



ARTICLE

# Gait rehabilitation in persons with spinal cord injury using innovative technologies: an observational study

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## Abstract

**Study design** Prospective, quasi-experimental study, pre- and post-design, single arm study.

**Objectives** Investigate whether persons affected by SCI can safely experience walking function using Robotic Exoskeletons and Functional Electrical Stimulation (FES).

**Setting** Inpatient

**Methods** 52 persons with SCI were recruited (36 completed the protocol) and assigned to one of two groups based on their Lower Limb Motor Scores (LEMS): Group A: LEMS  $\geq 10$  and Group B: LEMS  $< 10$ . Participants in Group A ( $n = 19$ ) underwent 20 sessions of Robot-Assisted Gait Training (RAGT) on a treadmill followed by 20 sessions of FES during Overground Gait (FES-OG). Participants in Group B ( $n = 17$ ) received 20 sessions of FES-cycling followed by 20 sessions of overground RAGT. The main outcome measures were: WISCI-II, 10MWT, 6MWT, TUG and SCIM-II.

**Results** 36 persons completed the study with no complications; only 4 of the 16 dropped out because of mild complications during the RAGT. Participants in Group A exhibited significant improvements in WISCI-II, 10MWT, 6MWT and TUG ( $p < 0.05$ ), while those in Group B did not significantly improve their gait function but their walking velocity and resistance with the assistance of the robotic exoskeleton increased. SCIM-II scores increased followed therapy only in Group A.

**Conclusions** Persons affected by SCI can safely experience their walking function with RAGT and FES therapy; only few mild complications were observed. Our data provides initial evidence of the potential value of these technologies, especially in persons with SCI having LEMS  $> 10$ .

## Introduction

Walking functions are frequently lost or impaired in persons affected by spinal cord injury (SCI) and SCI-related motor impairments are associated with general dissatisfaction and reduced quality of life [1]. The recovery of locomotor function is thus considered an important rehabilitation goal both by patients, their relatives and friends, physicians, physiotherapists and nurses [2].

Gait recovery is related to neurological function. The correlation between the American Spinal Injury Association Impairment Scale (AIS) [3] and the prognosis of gait

recovery is important to identify the correct rehabilitation programme in order to obtain the best results [4].

For instance, persons with AIS A (complete sensory and motor lesion) have a 2.5% probability of neurological recovery, whereas the probability of regaining the ability to walk is 33% in persons with AIS B (complete motor, incomplete sensory lesion), and 75% for AIS C (incomplete lesion with  $< 50\%$  Motor Scores  $\geq 3$ ) and 100% in AIS D (incomplete lesion with  $\geq 50\%$  Motor Scores  $\geq 3$ ), respectively [5]. Higher motor strength and “pinprick” sensory integrity are associated with a strong recovery [4].

The introduction of Body Weight Support (BWS) during walking on treadmill has increased the clinical application of gait training in persons with a SCI. It permits a more normal walking pattern compared with the gait practice on treadmill without BWS, as BWS has been shown to reduce the muscle spasticity [6]. Robotic devices for treadmill training with BWS have been developed to improve gait recovery; these technologies facilitate a high quality of gait training, which maintains very similar joint ranges of

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**Table 1** Inclusion and exclusion criteria.

Eligibility Criteria					
Inclusion			Exclusion		
Age ranging from 18 to 75 years; no episode of autonomic dysreflexia; tolerability to orthostatic position for more than 30 min. No important limitations in Range of Motion on hip, knee or ankle.			Cognitive deficits; psychiatric diseases; cancer; recent fractures.		
FES		ORET		BWSTRT	
Inclusion	Exclusion	Inclusion	Exclusion	Inclusion	Exclusion
Excitable muscles; FES tolerability.	Cardiac pacemaker; epilepsy; pregnancy; metallic implants.	Body weight <100 kg; height ranging from 150 to 190 cm; no asymmetry in lower limbs.	MAS > 3/5 in any lower limb segments.	Body weight <100 kg; height ranging from 110 to 200 cm.	MAS > 3/5 in any lower limb segments.

*FES* Functional Electrical Stimulation, *ORET* Overground Robotic Exoskeleton training, *BWSTRT* Body Weight Support Treadmill-based Robotic Training, *MAS* Modified Ashworth Scale.

motion during the different gait phases. In particular, Robot-Assisted Gait Training (RAGT) on a treadmill activates central pattern generator using a robotic exoskeleton in addition to BWS [7]. This training modality induces plastic changes in muscle recruitment and in sensory-motor cortex in patients with incomplete lesions [8–10].

Nowadays adjustable exoskeletons for overground RAGT are available for walking rehabilitation [11]. People with complete spinal lesions can walk with the assistance of robotic exoskeletons [12], thereby increasing their daily physical activity and improving their body composition [13].

