



Original Research

# Safety and Feasibility of Various Functional Electrical Stimulation Cycling Protocols in Individuals With Multiple Sclerosis Who Are Nonambulatory



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## KEYWORDS

Exercise;  
Health;  
Multiple sclerosis;  
Rehabilitation

**Abstract Objective:** To examine the safety, feasibility, and response to functional electrical stimulation (FES) cycling protocols requiring differing levels of effort in people with multiple sclerosis (MS) who are nonambulatory.

**Design:** Pilot study with pre-post intervention testing.

**Setting:** Outpatient clinic setting of a long-term acute care hospital.

**Participants:** Individuals (N=10) with MS (6 men; mean age 58.6±9.86y) who use a wheelchair for community mobility. Participants' Expanded Disability Status Scale score ranged from 6.5 to 8.5 (median 7.5).

**Intervention:** Participants performed 3 or 4 FES cycling protocols requiring different levels of volitional effort during 6-8 testing sessions.

**Main Outcome Measures:** The primary outcome was safety, measured by adverse events and increase in MS symptoms, all assessed throughout, immediately post- and 1 day postsession. FES cycling performance for each protocol was also recorded. Exploratory outcome measures collected before and after all testing sessions included functional assessment of MS, MS Impact

**List of abbreviations:** ADLs, activities of daily living; EDSS, Expanded Disability Status Scale; ESES, Exercise Self-Efficacy Scale; FAMS, functional assessment of multiple sclerosis; FES, functional electrical stimulation; I-Resist, resistance interval; I-Rest, rest interval; I-Stim, stimulation interval; MA, motor assist; MS, multiple sclerosis; MSIS-29, 29-Item Multiple Sclerosis Impact Scale; PHQ-9, 9-Item Patient Health Questionnaire; QOL, quality of life; rpm, revolutions per minute; S, standard protocol; VAS-P, visual analog scale of pain; VAS-S, visual analog scale of spasticity.

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Scale, Exercise Self Efficacy Scale, Patient Health Questionnaire-9 item, and the Zarit Care-giver Burden Scale.

**Results:** All participants (4 women, 6 men) completed all testing sessions. There were no serious adverse events or differences in vitals or symptoms between protocols. Two participants had an isolated episode of mild hypotension. Changes in pain, spasticity, and fatigue were minimal. Five participants were able to cycle for 30 minutes and completed interval training protocols requiring increasing difficulty. The remainder cycled for <3 minutes and completed a rest interval protocol. There was modest improvement on the exploratory outcome measures.

**Conclusions:** People with MS who use a wheelchair for community mobility can safely perform FES cycling requiring more effort than previously reported research. Therefore, the individuals may experience greater benefits than previously reported. Further study is required to better understand the potential benefits for optimizing function and improving health in people with MS.

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People with multiple sclerosis (MS) who are significantly limited in walking and mobility face a myriad of problems associated with their immobility. Decreased mobility leads to less physical activity, and physical inactivity leads to deconditioning<sup>1,2</sup> and further functional impairments. The decline in mobility and deconditioning also predisposes people who require a wheelchair to worsening of MS symptoms, such as pain, spasticity, and fatigue.<sup>3</sup> Immobility combined with these symptoms leads to secondary adverse health conditions which can lead to decline in health and participation and reduced quality of life (QOL).<sup>4,5</sup> Preventing the decline in mobility may help slow the progression of disability, worsening of MS symptoms, and perhaps decline in health, in people with MS. Exercise can improve mobility, as well as decrease symptoms, in people with MS who are ambulatory.<sup>6-9</sup> However, individuals with MS who are limited in walking ability and require a wheelchair for community mobility face barriers to interventions for increasing physical activity, and specifically for improving lower extremity strength and muscle endurance.<sup>10,11</sup>

Functional electrical stimulation (FES) cycling offers an opportunity for people with severe weakness or paralysis to exercise and to directly train their muscles.<sup>12-14</sup> Several studies have demonstrated modest improvement in FES cycling performance, increased cardiorespiratory and muscle responses, decreased symptoms, and improved QOL in people with MS after FES cycling.<sup>15-19</sup> However, the FES cycling protocols used in these studies required participants to cycle with maximal electrical stimulation they could tolerate to promote muscle strengthening and hypertrophy. In addition, these protocols were used to minimize fatigue due to the concern that people with MS who have severe weakness, fatigue, spasticity and pain might be harmed by working *too hard*. In fact, there are few studies evaluating the safety and potential efficacy of high-intensity exercise interventions for people with MS who have significant mobility limitations but who may be at greater risk for exacerbation of their MS symptoms with effort. Thus, it is important to evaluate whether performing FES cycling at a

greater intensity is safe or if there is any effect of this on symptoms, functional abilities, or QOL.

