Clinical assessment of upper extremity performance in individuals with spinal cord injury using the LIFT System to deliver non-invasive electrical spinal stimulation (ARC Therapy)

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Safety: To provide confirmatory evidence that use of the LIFT System, inclusive of all components and accessories, is safe.Effectiveness: To provide confirmatory evidence that use of the LIFT System provides an effective treatment for the...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Spinal cord and nerve root disorders
Study type	Observational non invasive

Summary

ID

NL-OMON51027

Source
ToetsingOnline

Brief title
The Up-LIFT Study of Non-Invasive ARC Therapy for Spinal Cord Injury

Condition

- Spinal cord and nerve root disorders

Synonym
SCI, Tetraplegia

Research involving
Human

Sponsors and support

Primary sponsor: ONWARD Medical, Inc.
Source(s) of monetary or material Support: ONWARD Medical;Inc.

Intervention

Keyword: ARC Therapy, SCI, Tetraplegia

Outcome measures

Primary outcome

Safety: Observational data regarding the incidence of serious adverse events (SAEs) related to the use of the study device and treatment procedures will be reported.

Effectiveness: The primary effectiveness outcome measure will test the hypothesis that a majority of the subjects will experience clinically significant improvement in selected strength and functional performance metrics after treatment with ARC Therapy administered by the LIFT System and FTP. A subject will be considered a treatment responder if she/he reports clinically relevant improvements in at least one outcome each in the Strength and Function domains as follows:

Strength: ISNCSCI-UEMS, GRASSP-Strength, CUE-T, Pinch force, Grasp force

Function: GRASSP-Prehension, CUE-T

Secondary outcome

Safety: All adverse events (AEs) and SAEs in the study will be reported.

Effectiveness: To capture meaningful improvements in established outcomes assessing upper extremity function, the following hierarchical testing will be carried out. These endpoints will be tested in descending order of importance through hierarchical testing as described in the Statistical Analysis Plan (SAP).

- Superiority of combined MPT and ARC Therapy with LIFT vs. FTP alone as described by statistically significant difference in responder rates (comparison of change from enrollment baseline to end of FTP with the change from enrollment baseline to end of combined FTP and ARC Therapy with LIFT)
- Quantitative comparison of individual performance metrics to establish superiority of FTP and ARC Therapy with LIFT compared to FTP alone:
- Pinch force
- GRASSP-Prehension
- GRASSP-Strength
- ISNCSCI-UEMS
- ISNCSCI-Total sensory score
- EQ-5D-5L
- SCIM
- WHOQOL-BREF

Study description

Background summary

Non-invasive Electrical Spinal Cord Stimulation may be used in conjunction with conventional rehabilitation therapy in patients with Spinal Cord Injury (SCI) to improve the recovery of physiological function following injury. The LIFT System from ONWARD Medical, Inc. is designed to help people experiencing paralysis due to injury, to help regain mobility, independence, and an improved quality of life. The LIFT System is a transcutaneous spinal cord stimulator that is externally connected to the patient using body surface electrodes. Stimulation pulses are provided to the patient to reactivate damaged and dormant neural circuits through neuromodulation of the spinal cord. The patients are able to re-learn patterns of activation associated with pre-injury function. The LIFT System is designed to be used in the hospital and at a rehabilitation therapy clinic.
The scientific basis for development of the LIFT System is predicated upon research studies performed on animal and human subjects with SCI that demonstrated that residual (spared) sensory and motor pathways were critical in mediating the voluntary movements that are possible when ARC Therapy delivered by the LIFT system is paired with task-based training by the individual. These studies demonstrated that either hand or lower extremity training combined with repetitive spinal cord stimulation drove neural plasticity that eventually resulted in the ability to improve voluntarily hand function and standing, respectively. Application of ARC Therapy combined with rehabilitation therapy could be used not just to restore physical movement of upper and lower extremities but also for improvement of autonomic functions and stroke rehabilitation to SCI patients afflicted with paralysis.

Study objective

Safety: To provide confirmatory evidence that use of the LIFT System, inclusive of all components and accessories, is safe.

Effectiveness: To provide confirmatory evidence that use of the LIFT System provides an effective treatment for the restoration or improvement in UE strength and function.

Other: To provide data regarding the potential benefits of the LIFT System to achieve other secondary outcomes such as improvement in pain, spasticity, quality of life, cardiovascular (blood pressure) and autonomic function.

Study design

The Up-LIFT Study is a prospective, single-arm study designed to evaluate the safety and effectiveness of non-invasive electrical spinal stimulation (ARC Therapy) administered by the LIFT System to treat upper extremity functional deficits in people with chronic tetraplegia. The primary endpoint of this pivotal study will report device related safety and changes in

established metrics of upper extremity function and strength after treatment with the study device.