Functional Electrical Stimulation (FES) involves the electrical activation of muscles by means of stimulation in order to reproduce functional activities. FES for Overground Gait (FES-OG) could be used in persons with incomplete SCI to rehabilitate different phases of the gait cycle [14]. FES-Cycling (FES-C) can be also used to reproduce a cycling motion in persons with SCI to induce an improvement in body structures and quality of life [15–18].

At present many robots for walking are available [19, 20]; the BWS treadmill-based robotic training (BWSTRT) has been used to recover walking ability in incomplete SCI persons [21]. The combination of this training with a following FES-OG is not proposed till now, therefore its effects on gait rehabilitation of incomplete SCI persons should be investigated.

More recently robotic exoskeletons for overground walking have been proposed: they can be used in persons with both incomplete and complete SCI [19, 20]. The rationale of using an overground robotic system in persons with complete SCI has twofold aims: (1) to verify if the application of this technology produces any relevant collateral effects; (2) to analyse the possibility to increase the person's ability of using an overground robot with the objective of walking in the daily time with a personalised exoskeleton.

In addition, FES-C training can be used to increase muscle, joint and bone tropisms, which are usually compromised in persons with complete SCI lesions [15–18].

The aim of this study was to investigate whether persons affected by SCI can safely experience their walking function via RAGT and FES therapy.

## Methods

### Study design

Two-hundred-forty-nine SCI inpatients were assessed for inclusion in this study between January 2015 and January 2018, according to the eligibility criteria listed in Table 1. After a neurological evaluation, participants were allocated to one of two rehabilitation groups, according to their Lower Limb Motor Scores (LEMS): those with an LEMS  $\geq 10$  were assigned to Group A, and those with LEMS Scores < 10 were assigned to Group B.

The following evaluations were administered at the beginning and at the end of the training protocol: (i) clinical neurological evaluation using the ASIA Impairment Scale (AIS) [3]; (ii) general function using the Spinal Cord Independence Measure (SCIM-II) [22]; (iii) locomotor functional evaluation using the Walking Index for SCI scale (WISCI-II) [23].

The safety of the proposed rehabilitation treatments was assessed via the number and severity of possible complications.

### Group A

The first group (Group A) underwent 20 sessions of BWSTRT followed by 20 sessions of lower limb FES-OG. The BWSTRT was carried out by means of a bilateral robotic exoskeleton system (Lokomat system, Hocoma, Volketswil, Switzerland) with two degrees of freedom per leg for sagittal knee and hip rotation under BWS [7]. The FES device for FES-OG (Microstim, Medel, Hamburg, Germany) provided two channels stimulation of the hip and/or ankle flexor

muscles, with gait phase synchronisation enabled by pressure sensors located on the sole of each foot. After an initial session of 30 min for subject familiarisation with the use of the exoskeleton on a treadmill, the other sessions of BWSTRT had a duration ranging from 40 to 60 min. The participants used FES-OG device on only one leg in order to stimulate hip and ankle flexors, or on both legs, to stimulate only the hip flexors or the ankle flexors bilaterally; the choice was centred on patients' specific needs.

Stimulation parameters: FES-OG was delivered using a biphasic square pulse, with amplitude of 30–70 mA, frequency of 35 Hz, and pulse width of 250  $\mu$ s. Subjects completed three training sessions per week, with each session lasting ~30 min. The whole rehabilitation programme lasted 14 weeks.

The gait assessment of Group A participants was performed, before and after training protocol, without the exoskeleton, but with the use of any additional assistive devices (cane, etc.) or orthoses routinely used by the patient and needed for safety. Outcome measures assessed included the 10-Metres Walk Test (10MWT), 6-Minutes Walk Test (6MWT) and Timed Up and Go test (TUG) [24].

## Group B

Participants of Group B underwent 20 sessions of FES-C training for reconditioning the joints and the muscles because most had previously experienced long periods of prior immobilisation. After one session of familiarisation, they were trained with 20 sessions of walking by using the Overground Robotic Exoskeleton. FES-C is a FES system, which permits to integrate a cyclo-ergometer system with an electronic interface (Pegaso, Biotech Srl, Bologna, Italy). The quadriceps and the femoral biceps of both legs were stimulated using an alternating biphasic square alternated pulse, amplitude from 35 to 75 mA for quadriceps and from 25 to 50 mA for biceps, frequency 50 Hz, pulse width 300  $\mu$ s. Each FES-C session lasted about 30 min.

To evaluate the modifications of thigh volume after FES-C training, on the two legs, four thighs circumferences were measured in the first and last sessions at four different distances (5, 10, 15 and 20 cm, respectively) proximal to the superior margin of the patella, towards the hip.