Notably, Backus et al<sup>15</sup> demonstrated variability in response to FES cycling in people with MS who were non-ambulatory and trained 3 times a week for 12 weeks.<sup>15</sup> All (N=14) participants were able to cycle without an increase in MS symptoms. However, some participants (n=7) were able to cycle for >25 minutes (maximum 30min) without stopping, whereas others (n=7) were not able to cycle for 30 minutes but were able to increase the duration of active cycling throughout a 12-week training period. In addition, although the FES cycling protocol used did not require volitional effort and instead increased stimulation to the maximum amount tolerated, several of the study participants were able to volitionally increase the speed (revolutions per minute [rpm]) and decrease the amount of stimulation required. Furthermore, the perceived level of effort rated with the *rating of perceived exertion* scale, participant ratings averaged 2.19 (EASY) and ranged from 0 (REST) to 4 (SORT OF HARD) (reference added after unblinding). These findings suggest that these participants might be able to put forth greater effort during cycling and further raise the question of whether protocols adjusted for an individual's ability will lead to more meaningful outcomes. Specifically, would requiring volitional muscle activation that is augmented, not substituted for, with FES, lead to greater training or functional improvements, without detrimental fatigue or increase in MS symptoms? Similarly, in those who are unable to cycle more than a few minutes, would an interval training protocol be more effective for increasing the ability to cycle and potentially provide a more intense exercise stimulus for people who would otherwise not be able to exercise as long? The safety, feasibility, and efficacy of moderate- to higher-intensity exercise protocols have not yet been established in individuals with moderate to severe MS.

The purpose of this pilot study was to evaluate the safety and feasibility of FES cycling protocols requiring different levels of effort. In addition, the secondary aim of

**Table 1** Inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
At least 18 y old	Experienced diagnosed MS relapse in the past 6 mo
Diagnosed with MS by a physician	Ability to ambulate >150 ft
Cleared medically by their physician	Any cardiovascular disease (ie, previous myocardial infarct, unstable angina, congestive heart failure, history of arrhythmia, or stroke) or uncontrolled blood pressure
Use wheelchair as primary means of community mobility	History of epileptic seizures
Willing to stop using electrical stimulation at least 2 wk prior to starting the study	Any implanted device(s) other than a Baclofen pump
Willing to not add any other therapy or exercises to their normal daily routine during the length of the study	Current unstable long bone fracture(s) in lower extremities or trunk
	Unable to tolerate sitting upright for 1 h
	Currently participating in another research study
	Investigators were unable to generate a muscle contraction from the quadriceps, hamstrings, and/or gluteus maximus muscles using electrical stimulation

this study was to evaluate the potential efficacy for decreasing symptoms and improving function in people with MS who are nonambulatory.

## Methods

### Participants

Using convenience sampling, individuals were recruited from the clinical program and the local community via phone calls, flyers posted in local clinics, and word of mouth. All participants who satisfied the inclusion and exclusion criteria (table 1) were enrolled in the study after providing written informed consent.

### Procedures

All study procedures were approved by the institution's research review board. The principal investigator is a licensed physical therapist and oversaw all aspects of the study. A licensed physical therapist researcher, an exercise specialist, and trained research assistants performed assessments and implemented all aspects of the testing sessions. All investigators were trained on how to use the FES cycle and to administer all outcome measures.

Figure 1 shows the flow of a participant's activity throughout the study. All study activities were conducted in an outpatient clinic setting. Once enrolled in the study, participants provided demographic information, including age, estimated time since diagnosis, type of MS, and medications. Participants also completed the interview version of the Expanded Disability Status Scale (EDSS)<sup>20</sup> to allow investigators to characterize participants for data interpretation. Participants completed 6-8 FES testing sessions (3-4 protocols administered in a standardized order) per the protocol sequence with at least 1 day of rest between each session for 4-8 weeks.

### FES lower extremity cycling testing protocols

FES cycle testing was performed on the RT 300 cycle.<sup>a</sup> Participants remained seated in their wheelchair to cycle. For all sessions, an investigator applied surface electrodes to participants' bilateral quadriceps, hamstrings, and gluteus maximus muscles and safely positioned the participant's feet on the pedals of the cycle. Participants then cycled independently with the assistance of FES and the ergometer motor as needed.

FES parameters were predetermined based on previous studies of FES cycling in people with MS.<sup>15</sup> The stimulation intensity was set to encourage the maximum amount of volitional cycling within the participants' tolerance. Stimulation assistance was provided as necessary to achieve target pedaling rate of 30-45 rpm.

Each FES testing session consisted of a 2-minute passive (cycling caused by the ergometer, with no volitional cycling and no FES) warm-up at 35 rpm, a protocol-specific active cycling phase (either volitionally or with FES to augment), and a 2-minute passive cool down at 35 rpm. This study employed 5 protocols (table 2). Each participant first completed the 2 different continuous cycling protocols on 2 separate days: one without motor assist (MA) from the ergometer (standard: S) and one with MA. During protocol S, if a participant was unable to maintain at least 30 rpm, the electrical stimulation turned off, and the FES cycle went into passive mode (ie, the ergometer propelled the pedals). The time from the start of the active phase to that at which the FES cycle went into passive mode was recorded as the participant's maximum active cycling time. Protocol MA differed such that when the participant was unable to maintain 30 rpm, the ergometer provided motor assistance (MA), and the MA and FES remained on during the entire active phase, regardless of the amount of voluntary muscle activation the participant was able to provide.

