union

European Innovation Council

Why Neurinnov?

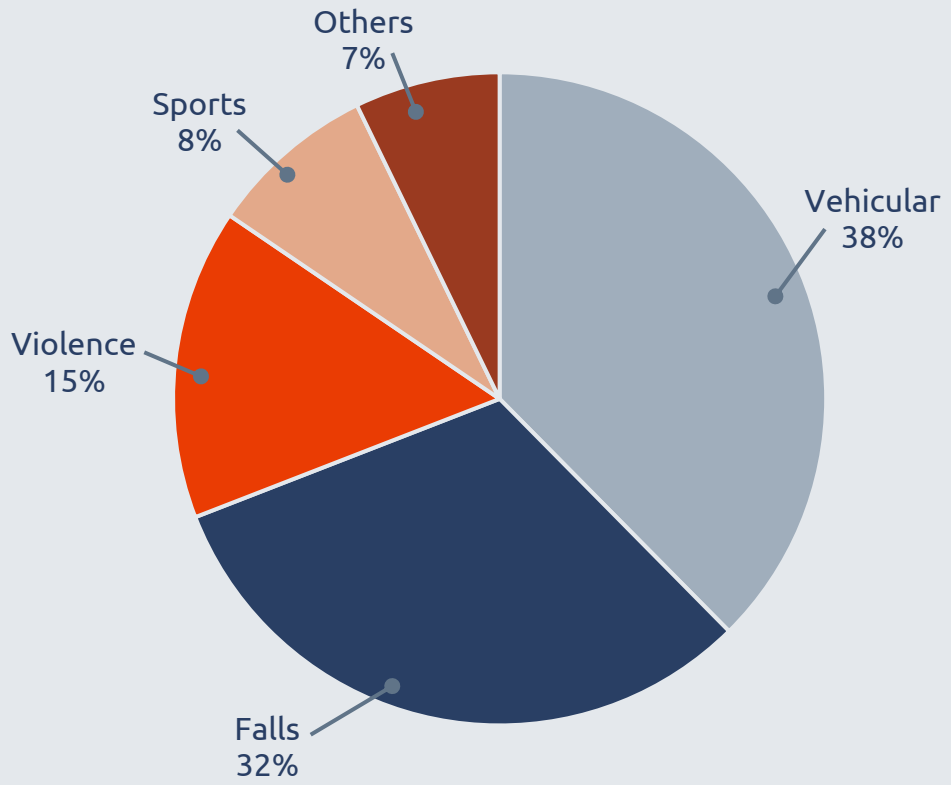
A COMPELLING OPPORTUNITY

- Living with a spine cord injury, an underserved market
- Highly differentiated selective neurostimulation platform
- Growing body of compelling clinical evidence demonstrating the safety and effectiveness of the productwith high-profile backers
- Growing IP portfolio protecting 15+ years of R&D
- Carefully drafted execution plan built upon the success of the team to meeting ambitious targets
- Clear commercialisation path
- Innovative technology with far-reaching potential
- A series of value-enhancing transforming events ahead
- Talented and experienced team with high-profile backers

