ARC Therapy to restore hemodynamic stability and trunk control in people with spinal cord injury

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Primary objective:• Assess the safety of ARC Therapy at supporting the management of hemodynamic instability in participants with sub-acute or chronic Spinal Cord Injury suffering from orthostatic hypotensionSecondary objectives with clinical...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Spinal cord and nerve root disorders
Study type	Interventional

Summary

ID

NL-OMON53314

Source
ToetsingOnline

Brief title
HemON-NL

Condition

- Spinal cord and nerve root disorders

Synonym
epidural lesion, Spinal cord injury

Research involving
Human

Sponsors and support

Primary sponsor: ONWARD Medical
Source(s) of monetary or material Support: ONWARD Medical

Intervention

Keyword: ARC Therapy, Epidural stimulation, Orthostatic hypotension, Spinal cord injury

Outcome measures

Primary outcome

The primary outcome of the study is the occurrence of serious adverse events and adverse events that are deemed related or possibly related to the study procedure or to the ARC-IM Thoracic System, from implantation up to the end of the study

Secondary outcome

Secondary outcomes with clinical impact:

• Preliminary efficacy of ARC Therapy at supporting management of hemodynamic instability will be assessed via orthostatic head-up tilt tests, via continuous blood pressure monitoring using a wearable device, via a steady BP measurement, a seated BP test, and via the Mapping of Rehab Training (MART) forms filled by therapists during rehabilitation sessions

• Effect of ARC Therapy on trunk control will be assessed with the Trunk Control Test (TCT), trunk stability measurements, wheelchair performance test, the Function In Sitting Test (FIST-SCI) test and CT scans.

• Effect of ARC Therapy on spasticity will be evaluated with spasticity questionnaires filled by the participants and via the Modified Ashworth Scale (MAS)

• Effect of ARC Therapy on daily life performance will be assessed with the Spinal Cord Independence Measure (SCIM III), with the Canadian Occupational Performance Measure (COPM) and with a daily life activities monitoring

assessment

Secondary outcomes with technical impact:

• Evaluation of the independent use of ARC-IM Thoracic System, will be assessed with a stimulation usage log and weekly questionnaires, filled by the participants

• Evaluation of the robustness of ARC-IM Thoracic System will be assessed based on the occurrence of Device Deficiencies, and by analysing the automatic logs recorded by the devices

• Evaluation of the usability and clinical procedures of the ARC-IM Thoracic System by the different users will be assessed with a surgical checklist and different questionnaires to be filled about the system

Study description

Background summary

The consequences of a Spinal Cord Injury (SCI) are dramatic. Not only do affected individuals lose the ability to move, but they also face repeated hypotensive episodes that can be life-threatening and reduce the potential for neurological recovery. In the chronic phase, daily hypotensive and hypertensive (i.e., autonomic dysreflexia) episodes increase the risk of stroke, heart disease and reduce engagement in social and professional activities. Individuals with spinal cord damage above the 6th thoracic vertebra often suffer from severe hemodynamic instability. Pharmacological management of hemodynamic instability is currently limited to long-acting pressor agents (e.g., midodrine) and anti-hypertensives (e.g., prazosin, nifedipine). These drugs require approximately one hour to become active and exert prolonged cardiovascular effects. Conversely, the hemodynamic instability experienced by people with SCI occurs most commonly over just a few minutes and tends to cease rapidly. Using long-acting agents to manage short-acting conditions is, thus, not the ideal approach. Indeed, this temporal discrepancy can predispose individuals to more extreme hemodynamic instability or adverse events. In the

absence of alternative treatment options, clinicians have resorted to therapies that are arduous and are not supported by rigorous evidence (e.g., abdominal binding, compression stockings, high-sodium diet). Importantly, the quality of life of people with SCI strongly depends on recovering both autonomic and motor functions. In particular, the recovery of hemodynamic stability and trunk stability are associated with greater independence and are consistently ranked by people with cervical SCI as top health priorities.