An Overground Robotic Exoskeleton Training (ORET) was performed by using a powered exoskeleton for overground walking (Ekso, Ekso Bionics, Richmond, CA, USA) [11].

Each ORET session lasted from 50 to 68 min, and participants completed three sessions per week, for a total rehabilitation programme of 14 weeks.

The gait assessment of Group B participants was performed by using the overground robotic exoskeleton, with the following outcome measures: 10MWT-exo, 6MWT-

exo, TUG-exo and Endurance Test (Endurance-exo) at the first and last session of training; during Endurance-exo each participant was asked to walk with the assistance of the robotic exoskeleton as long as possible without any break (the score was expressed in seconds). During the "6MWT-exo" patients performed from 1 to 3 turns.

## Statistical analysis

Statistical analysis was performed using Sigma Stat v3.5 statistical package (System Software Inc., San Jose, CA, USA). The results on thigh circumferences, walking ability tests and Endurance-exo are expressed as Mean  $\pm$  Standard Deviation ( $M \pm SD$ ), those on SCIM-II and WISCI-II as median and interquartile range (median; IQR). The differences between Pre- and Post-treatment scores were analysed by means of the Student *t* test and the Wilcoxon–Mann–Whitney test. Significance has been set at  $p < 0.05$ .

## Results

Out of two-hundred and forty-nine inpatients with SCI evaluated in three years, 52 persons (21%) were recruited: 38 males, 14 females, ratio men/women: 2,7:1, mean age (SD): 49.0 (15.3) years, range: 22–75 years (Table 2).

Different distributions of participants with Traumatic (*T*) vs. Non-Traumatic (*NT*) and complete vs. incomplete lesions were observed between the two groups: Group A included a greater number of *NT* and incomplete motor injuries, whereas in the Group B a greater number of *T* and complete motor injuries were observed. The distribution of time since injury between the two groups is different with a predominance of <1 year in the Group A. Even the age was different in the two groups: the persons of Group A were older on average than those in Group B, in line with epidemiologic literature reporting a higher mean age in persons with *NT* SC lesions [25, 26].

Sixteen participants (eight from Group A and eight from Group B) did not complete the treatment but only four from Group B dropped out because of complications during the ORET: one presented a shoulder pain during the ambulation, one had muscular haemorrhage and two developed skin lesions. Six persons stopped the training due to SCI comorbidity and six abandoned the training for personal reasons. Except in two cases, showing a shift respectively from AIS B to C and AIS C to D, AIS did not change after the rehabilitation treatment.

## Functional electrical stimulation

Thirteen participants of group A used FES-OG on only one limb. Among them FES-OG was applied on the ankle dorsal

**Table 2** Participants characteristics.

Characteristics	Tot [n, (%)]	Group A [n, (%)]	Group B [n, (%)]
Participants	52 (100)	27 (52)	25 (48)
Age (years) (Mean $\pm$ SD)	49.0 $\pm$ 15.3	58.3 $\pm$ 12.0	38.9 $\pm$ 11.1
Lesion onset			
Median (IQR)	1 (1–5)	1 (1–2)	3 (1–5)
$\leq 1$ year	30 (58)	19 (70)	11 (44)
1 < t $\leq$ 5 years	11 (21)	3 (11)	8 (32)
5 < t $\leq$ 10 years	2 (4)	1 (4)	1 (4)
>10 years	9 (17)	4 (15)	5 (20)
Sex			
M	38 (73)	17 (63)	21 (84)
F	14 (27)	10 (37)	4 (16)
Lesion aetiology			
T	26 (50)	4 (15)	22 (88)
NT	26 (50)	23 (85)	3 (12)
AIS			
A	15 (29)	0 (0)	15 (60)
B	9 (17)	0 (0)	9 (36)
C	10 (19)	9 (33)	1 (4)
D	18 (35)	18 (67)	0 (0)
Injury severity			
C1–C4	6 (11)	5 (18)	1 (4)
C5–C8	5 (10)	1 (4)	4 (16)
T1–S5	23 (44)	3 (11)	20 (80)
AIS D	18 (35)	18 (67)	0 (0)
Drop Out	16 (31)	8 (30)	8 (32)

M Male, F Female, T Traumatic, NT Non-Traumatic, AIS ASIA Impairment Scale.

flexors ( $n = 8$ ) or on both hip and ankle flexors ( $n = 5$ ). Bilateral FES application was used in six persons on ankle dorsal flexors. Participants of Group B ( $n = 17$ ) underwent 20 sessions of FES-C in order to improve the bone, muscle and joint reconditioning. Thigh circumferences increased significantly after the 20 FES-C sessions (Fig. 1) (Table 3).