Each participant's maximum active cycling time from protocol S determined which interval protocol(s) they completed (see table 2) (fig 2). If the participant actively

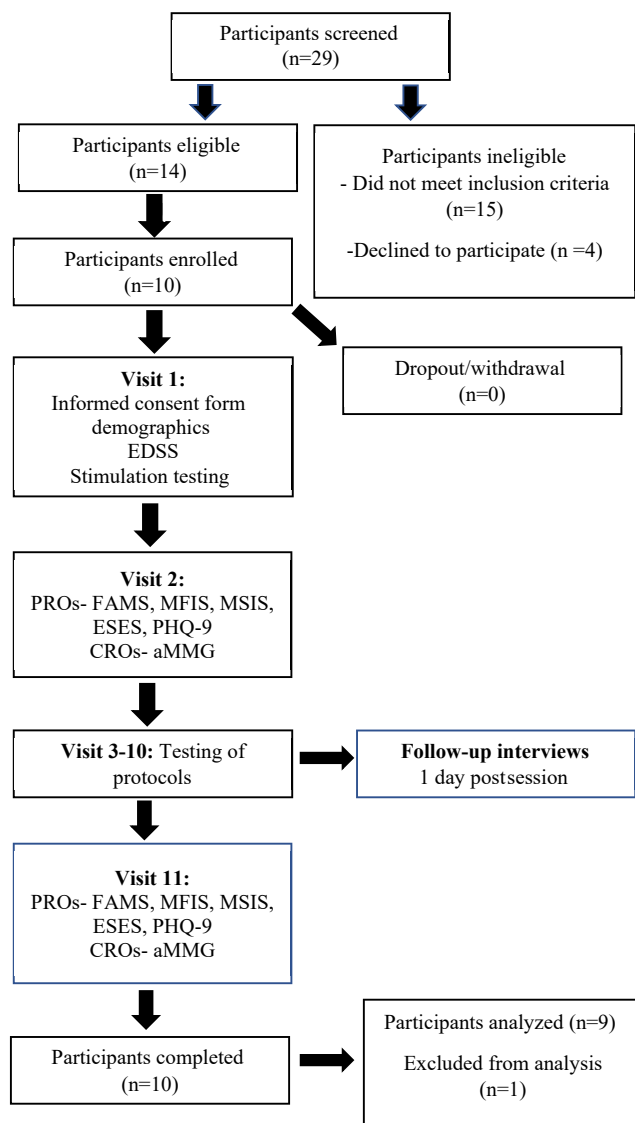


Fig 1 Flow chart of study procedure.

cycled for 30 minutes, they performed 2 interval protocols: one with varied electrical stimulation (stimulation interval [I-Stim]) and one with varied resistance (resistance interval [I-Resist] protocol) (fig 2A). For I-Stim, the intervals increased in difficulty by decreasing stimulation available and for I-Resist by increasing resistance. As the difficulty of the intervals increased, the RPM rate a participant was required to maintain decreased stepwise in accordance with the intervals protocols (range 20-45 rpm). If a

participant was unable to maintain active cycling for 30 minutes in protocol S, they continued to a variation of rest interval (I-Rest) protocol (fig 2B). Each assigned protocol was completed twice in a standardized sequence.

## Outcome measures

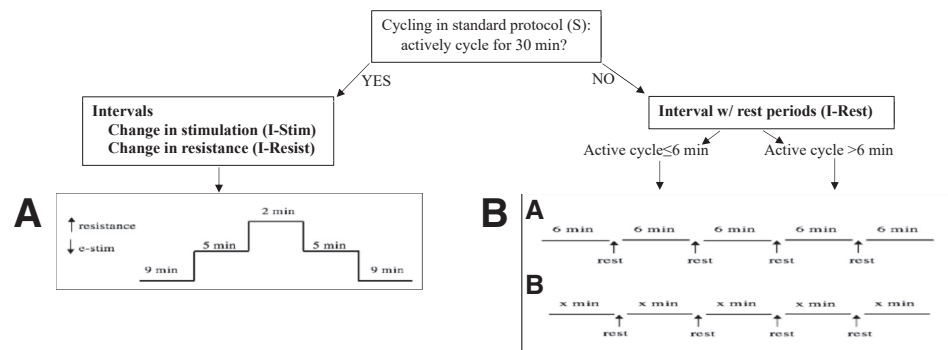
The primary aim of this study was to assess the safety of these FES cycling protocols for people with MS who are severely limited in walking ability and primarily use a wheelchair for mobility. Participants were closely monitored for adverse signs or increase in symptoms associated with cycling during each session and 1 day postsession. Each participant completed the visual analog scales of fatigue, spasticity (VAS-S), and pain (VAS-P) at the beginning and end of every testing session.<sup>21</sup> Each is a likert scale ranging from 0 (no symptom) to 10 (severe symptoms). Participants were also contacted the day after the session via phone and interviewed about their symptoms related to fatigue, spasticity, and pain using a 10-point Likert scale and any other potential adverse events that may have occurred after the session. Specifically, it was important to determine whether there was an increase in MS-related symptoms. For example, a participant may have experienced muscle soreness due to testing and would not consider this a poor response or adverse event to a given protocol or FES cycling in general. If a participant reported an increase in neurogenic pain or developed it as a new symptom after cycling, this was considered an adverse event.