To ensure that the benefits realized in the study are directly attributable to the ARC Therapy administered by the LIFT System, all enrolled subjects will first undergo a guided, in-clinic conventional functional task practice (FTP) program lasting approximately two months to regain strength and function of their upper extremities (UE). Performance gains realized during the wash-in period provide a subject specific control that reflects the limits of conventional FTP without stimulation (standard of care). At the conclusion of the wash-in period, subjects will complete pre-stimulation baseline testing of UE function.

To test the additive benefit of training with stimulation, combined FTP and ARC Therapy will then be administered over a period of approximately two months using the LIFT System. FTP will follow established rehabilitation protocols that are specific to the individual subject*s specific needs and capabilities (Gomes-Osman, Tibbett, Poe, & Field-Fote, 2017). Training will be graded to accommodate performance improvement over time, thus maximizing the potential benefit to subjects. To ensure consistency and safety, subjects will participate in a minimum of 12 and a maximum of 20 in-clinic training sessions per month. At the conclusion of this primary training period, changes in UE strength and function will be measured without active stimulation therapy and used to assess the primary study endpoints.

The choice of primary outcome measures for this pivotal study is dictated by the following factors-
1. Safety,
2. Relevance to UE function,
3. Capture improvements in both strength and function, and
4. Magnitude of changes that are clinically meaningful

All performance metrics will be assessed at enrollment, at the completion of the wash-in period and at the end of the ARC Therapy assessment period. Subjects with clinically meaningful gains in multiple performance domains resulting from the ARC Therapy with LIFT will be considered responders. Additionally, gains during the wash-in (control) period will be compared to gains during the ARC Therapy with LIFT (test) period. Safety will be evaluated throughout the entire study through periodic monitoring and analysis of all reported adverse events.

Study burden and risks

Living with SCI has historically meant learning to cope with disability and worsening symptoms over time. In contrast, it has been shown through research studies that using neuromodulatory techniques to alter physiological state of

spinal networks yields significant levels of retained clinically relevant function in subjects with varying levels of paralysis as a result of spinal cord injury. This has been proven using both transcutaneous and epidural spinal cord stimulation systems on human subjects. Patient benefits have included recovery or improvement in voluntary movement of the lower and upper extremities, trunk control, cardiovascular function, thermoregulation, independent standing, activities of daily living, and quality of life. In some cases, these benefits have resulted in a decrease of healthcare costs for the patients.

Potential Benefits to Study Subjects
Receiving benefit from participation in the study is not guaranteed. Anticipated benefits to subjects may include, but are not limited to, the following:
- Improved hand and/or arm muscle strength and prehension (ability to pinch, grasp)
- Improved light touch and/or pinprick sensation in the dermatomes at, below or above the level of lesion
- Improved quality of life
- Improved bladder, bowel, or sexual function
- Reduced frequency of spasticity (if present at baseline)

Potential Risks to Study Subjects
Risks to study subjects enrolled in this study include all those risks commonly associated with all TENS and NMES devices including skin rash at the site of application of the surface electrode, electric shock from the stimulator unit, unpleasant tingling or buzzing sensation at skin surface and cramping of the muscles. Other risks are identified in Sections 13.4 and 13.5.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Key Inclusion Criteria:
Subjects must meet all the following criteria:
1. At least 22 years old and no older than 75 years old at the time of enrollment
2. Non-progressive cervical spinal cord injury from C2-C8 inclusive
3. American Spinal Injury Association (ASIA) Impairment Scale (AIS) classification B, C, or D
4. Indicated for upper extremity training procedures by subject's treating physician or a physical therapist
5. Minimum 12 months post-injury
6. Capable of providing informed consent

Exclusion criteria

Key Exclusion Criteria:
Subjects must not meet any of the following criteria:
1. Has uncontrolled cardiopulmonary disease or cardiac symptoms as determined by the Investigator
2. Has any unstable or significant medical condition that is likely to interfere with study procedures or likely to confound study endpoint evaluations like severe neuropathic pain, depression, mood disorders or other cognitive disorders
3. Has been diagnosed with autonomic dysreflexia that is severe, unstable, and uncontrolled
4. Requires ventilator support
5. Has an autoimmune etiology of spinal cord dysfunction/injury
6. Spasms that limit the ability of the subjects to participate in the study training as determined by the Investigator

7. Breakdown in skin area that will come into contact with electrodes
8. Has any active implanted medical device
9. Pregnant, planning to become pregnant or currently breastfeeding
10. Concurrent participation in another drug or device trial that may interfere with this study
11. Presence of syringomyelia as confirmed by an MRI
12.Total baclofen dose >30 mg per day
13. In the opinion of the investigators, the study is not safe or appropriate for the participant

Study design

Design

Study phase:	3
Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-08-2021
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO

Date:	06-05-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	12-10-2021
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
ClinicalTrials.gov	NCT04697472
CCMO	NL76734.091.21