### Group A

In Group A, seven participants, whose SCI occurred recently (i.e., <12 months), were unable to walk (WISCI-II score = 0) before gait training; after the BWSTRT, WISCI-II score increased. No further score increase were observed after the FES-OG (Table 4); on the other hand, a significant difference of WISCI-II score was observed between pre- and post-treatment (i.e., BWSTRT plus FES-OG) (Table 4).

Twelve participants were able to walk and a significant increase of the WISCI-II scores after the BWSTRT (Table 4), but no further increase after the FES-OG, was observed (Table 4).

It was possible to perform the walking tests (before and after the training) only in seven participants among them

with an initial WISCI-II score  $\geq 6$ : 10MWT, 6MWT and TUG improved after the BWSTRT (Table 4); no further improvement was observed after the FES-OG; the difference of 10MWT, 6MWT and TUG score between pre- and post- treatment (BWSTRT plus FES-OG) was significant (Fig. 2) (Table 4).

Median SCIM-II scores of persons in Group A was 46 (IQR 25.2–67.0) before treatment and 58 (IQR 40.5–85.7) after the training (BWSTRT plus FES-OG) with the difference registering as significant ( $p = 0.001$ ).

### Group B

All participants of Group B ( $n = 17$ ) were unable to walk at baseline (WISCI-II score = 0) and exhibited no change in WISCI-II score at the end of the training. During the training with the overground exoskeleton, the walking time and the number of steps increased from 16.9 (5.6) min and 282 (129) steps in the first session to 30.5 (16.4) min and 906 (489) steps in the last session, respectively.

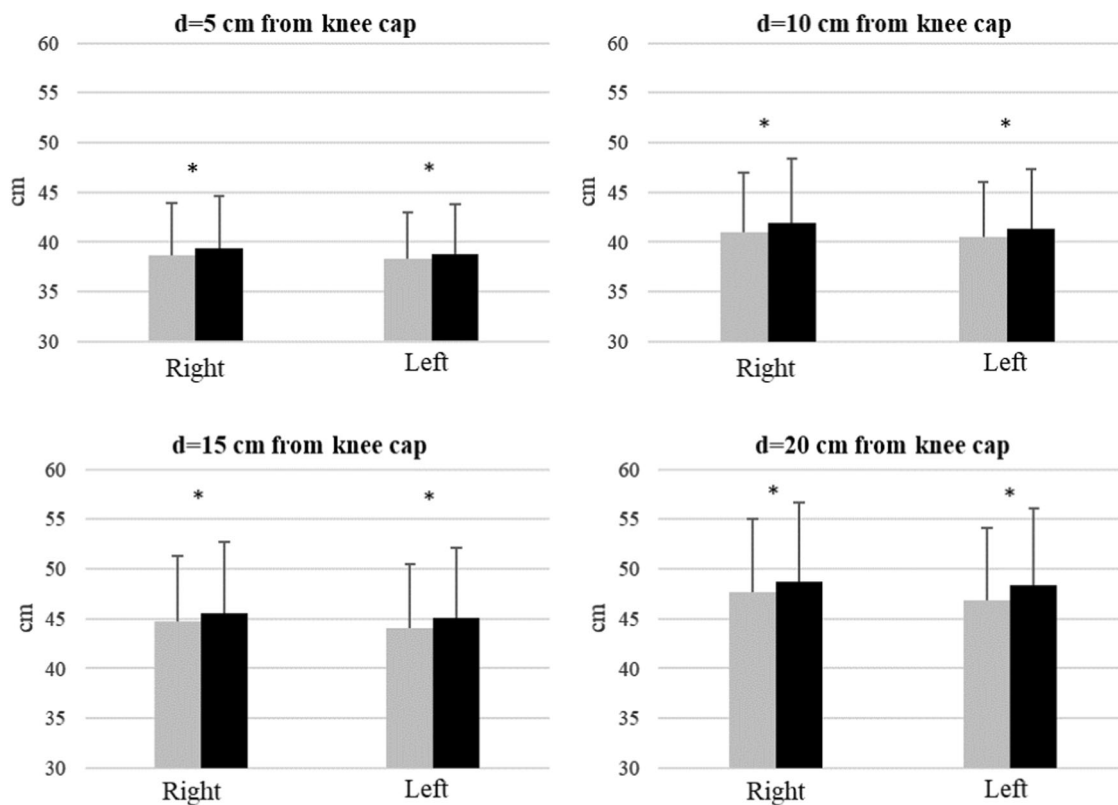
For the Group B, walking tests were carried out using the overground robotic exoskeleton: 10MWT-exo, 6MWT-exo, TUG-exo and Endurance-exo score improved significantly from the first session and the last session of ORET (Fig. 3, Table 5).

In Group B, no statistically significant difference was observed ( $p = 0.59$ ) in the SCIM-II scores before (median 66, IQR 60.0–72.0) vs. after (median 67, IQR 61.0–72.2) FES-C plus ORET training.