Researchers recently dissected the anatomical topology and physiological dynamics of the sympathetic circuitry and developed the mechanisms behind how Epidural Electrical Stimulation (EES) can target these physiological processes and modulate blood pressure. They identified a clear anatomical and functional enrichment at the three most caudal thoracic spinal segments which they termed the hemodynamic hotspots. The EES protocol immediately stabilized hemodynamic in rodent and non-human primate models of SCI. They also validated the features of hemodynamic EES in ten patients. Moreover, 7 weeks of daily hemodynamic EES in rodents abrogated autonomic dysreflexia. Consequently, EES has the potential to become the first-line treatment for hemodynamic instability in people with chronic or sub-acute SCI. However, its clinical deployment relies on medical-grade implantable spinal-cord stimulation technologies that are optimized for hemodynamic management. In addition, spinal segments associated with trunk stability and spasticity overlap with the hemodynamic hotspots.

In this study, we aim to stimulate specific circuits in the spinal cord thanks to a new EES therapy named ARC Therapy to manage the regulation of blood pressure in people with sub-acute and chronic spinal cord injury located between C3 and T6 and who suffer from orthostatic hypotension.
This therapy also aims to have a positive impact on other clinical functions such as trunk stability, spasticity (through muscle tone normalization), respiratory function, cognitive functions, overall quality of life and daily life activities.

Study objective

Primary objective:
• Assess the safety of ARC Therapy at supporting the management of hemodynamic instability in participants with sub-acute or chronic Spinal Cord Injury suffering from orthostatic hypotension

Secondary objectives with clinical impact:
• Evaluation of the preliminary efficacy of ARC Therapy at supporting management of hemodynamic instability in participants with sub-acute or chronic Spinal Cord Injury suffering from orthostatic hypotension
• Evaluation of effect of ARC Therapy on trunk control in participants with sub-acute or chronic Spinal Cord Injury
• Evaluation of effect of ARC Therapy on spasticity in participants with sub-acute or chronic Spinal Cord Injury

• Evaluation of effect of ARC Therapy on daily life performance in participants with sub-acute or chronic Spinal Cord Injury

Secondary objectives with technical impact:
• Evaluation of the independent use of ARC-IM Thoracic System by study participants
• Evaluation of the robustness of ARC-IM Thoracic System including effectiveness of risk mitigation
• Evaluation of the usability of ARC-IM Thoracic System for clinicians and study participants

Other objectives:
• Evaluation of the effect of ARC Therapy on:
o Respiratory function
o Cognitive function
o Vascular anatomy
o Autonomic dysreflexia
o Pressure sores prevention
o Participants Reported Outcomes Measures (PROMs) (quality of life, sleep, mental,...)

Study design

This study is single site, single arm, non-blinded, non-randomized, interventional.

Intervention

Consent and eligibility
• Patients fulfilling eligibility criteria and willing to provide signed informed consent are enrolled.

Baseline assessments (up to 8 weeks)
• A comprehensive assessment of demographics, history of injury, health history, family history, and history of hospitalizations, surgeries and interventions will be assessed.
• Medication history for the previous two years will be documented and a questionnaire about substance use, including alcohol and substances, will be administered via the CAGE-AID Questionnaire.
• For women of childbearing potential who are participants in the study, a pregnancy test will be performed.
• A thorough history of rehabilitation will be documented. Rehabilitation history will apply to all events occurring after the initial spinal cord injury and will include questions about the type and duration of rehabilitation interventions received (I.e., tilt-test training).
• After enrolment in the study, baseline data are collected (a pre-operative

MRI, X-ray, and CT scan).
• Further assessments: ASIA impairment scale classification, orthostatic challenge, seated BP test, steady BP measurement, autonomic dysreflexia following spinal cord injury (ADFSCI) questionnaire, quality of life questionnaires, measures of respiratory function, cognitive functions, trunk stability, daily life performance, spasticity, and vascular anatomy.

Surgical procedure
• Standard pre-surgical procedures are performed (i.e., visit with anesthesiologist).
• Pre-operative MRI combined with CT-scan acquisitions are used to guide the precise placement of the paddle array and define the entry point prior to surgery.
• The ARC-IM Thoracic System will be implanted and guided with intra-operative electrophysiology and surgical imaging.
• A post-operative CT-scan will be performed.

Configuration phase (phase 1 - 1 month)
• Configuration will include testing a variety of stimulation configurations and parameters to understand the optimal use of the ARC-IM Thoracic System for hemodynamic control, trunk stability, improvement of respiratory function and spasticity.
• Different technical assessments will be performed during this phase.
• Participant will perform standard rehabilitation sessions and optimization sessions to configure the neuromodulation system.