To determine the feasibility of these protocols and that the participants were able to complete each of the protocols, FES cycling performance parameters (distance cycled, active time, power output, rpm, stimulation) were collected during each session by the RTI software and analyzed offline. The participants' perceived level of effort during cycling was also recorded for each session.

The participants in this study had decreased physical activity due to their mobility challenges, that is, they used a wheelchair for mobility and walked significantly limited distances. Given that the increase in physical activity and exercise may have a positive effect on an individual's perception of their ability, mood, and health, and that they may experience a training effect from the FES cycling testing (6-8 sessions of 30min), the following outcome measures were administered before and after the completion of all testing sessions to gather preliminary data related to potential for efficacy of FES cycling for this population to use for future studies: (i) The 29-item Multiple Sclerosis Impact Scale (MSIS-29)<sup>22</sup> measures an

Table 2 Description of the 5 FES cycle testing protocols. MA=ergometer from FES cycle provides passive support for cycling the leg

Variable Changed	Without MA (S)	MA	I-Stim	I-Resist	I-Rest
	Standard	Add MA	Stimulation (Decrease)	Resistance (Increase)	Rest Period
Stimulation (stim) allowed	100% of max stim tolerated	100% of max stim tolerated	Varied (0%-100%)	100% of max stim tolerated	100% of max stim tolerated
Resistance	0.5 N·m	0.5 N·m	0.5 N·m	Varied (0.5-0.77 N·m)	0.5 N·m
Target speed	45 rpm	45 rpm	Varied (30-45 rpm)	Varied (30-45 rpm)	45 rpm



**Fig 2** Algorithm for interval protocol selection. (A) Protocol I-Stim and I-Resist for individuals able to cycle 30 minutes in protocol S. (B) Protocol I-Rest for individuals able to cycle <30 minutes in protocol A.

individual's perception of the effect of MS on daily life. Changes on the MSIS-29 are clinically significant if there is an 8-point change<sup>23</sup> between outcome administrations. (ii) The functional assessment of multiple sclerosis (FAMS)<sup>24</sup> is a self-report survey that measures the effect of MS on an individual's perception of health, functional mobility, and daily activities. Although higher scores on the FAMS indicate a higher QOL such that there is less of an effect of MS on an individual's daily life, cutoff scores determining minimally important differences have not been established. (iii) The Exercise Self-Efficacy Scale (ESES)<sup>25</sup> measures an individual's belief in their ability to participate in exercise. Although higher scores indicate increasing confidence and self-efficacy, minimal detectable change or minimal clinically important difference values have not been established. (iv) The 9-item Patient Health Questionnaire (PHQ-9)<sup>26</sup> measures participant's mood in a variety of situations within the last 2 weeks with a change of at least 5 points being clinically significant.

Given that caregivers have subjectively reported increased ease with transfers, activities of daily living (ADL), and household ambulation in several earlier studies,<sup>15,16</sup> the Zarit Caregiver Burden<sup>27</sup> was also administered to assess for the caregiver's perception of the effect of any changes in bed mobility, transfers, and ADLs after FES cycling on their own health and wellness.

Both the MSIS-29 and FAMS scales are validated in MS and are recommended as outcome measures for MS by the American Physical Therapy Association EDGE MS Task Force 2011.<sup>28</sup> Although the other instruments have not been directly validated within the MS population, they are used within spinal cord injury,<sup>26,29-31</sup> brain injury,<sup>32</sup> and stroke populations,<sup>33</sup> as well as in other MS literature.<sup>34,35</sup> Given the functional similarities the participants may have shared with these other neurologic populations, the outcome measures were included to allow for easier comparison on effects across other studies in MS and other populations.

## Data analysis

Data were compiled into an Excel spreadsheet for analyses. Descriptive statistics were performed on all outcome measures to assess mean, median, and change scores. We assessed clinically meaningful change using minimal clinically important difference and effect size. Effect size was

computed using Cohen's  $d$ ,<sup>36,37</sup> where 0.2 is considered a small effect size, 0.5 a medium effect size, and 0.8 a large effect size.<sup>37</sup> Post-hoc analyses included assessment of the magnitude of the difference between 2 groups that emerged based on the participants' ability to cycle 30 minutes.