## Discussion

This study confirms that when using robotic exoskeletons for walking, careful monitoring is recommended to avoid skin lesions [11]. Specifically, 8% of persons of Group B exhibited skin redness at the end of one of ORET sessions, and further adverse health effects (e.g., bedsores) were avoided via the prompt interruption of the training. Bone density should also be examined before training because bone fractures have been reported in persons with SCI undergoing overground robotic exoskeleton gait training [27].

In the clinical spinal cord unit where study participants were recruited, an osteoporosis evaluation and a treatment protocol were applied as standard care, thus reducing the risk of bone fractures. During the ORET, a walker or two crutches are held by the upper limbs; this can lead to a musculoskeletal pain, in particular localised in the shoulders [27]. Muscle haemorrhage lesions are another adverse event that can arise in persons with SCI during robotic gait training, and the anticoagulant drugs often used in these persons could be, partially responsible.



**Fig. 1 Thigh circumferences in Group B.** Pre- (grey) and post- (black) FES-C treatment bilateral thigh circumferences (expressed as mean  $\pm$  standard deviation) recorded at distance (d) of 5 cm (top row,

left plot), 10 cm (top row, right plot), 15 cm (bottom row, left plot) and 20 cm (bottom row, right plot) from the knee cap (\* $p < 0.05$ ) (colour figure online).

**Table 3** Thigh circumferences measurements (values expressed as mean  $\pm$  standard deviation).

<i>d</i>	Left				Right			
	Pre-treatment	Post-treatment	Change	<i>p</i>	Pre-treatment	Post-treatment	Change	<i>p</i>
5	38.3 $\pm$ 4.7	38.8 $\pm$ 5.0	0.5 $\pm$ 1.0	0.049	38.6 $\pm$ 5.3	39.3 $\pm$ 5.3	0.7 $\pm$ 0.9	0.004
10	40.5 $\pm$ 5.5	41.4 $\pm$ 5.9	0.9 $\pm$ 1.5	0.026	41.0 $\pm$ 5.9	41.9 $\pm$ 6.4	0.9 $\pm$ 0.3	0.010
15	44.0 $\pm$ 6.5	45.1 $\pm$ 7.0	1.2 $\pm$ 1.4	0.003	44.7 $\pm$ 6.6	45.6 $\pm$ 7.1	0.9 $\pm$ 1.2	0.006
20	46.9 $\pm$ 7.2	48.4 $\pm$ 7.7	1.4 $\pm$ 1.1	0.0001	47.7 $\pm$ 7.3	48.7 $\pm$ 8.0	1.1 $\pm$ 1.6	0.013

*d* distance from the knee cap (centimeters).

Enrolled participants accounted for just 21% of the examined persons with SCI lesions. This low enrolment percentage may be attributed to several factors, including (a) the time-intensiveness of the prescribed rehabilitation programme (requiring from two to four months of uninterrupted participation); (b) more than one instrument with different eligibility criteria (Table 1) was used to complete the training; (c) persons with SCI have a delicate state of health with numerous concurrent comorbidity, often requiring interruption of training. Among these factors, this last reason accounted for a high percentage (38%) of study withdrawals, with a comparable number of participants citing personal reasons relating to their difficulty

maintaining participation for the long duration of the rehabilitation programme (38%).

Only 24% of study withdrawals were attributed to complications related to the robotic training, including skin lesions, pain and muscle haemorrhagic lesions.

The safety of the proposed rehabilitation programme as regards Group A (i.e., higher functioning group) was demonstrated by the absence of any such complication. On the other hand, some mild complications affected participants in Group B.

The selected study population comprises a range severity of functional deficits, including persons with paraplegia (44%), tetraplegia in high cervical injury (11%),