APPENDIX

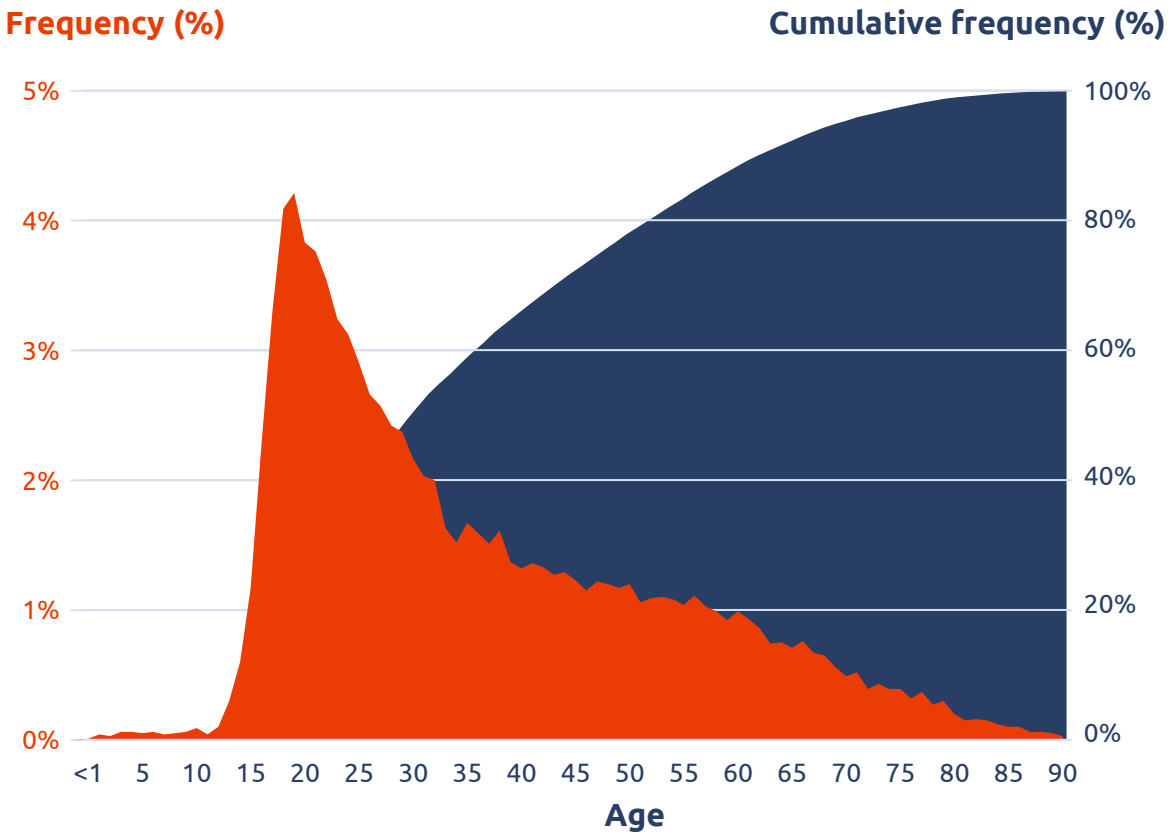
Nearly half of the SCI injuries occur before 30-yr-old

ETIOLOGY OF SCI[19]