## Results

### Participant characteristics

Twenty-nine people with MS were screened, 14 were eligible, 10 enrolled, and 10 participants (6 men; mean age  $58.6 \pm 9.86$ y) completed all aspects of the study. One participant who completed the study was withdrawn from data analysis as she did not complete the study flow according to the protocol as designed. Therefore, all results presented are based on a sample size of 9 participants. Participants represented all MS subtypes (relapsing-remitting = 4, primary progressive = 3, secondary progressive = 2) with an average of 17.22 years since diagnosis (range 7-27 years) and were on a variety of medications. Seven participants (70%) received disease-modifying therapies including ocrelizumab ( $n=3$ ), fingolimod ( $n=1$ ), teriflunomide ( $n=1$ ), dimethyl fumarate ( $n=1$ ), and glatiramer acetate ( $n=1$ ). All participants were unable to ambulate >150 ft and used a wheelchair as their primary means of community mobility; participants self-identified EDSS scores ranging from 6.5 to 8.5 (median 7.5) on the EDSS interview.<sup>38</sup> One participant reported an EDSS score of 6.5; however, this individual was only able to ambulate 80 ft with bilateral assistance and used a wheelchair in the community. Five of the 9 participants had a caregiver to assist with bed mobility, transfers, and ADL.

### Safety outcomes

#### Adverse events

There were no serious adverse events or differences in protocols related to vital signs or symptoms overall. There were 2 separate orthostatic events. Each event occurred in a different participant after 1 instance of the protocol with MA; each of these was determined to be an isolated incident that resolved within 10 minutes postcycling. Participants were cleared by the principal investigator and able to

**Table 3** Average symptoms after an FES testing session

Scales	Group Average Symptoms														
	I-S (n=9)			I-MA (n=9)			I-Rest (n=4)			I-Stim (n=5)			I-Resist (n=5)		
	Pre	Post	Range	Pre	Post	Range	Pre	Post	Range	Pre	Post	Range	Pre	Post	Range
VAS-P	0.92 (0-3)	0.69 (0-3)	0.83 (0-3)	0.94 (0-4)	0.50 (0-2)	1.13 (0-4)	0.80 (0-3)	0.80 (0-3)	0.80 (0-3)	0.70 (0-3)	0.80 (0-3)	0.70 (0-3)	0.70 (0-3)	0.80 (0-3)	0.70 (0-3)
VAS-S	1.28 (0-3)	1.08 (0-4)	1.00 (0-2)	0.94 (0-4)	1.00 (0-3)	1.13 (0-3)	0.80 (0-3)	0.80 (0-3)	0.80 (0-3)	0.70 (0-3)	0.80 (0-3)	0.70 (0-3)	0.70 (0-3)	0.70 (0-3)	0.70 (0-2)
VAS-F	0.97 (0-4)	2.86 (0-7)	1.78 (0-7)	2.06 (0-6)	3.88 (0-7)	0.75 (0-3)	0.70 (0-2)	0.70 (0-2)	0.70 (0-2)	1.60 (0-6)	1.60 (0-6)	0.60 (0-2)	0.60 (0-2)	1.00 (0-2)	1.00 (0-2)
Session RPE	2.06 (0-7)		1.83 (0-4)			1.63 (0-3)	2.10 (0-4)					2.00 (0-4)			

NOTE. Scores are reported mean (range).

Abbreviations: VAS-F, visual analog scale of fatigue; RPE, rating of perceived exertion.

continue study participation with close monitoring and without further incident.

### Spasticity

There were minimal changes in spasticity (VAS-S; average change  $0.22 \pm 0.75$ ) (table 3). For 70% of all participant sessions, spasticity decreased or remained unchanged immediately after FES cycling, and these changes were maintained or returned to baseline 1 day postsession.

### Pain

There also were minimal changes in pain (VAS-P; average change  $-0.18 \pm 0.94$ ) across all protocols (see table 3). For 91% of participant sessions (58/64), any pain experienced returned to baseline levels 1 day postsession or by the next testing session.

### Fatigue

All but 1 participant who had an increase in fatigue immediately postsession returned to baseline the next day (average change  $-0.10 \pm 1.73$ ) (see table 3). Participants who reported an increase in fatigue at 1 day post returned to baseline before the next session.

One individual experienced a substantial increase in visual analog scale of fatigue +5, VAS-S +3, and VAS-P +4 1 day after I-Rest. However, the participant reported he was not consistent with his usual medication regimen. The participant continued study participation and repeated the protocol without incident after resuming his regular medication schedule.

### Feasibility

#### Perceived exertion

All participants completed each protocol with an average level of effort of the Rating of Perceived Exertion (RPE) scale of  $1.94 \pm 1.55$  with ratings ranging from 0 to 10 (resting, no work) to 7 of 10 (moderately hard). There were minimal differences between participants' Rating of Perceived Exertion ratings between protocols (see table 3).