**Table 4** Gait outcomes in Group A.

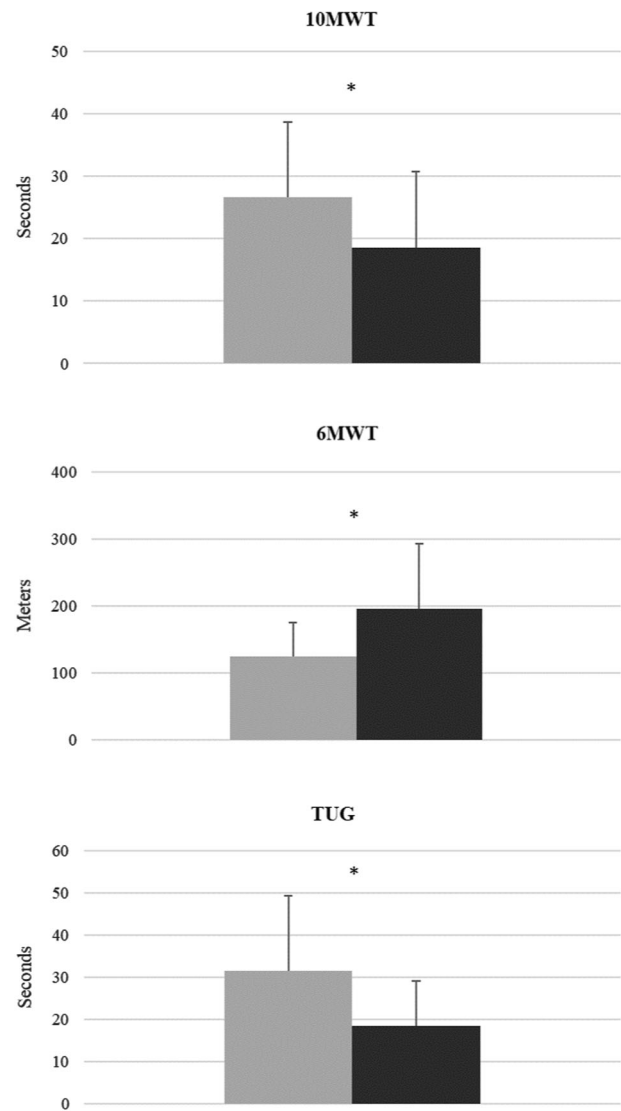
	Pre-treatment	Post-BWSTRT	Change	<i>p</i>	Pre-FES-OG	Post-FES-OG	Change	<i>p</i>	Pre-treatment <sup>d</sup>	Post-treatment <sup>d</sup>	Change	<i>p</i>
WISCI-II <sup>b</sup>	(7) 0; 0-0 (12) 7; 1.0-13.5	8; 3.5-13.0 15; 7.5-16.7	8; 3.5-13.0 5; 0-8.0	<0.05 <0.05	8; 3.5-13.0 15; 7.5-16.7	8; 8.0-13.0 16; 11.7-19.2	1.5; 0-5.0 0.5; 0-2.2	NS NS	(7) 0; 0-0 (12) 7; 1.0-13.5	8; 8.0-13.0 16; 11.7-19.2	14.5; 8.0-13.0 14.5; 3.7-10.2	<0.001 <0.05
10MWT (s) <sup>c</sup>	26.6 ± 12.1	19.6 ± 13.9	-7.0 ± 7.1	0.009	19.6 ± 13.9	18.6 ± 12.2	-1.0 ± 6.4	NS	26.6 ± 12.1	18.6 ± 12.2	-8.0 ± 0.7 (30%)	0.01
6MWT (m) <sup>c</sup>	124.1 ± 50.9	196.3 ± 92.6	72.1 ± 8.5	0.01	196.3 ± 92.6	195.6 ± 97.4	-0.7 ± 14.8	NS	124.1 ± 50.9	195.6 ± 97.4	71.4 ± 6.4 (58%)	0.02
TUG (s) <sup>c</sup>	31.4 ± 17.9	21.9 ± 11.4	-9.6 ± 12.0	0.045	21.9 ± 11.4	18.6 ± 10.5	-3.3 ± 3.4	NS	31.4 ± 17.9	18.6 ± 10.5	-12.9 ± 10.6 (41%)	0.009

NS Not Significant.

<sup>a</sup>BWSTRT plus FES-OG.

<sup>b</sup>Values expressed as median; interquartile range.

<sup>c</sup>Values expressed as mean ± standard deviation. Computed among a subgroup of participants whose initial WISCI-II score was ≥6.