Supported use phase (phase 2 - 1 month)
• Participants will use the ARC-IM Thoracic System by themselves through the support of the study team via supported use sessions (telemonitoring).
• Optimization sessions will also be planned to manage the configuration of ARC-IM Thoracic System.

Independent use phases (phases 3 and 4 - 10 months)
• Participants will use ARC-IM Thoracic System by themselves, during daily life activities.
• Optimization sessions and telemonitoring sessions will be scheduled upon request of the study team or of the participants.

Assessments
• Different assessments will be planned throughout the course of the study, after phases 1, 3 and at the end of the study, with and/or without stimulation:
o Clinical assessments, hemodynamic assessments, trunk assessments, spasticity assessments, daily life functional assessments, respiratory assessments, cognitive assessments, and vascular assessments
• Participants Reported Outcomes Measures will be collected:
o Monthly via PROMs questionnaires
o Every 6 months via semi structured interviews

o Weekly via other questionnaires

End of the study
• After final clinical evaluation, the participant may choose between inactivation of the stimulator or explant of the investigational system, unless further use is deemed beneficial for the participant as assessed by the investigators. Cost of explant will be covered by the sponsor. The study ends after the final study procedures

Study burden and risks

Participation burden:
Participants will be enrolled for approximately 15.5 months in this study. A daily presence on-site will be asked during the first 2 months and then, during 2 weeks every 6 months.

Study risks:
1. Risks and side effects associated to the surgery procedure (risks associated with general anaesthesia, risks associated with implants surgery such as cerebrospinal fluid leak, infection or inflammation, wound complications, pain,...)
2. Risks associated to ARC Therapy such as pain, discomfort, overstimulation feeling, muscle contraction, fluctuation of mood or stress
3. Risks associated with the implanted devices such as failure or malfunction of the devices, components migration, allergic or immune system response

Study benefits:
The ARC Therapy aims to manage the regulation of blood pressure in people with sub-acute and chronic spinal cord injury located between C3 and T6 and who suffer from orthostatic hypotension.
This therapy also aims to have a positive impact on other clinical functions such as trunk stability, spasticity (through muscle tone normalization), respiratory function, cognitive functions, overall quality of life and daily life activities.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- 18 years of age or older
- Must provide and sign the Informed Consent prior to any study-related procedures
- Traumatic spinal cord injury
- Spinal cord injury lesion level between C3 and T6 (inclusive)
- AIS- A, B, C or D
- SCI >= 1month
- Confirmed orthostatic hypotension
- Stable medical, physical and psychological condition as considered by the investigators
- Able to understand and interact with the study team in Dutch or English
- Agrees to comply in good faith with all conditions of the study and to attend all scheduled appointments
- In case participants need continuous support from a personal caregiver in daily life, then the presence of their caregiver during the visits to the study site is needed, including independent transport (not dependent on a cab)

Exclusion criteria

- Diseases and conditions that would increase the morbidity and mortality of spinal cord injury surgery

- The inability to withhold antiplatelet/anticoagulation agents perioperatively
- History of myocardial infarction or cerebrovascular event within the past 6 months
- Other conditions that would make the subject unable to participate in testing in the judgement of the investigators
- Clinically significant mental illness in the judgement of the investigators
- Botulinum toxin non-vesical and vesical injections in the previous 3 months before the enrolment
- Presence of significant pressure ulcers
- Recurrent urinary tract infection refractory to antibiotics
- Presence of indwelling baclofen or insulin pump
- Women who are pregnant (pregnancy test obligatory for woman of childbearing potential) or breast feeding,
- Lack of safe contraception for women of childbearing capacity,
- Intention to become pregnant during the course of the study,
- Other clinically significant concomitant disease states (e.g., renal failure, hepatic dysfunction, cardiovascular disease, etc.),
- Inability to follow the procedures of the study, e.g. due to language problems, psychological disorders, or dementia of the participant,
- Participation in another study with investigational drug within the 30 days preceding and during the present study,
- Enrolment of the investigator, his/her family members, employees, and other dependent persons.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-09-2023
Enrollment:	8
Type:	Actual

Medical products/devices used

Generic name:	ARC-IM Thoracic System
Registration:	No

Ethics review

Approved WMO Date:	08-08-2023
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-04-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-06-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL83694.000.23