#### FES cycling performance

FES cycling performance varied for distance cycled, active time, power output, rpm, and stimulation across protocols and between participants (table 4). Four participants cycled for approximately 2-3 minutes of continuous cycling (standard protocol; S). They were categorized in the <30-minute group and completed protocols S, MA, and I-Rest. Five participants cycled the full 30 minutes of continuous cycling with some level of stimulation assistance and completed protocols S, MA, I-Stim, and I-Resist.

Of all participants, 3 of the 9 were FES naïve. One of the 3 (EDSS 7.0) could actively cycle for no >3 minutes without MA, whereas the other 2 (EDSS 7.0 and 7.5) were able to cycle the full 30 minutes. Of the remaining 6 participants who were not FES naïve, 3 were unable to actively cycle >3 minutes (EDSS 8.0, 8.0, 8.5), whereas 3 could complete 30 minutes (EDSS 6.5, 7.0, 7.5).

**Table 4** Group averages of FES cycle performance parameters

Performance Parameters	FES Performance Parameters						
	<30-min group (n=4)			=30-min group (n=5)			
	Protocol S	Protocol MA	Protocol I-Rest	Protocol S	Protocol MA	Protocol I-Stim	Protocol I-Resist
Active time (min)	2:38 (0:55)	30:00 (0:00)	10:00 (0:00)	30:00 (0:00)	30:00 (0:00)	30:00 (0:00)	30:00 (0:00)
Distance (miles)	0.58 (0.31)	3.70 (0.09)	1.68 (0.4)	2.08 (0.97)	5.54 (0.99)	5.43 (0.73)	5.58 (1.14)
Energy Expended (kcal/h)	0.37 (0.32)	0.27 (0.32)	0.26 (0.08)	2.01 (0.45)	2.02 (0.44)	1.93 (0.41)	2.23 (0.69)
Power (W)	0.87 (0.43)	0.39 (0.44)	0.93 (0.54)	2.33 (0.48)	2.31 (0.41)	2.46 (0.57)	2.60 (0.77)
rpm	21.98 (8.08)	30.37 (0.74)	38.38 (2.89)	45.36 (9.55)	46.61 (8.47)	45.48 (6.46)	47.11 (9.67)
Stimulation (uC)	12.81 (2.80)	13.73 (3.97)	13.67 (3.60)	7.80 (4.12)	8.38 (3.75)	6.72 (3.58)	6.73 (3.52)

NOTE. Unless noted values reflect average (standard deviation).

### < 30-minute cycling group

For the 4 participants in the <30-minute group, average active cycling time was 2 minutes,  $38 \pm 0:55$  seconds in protocol S,  $30 \pm 0:00$  minutes during protocol MA, and  $10 \pm 0:00$  minutes total (five 2-min interval) in I-Rest. In this group, all participants increased their active cycle time (by an average of 400%), distance cycled (correlated with increased time cycling), and performed with greater power output during I-Rest. Participants in the <30-minute group varied in their rpm during the active cycle time with the highest rpm during I-Rest (range across 3 protocols 21.98-38.38 rpm).

### 30-minute group

All 5 participants in the 30-minute group actively cycled for 30 minutes during all protocols. In these individuals, power output and RPMs were all highest for protocol I-Resist. Average stimulation used was highest for protocol MA.

Participants in this group were able to maintain a steady average rpm rate of  $46.14 \pm 0.86$  rpm. Three of the 5 participants in this group required progressively less stimulation within a single cycling session.

### Participant-reported outcomes

The participant-reported outcomes and caregiver reported outcomes are summarized in table 5. Across all

participants, there was a small improvement (Cohen's  $d=0.16$ ) in average FAMS score ( $+4.83 \pm 8.25\%$ ), but the score decreased in 1 participant by 11.57%. There was a moderate (Cohen's  $d=0.41$ ) and clinically significant improvement in MSIS-29 scores for all but 1 participant (group average change  $-13.6 \pm 12.66$  points). The average score for the ESES improved or stayed the same for all but 1 participant ( $5.64 \pm 7.08\%$ , Cohen's  $d=0.26$ ) who reported a decrease of 19 points (65.52% change) on the ESES. Across all participants, scores for the PHQ-9 worsened, but stayed within the mild-to-moderate range for depression ( $12.99 \pm 55.17\%$ , Cohen's  $d=0.30$ ).

Six caregivers completed the Zarit, and scores improved or stayed the same for all participants ( $-9.02 \pm 12.20\%$ , Cohen's  $d=0.25$ ). Two of 6 caregivers reported a decrease in the assistance the participant required immediately after the FES cycling session and after the completion of all the FES cycling sessions.