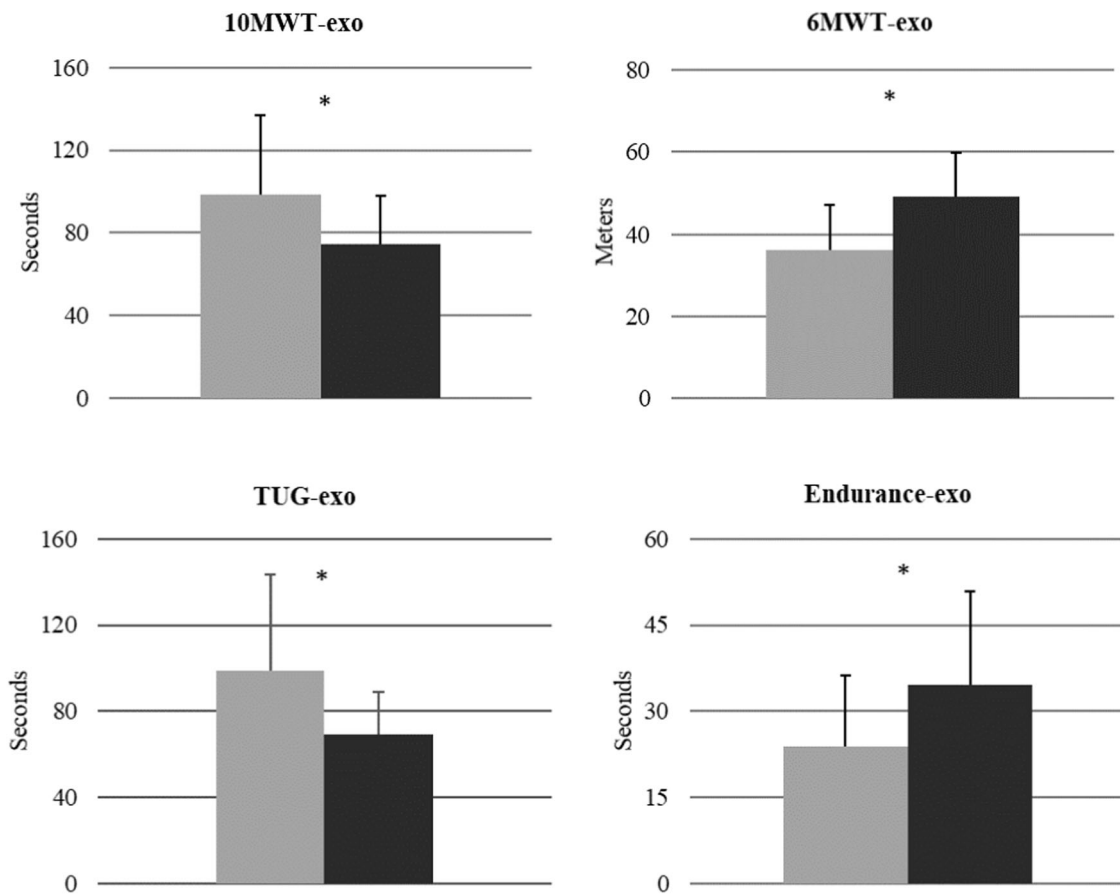


**Fig. 2** BWSTRT plus FES-OG walking tests scores. 10MWT (seconds) (top plot), 6MWT (metres) (middle plot), TUG (seconds) (bottom plot), expressed as mean ± standard deviation, at pre- (grey) and post- (black) treatment in *n* = 7 persons able to walk out of *n* = 19 persons of Group A; \**p* < 0.05 (colour figure online).

and tetraplegia in low cervical injury (10%), as well as a large portion of participants (35%) with AIS D lesions and a clinical prognosis of a strong possibility of complete gait recovery.

**Group A**

Gait recovery was evaluated using validated and widely accepted clinical assessment scales, including the 10MWT, 6MWT and TUG [24]. The results of the present study suggest that the application of a rehabilitation protocol featuring combined BWSTRT plus FES-OG allows many persons affected by incomplete SCI to regain locomotor function.



**Fig. 3** ORET tests scores. 10MWT-exo (seconds) (top row, left plot), 6MWT-exo (metres) (top row, right plot), TUG-exo (seconds) (bottom row, left plot), Endurance-exo (seconds) (bottom row, right plot) at

pre- (grey) and post- (black) treatment in  $n = 17$  persons of Group B. Note: the tests were carried out with the assistance of the overground robotic exoskeleton; \* $p < 0.05$  (colour figure online).

**Table 5** Outcomes in Group B.

	ORET first session	ORET last session	Change	<i>p</i>
10MWT-exo (s)	98.3 ± 38.6	74.2 ± 23.7	24.1 ± 17.0 (25%)	<0.001
6MWT-exo (m)	36.2 ± 10.9	49.0 ± 10.7	12.8 ± 3.9 (35%)	<0.001
TUG-exo (s)	99.0 ± 44.2	69.0 ± 20.0	30.0 ± 27.2 (30%)	<0.001
Endurance-exo (s)	23.9 ± 12.3	34.5 ± 16.3	10.6 ± 8.4 (44%)	<0.001

Values expressed as mean ± standard deviation.

Participants in Group A increased their mean walking speed by 30% ( $0.7 \pm 0.4$  m/s), reaching a value similar to uninjured individuals (0.8 m/s). This increased walking velocity and resistance was observed at the end of the treatment. In addition, an improvement of 58 and 41% was observed in resistance and transfer ability, respectively (Table 4).

On the other hand, persons who were not able to walk before the treatment regained their walking ability after the BWSTRT plus FES-OG. The use of robotic exoskeletons facilitates the walking recovery in persons with SCI and LEMS  $\geq 10$ , probably by activating a neural plasticity: in

fact, all persons with SCI recruited recovered their walking capacity [8, 9].