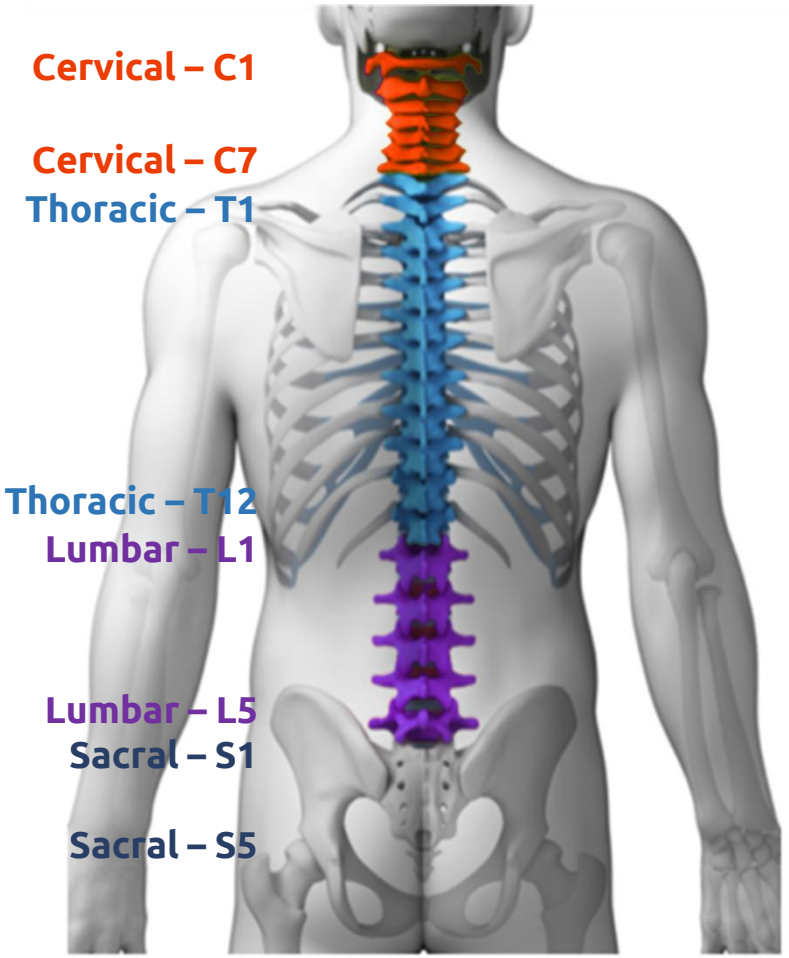


SCI: Spine Cord Injury
Etiology based on US data, since 2015

AGE AT INJURY FREQUENCY DISTRIBUTION[19]



Neurinnov's current focus: C4-C7



LESION SITE	IMPAIRMENT[20]
C1-C3	Respiratory functions (mechanical ventilation needed), swallowing, communication, limited head & neck movements
C3-C4	Respiratory functions, shoulder shrug
C5	Shoulder and elbow movements
C6-C7	Wrist and elbow movements
C7-T1	Hand and finger movements
T1-T12	Temperature stability, trunk stability
T11-L2	Hip movements, ejaculation
L4-S1	Feet and knee movements, vesicle and intestinal functions
S2-S4	Penile erection, vesicle and intestinal functions

Sources and references

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4) Calculated by annual incidence; from Onward Medical NV (2022 annual report)
5) Kumar et al. 2018, Traumatic Spinal Injury; Global Epidemiology and Worldwide Volume
6) For people living in the US with SCI surviving at least one year post injury (AIS ABC: C1-C4); National Spinal Cord Injury Statistical Center, annual report 2023
7) NervGen Investor Presentation, July 2023; https://nervgen.com/wp-content/uploads/2023/08/NervGen-Corporate-Presentation-08.14.23-web-version.pdf
8) Average yearly expenses, including healthcare costs and living expenses (in 2022 dollars), for high tetraplegia (C1-C4) AIS ABC; does not include any indirect costs such as losses in wages, fringe benefits and productivity (indirect costs averaged $89,000 p.a. in 2022 dollars); National Spinal Cord Injury Statistical Center, Traumatic Spinal Cord Injury Facts and Figures at a Glance. Birmingham, AL: University of Alabama at Birmingham, 2023; https://www.nscisc.uab.edu/public/Facts%20and%20Figures%202023%20-%20Final.pdf
9) Estimated lifetime cost for a 25-year-old individual (in 2022 dollars); National Spinal Cord Injury Statistical Center, Traumatic Spinal Cord Injury Facts and Figures at a Glance. Birmingham, AL: University of Alabama at Birmingham, 2023; https://www.nscisc.uab.edu/public/Facts%20and%20Figures%202023%20-%20Final.pdf
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12) Company data
13) Company estimates
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15) Spinal Cord Injury (SCI) 2016 Facts and Figures at a Glance. J Spinal Cord Med. 2016 Jul;39(4):493-4.
16) Alsulihem 2019
17) Nebahat Sezer 2015
18) Palma 2020
19) https://www.nscisc.uab.edu/public/AR2022_public%20version.pdf
20) https://cnfs.ca/pathologies/infarctus-du-myocarde/lesion-medullaire

1st prize
(2012)

Prix académique des sciences (2010)

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Bronze medal
(2005)

Innovation Prize of i-site
(2019)