When the participants' data are analyzed according to their FES cycling performance, the results differ between groups (see table 5). In the <30-minute group, the 3 of 4 participants' average PHQ-9 scores improved ( $-40.00 \pm 52.92\%$ , Cohen's  $d=-0.41$ ), whereas the 30-minute group scores did not ( $27.38 \pm 20.74\%$ , Cohen's  $d=0.34$ ). In addition, ESES scores improved ( $5.68 \pm 6.44\%$ , Cohen's  $d=0.28$ ) in the 30-min group and

**Table 5** Group average change in participant-reported outcomes after completion of all testing sessions

PRO Measures	Patient-Reported Outcomes (n=9)				
	Pre Average $\pm$ SD	Post Average $\pm$ SD	Average Change $\pm$ SD	Average % Change $\pm$ SD	Cohen's $d$
MSIS	78.56 $\pm$ 23.28	66.00 $\pm$ 28.86	-12.56 $\pm$ 12.96*	-17.49 $\pm$ 15.925*,†	0.41‡
FAMS	109.78 $\pm$ 23.83	114.67 $\pm$ 25.29	4.89 $\pm$ 9.40	4.83 $\pm$ 8.25†	0.16
ESES	31.25 $\pm$ 5.06	32.75 $\pm$ 3.69	1.50 $\pm$ 1.93	5.64 $\pm$ 7.08†	0.26
<30-min group (n=4)	29.5 $\pm$ 4.51	25.75 $\pm$ 10.90	-3.75 $\pm$ 10.34	-12.21 $\pm$ 36.39†	-0.42‡
30-min group (n=5)	32.2 $\pm$ 5.17	33.8 $\pm$ 3.70	1.6 $\pm$ 1.95	5.68 $\pm$ 6.44†	0.28
PHQ-9	5.11 $\pm$ 4.20	7.22 $\pm$ 8.09	2.11 $\pm$ 4.20	12.99 $\pm$ 55.17†	0.30
<30-min group (n=4)	2.33 $\pm$ 2.52	1.33 $\pm$ 2.31	-1.00 $\pm$ 1.00	-40.00 $\pm$ 52.92†	-0.41‡
30-min group (n=5)	5.6 $\pm$ 4.16	7.8 $\pm$ 6.87	2.2 $\pm$ 2.77	27.38 $\pm$ 20.74†	0.34‡
Zarit Caregiver Burden Scale (n=6)	38.17 $\pm$ 12.3	34.50 $\pm$ 10.82	-3.67 $\pm$ 5.09	-9.02 $\pm$ 12.20	0.25

\* Clinically significant.

† Improvement.

‡ Moderate effect size.

worsened ( $-12.21\% \pm 36.39\%$ , Cohen's  $d=0.42$ ) in the <30-minute group.

## Discussion

This study extends previous findings that people with MS who are nonambulatory can safely perform FES cycling and further demonstrates that they can perform FES cycling using protocols requiring more effort. Participants were able to complete all sessions with an *easy to moderately hard* level of effort rating with minimal changes in their baseline MS symptoms which suggests that cycling protocols requiring more volitional muscle activation are not harmful for these individuals.

### FES cycling performance

Although all participants were unable to ambulate >150 ft and used a wheelchair or scooter for community mobility, suggesting they were functionally similar, 2 distinct groups emerged based on cycling performance. One group ( $n=4$ ) was not able to cycle for >3 minutes continuously without MA, whereas the other group ( $n=5$ ) was able to cycle for a full 30 minutes with less stimulation and more resistance (ie, requiring more effort). This variability in ability to perform FES cycling has been reported previously for people with MS.<sup>15</sup> Neither EDSS classification nor prior use of electrical stimulation or an FES cycle correlated with cycling performance. The differences between these 2 groups may be due to different levels of volitional control or muscle condition<sup>18</sup> given the heterogeneity of symptoms within people with MS. This warrants further investigation and consideration for the choice of protocols to use clinically for people with severe MS.

All participants demonstrated improvement in FES cycling performance (see [table 4](#)). This supports research as described by Backus et al.<sup>15</sup> Most interestingly, in this study, participants who were unable to perform >3 minutes of continuous active FES cycling were able to cycle for the full 30 minutes during protocol MA and to complete an interval protocol with short rest breaks allowing them to improve their total active cycle time by an average of 400% without any increase in spasticity, pain, or fatigue. These findings suggest that even those with significant weakness who cannot sustain FES cycling for a prolonged period with the standard protocol have the potential to experience a greater exercise stimulus with different protocols. Future studies should evaluate whether training under conditions in which an individual can exercise longer (ie, with interval training or with MA) will lead to meaningful changes in symptoms, function, health, or QOL. If so, that would suggest that FES cycling might be useful for people with MS who have significant weakness and are limited in access to exercise or rehabilitation interventions.

### Outcome measures

Meaningful changes in functional mobility were not expected given that this was a testing; training, study, and

participants were not progressed to induce a training effect. However, 8 of 9 participants reported improvements in their perception of MS (ie, less of an effect of the MS) on their functional ability (FAMS) and less effect of MS on their daily lives (MSIS-29) after study participation. These findings may be because of an increase in physical activity in normally sedentary individuals positively influencing their outlook. These findings suggest that future studies are warranted to evaluate the potential for FES cycling to improve mobility and overall function and QOL in people with MS who are nonambulatory.