### Group B

Persons in Group B did not regain significant walking function on the clinical scales employed in this study. In fact, the increase observed in the walking ability (10MWT-exo, 6MWT-exo and TUG-exo) and endurance (Endurance-exo) means that a better skill in the use of the overground robotic exoskeleton for walking was reached, thus employing the most of the device's possibilities.

The gait speed during the ORET increased significantly from 0.11 (0.04) m/s to 0.15 (0.04) m/s, which remains clearly slower than the above-mentioned normal gait speed for healthy individuals.

Other factors which may influence the gait speed achieved in overground exoskeletons are highlighted in the medical literature. For instance, Louie and colleagues found significant correlations between walking velocity and increasing age, injury level and number of training sessions [28]. According to the literature, the mean number of rehabilitation sessions should be around 20 sessions; there are published experiences of persons who practised exoskeleton training for longer period obtaining better results [29].

At present, persons with SCI and poor lower limb motor activity can experience walking using overground robotic exoskeletons, with better health feeling and an increased ability to use the device. The use of robotic exoskeletons for walking may increase functionality in activities of daily living, thus contributing to improve the body composition [12, 13].

### Integration of gait training with exoskeleton and FES

The primary innovation of this study is represented by the integration of multiple advanced technologies in the functional rehabilitation of persons with SCI, including robotic exoskeletons, FES-C and FES-OG, with results supporting their combined use in multimodal rehabilitative programmes. In accordance with this opinion, a consensus among different clinical centres has been reported, applying across a variety of rehabilitation devices used by different rehabilitation hospitals, which develop and implement their own protocols [30].

In the present study, persons with SCI and LEMS < 10 underwent a joint, bone and neuromuscular reconditioning using FES-C before starting the robotic training. The results confirm that the thigh circumferences significantly increased after FES-C, in accordance with higher muscle volumes observed elsewhere [31]. The introduction of FES-C training before the robotic training requires participants to wait for a longer period before obtaining the physical and psychological benefits of the exoskeleton training, but has been reported to improve the safety of its use [32]. Persons with SCI, who have less compromised joint, bone and muscle composition thanks to residual motor voluntary activity at sublesional levels (LEMS  $\geq$  10), can start directly the robotic walking training. In this subgroup, a significant increase in the SCIM-II scores was observed after the treatment.

The 6-month and 12-month follow-up data, currently under investigation, may demonstrate a long-term improvement in terms of walking function and independence.

### Study limitations

The design of the current study is not sufficient to prove a cause-effect relationship due to the lack of a control group, a randomisation procedure, a sample size computation for statistical power and blinded assessors. These limitations should be carefully considered when weighing the strength of the results. Moreover, the rehabilitation protocol was challenging due to the required participant engagement of 8–12 weeks, and not all persons with SCI were eligible due to the instrumentation-specific requirements.

These limitations may have introduced a subject selection bias of the studied population, wherein only persons who have not contraindications regarding the use of the devices utilised in this study were included in the training. On the other hand, participants with different levels of functional impairment (complete, incomplete; AIS A, B, C and D) different spinal lesion levels of functional impairment (from C4 to L3), and different lesion onset have been included.

This subject heterogeneity could be a limitation of the study, as it resulted in a small sample size for the subgroups analysed.

### Conclusions

Although the present study design was not sufficient to prove a direct cause-effect relationship, the main findings of this study provide some encouraging evidence for the positive response of persons with SCI to multimodal rehabilitation paradigms using advanced robotic gait assistance and FES technologies. Persons affected by SCI, who have no contraindications to the use of robotic exoskeletons or FES, can safely experience walking function using these technologies, the use of which can contribute to improve the gait abilities in persons with SCI having LEMS > 10. In particular, BWSTRT followed by FES-OG training in persons with a relevant motor strength preservation improved not only the gait velocity and resistance, but also their functional walking abilities as assessed using clinical scales. On the other hand, persons with no or low motor strength preservation may experience walking function by means of the assistance of the overground robotic exoskeleton.

An ORET carried out after body reconditioning with FES-C is likely to be able to increase their abilities to interact with the device.

### Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.



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**Author contributions** GS was responsible of the study protocol, carried out patients’ selection, supervised clinical evaluations and treatments, supervised dataset production and analysed data, interpreted results, and drafted the paper. MO was responsible of dataset production, contributed to statistical analysis and contributed to drafted the paper. AR carried out patients’ physiotherapy evaluation and treatments, contributed to dataset production. CDA contributed to clinical evaluations. AG carried out clinical evaluations. SM contributed to design the study protocol, supervised statistical analysis, analysed the data, interpreted results and drafted the paper.

## Compliance with ethical standard

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** The study followed the guidelines of the Declaration of Helsinki. All applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research. All the necessary approvals were obtained, including local ethic committee (protocol number 410699).

**Informed consent** All participants received oral, as well as written information about the study, before informed consent was obtained.

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