On the Zarit Caregiver Burden Scale post all sessions, 2 of 6 caregivers reported a decrease in their perception of their burden to provide care for their respective participants after FES cycling. This is consistent with previous studies during which caregivers reported that their burden of care during assisted mobility and transfers was easier after FES cycling and that this seemed to be related to decreased spasticity (D. Backus, unpublished data, 2017). Future studies should evaluate the effect of FES cycling, as well as other interventions, not only for the people with MS but also on caregiver burden.

Multiple participants reported feelings of sadness at the study conclusion because they reported feeling less able to participate in exercise without access to an FES cycle. These feelings may have contributed to the decline in scores seen for PHQ-9 scores. When analyzed by group, posttesting self-efficacy (ESES) scores worsened in the <30-minute group suggesting that the FES cycle may allow individuals who are more functionally impaired to participate in physical activity to a greater degree than imagined. Conversely, individuals in the 30-minute group reported an average improvement in self-efficacy scores posttesting.

### Study limitations

Because of the small sample size and that participants in the study were nonambulatory, these results are limited to interpretation and are not generalizable to the entire MS population. Because this is not a training study, the results do not provide information regarding the long-term or functional effects of FES cycling. There was neither a control group nor randomization, and thus future study is warranted to evaluate the full effect of FES cycling with these different protocols on people with MS who are nonambulatory.

### Conclusions

Individuals with MS who are nonambulatory can safely perform FES cycling using parameters requiring more effort and is therefore a viable exercise tool for individuals with greater disability. FES cycling may therefore offer an opportunity for neuromuscular training and exercise benefits if cycling protocols are used that adequately challenge individuals. Future studies should assess the functional effects of FES cycling in people with severe MS who are nonambulatory.



## Supplier

a. RT 300 cycle; Restorative Therapies, Inc.

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## References

1. Willingham TB, Backus D, McCully KK. Muscle dysfunction and walking impairment in African American and Caucasian American women with multiple sclerosis. *Int J MS Care* 2019;21:249-56.
2. Klaren RE, Sandroff BM, Fernhall B, Motl RW. Comprehensive profile of cardiopulmonary exercise testing in ambulatory persons with multiple sclerosis. *Sports Med* 2012;46:1365-79.
3. Motl RW, Arnett PA, Smith MM, Barwick FH, Ahlstrom B, Stover EJ. Worsening of symptoms is associated with lower physical activity levels in individuals with multiple sclerosis. *Mult Scler* 2008;14:140-2.
4. Motl RW. Physical activity and irreversible disability in multiple sclerosis. *Exerc Sport Sci Rev* 2010;38:186-91.
5. Hemmett L, Holmes J, Barnes M, Russell N. What drives quality of life in multiple sclerosis? *QJM* 2004;97:671-6.
6. Edwards T, Pilutti LA. The effect of exercise training in adults with multiple sclerosis with severe mobility disability: a systematic review and future research directions. *Mult Scler Relat Disord* 2017;16:31-9.
7. Kalron A, Rosenblum U, Frid L, Achiron A. Pilates exercise training vs. physical therapy for improving walking and balance in people with multiple sclerosis: a randomized controlled trial. *Clin Rehabil* 2017;31:319-28.
8. Heine M, van de Port I, Rietberg M, van Wegen E, Kwakkel G. Exercise therapy for fatigue in multiple sclerosis. *Cochrane Database Syst Rev* 2015;9. CD009956.
9. Coote S, Uszynski M, Herring M, et al. Effect of exercising at minimum recommendations of the multiple sclerosis exercise guideline combined with structured education or attention control education – secondary results of the step it up randomised controlled trial. *BMC Neurol* 2017;17:119.
10. Backus D. Increasing physical activity and participation in people with multiple sclerosis: a review. *Arch Phys Med Rehabil* 2016;97:S210-7.
11. Learmonth Y, Rice I, Ostler T, Rice L, Motl R. Perspectives on physical activity among people with multiple sclerosis who are wheelchair users. *Int J MS Care* 2015;17:109-19.
12. Petrofsky J, Phillips C. The use of functional electrical stimulation for rehabilitation of spinal cord injured patients. *Cent Nerv Syst Trauma* 1984;1:57-74.
13. Donaldson N, Perkins T, Fitzwater R, Wood D, Middleton F. FES cycling may promote recovery of leg function after incomplete spinal cord injury. *Spinal Cord* 2000;38:680-2.
14. Hunt KJ, Fang J, Saengsuwan J, Grob M, Laubacher M. On the efficiency of FES cycling: a framework and systematic review. *Technol Health Care* 2012;20:395-422.
15. Backus D, Burdett B, Hawkins L, Manella C, McCully K, Sweatman M. Outcomes after functional electrical stimulation cycle training in individuals with multiple sclerosis who are nonambulatory. *Int J MS Care* 2017;19:113-21.
16. Fornusek C, Hoang P. Neuromuscular electrical stimulation cycling exercise for persons with advanced multiple sclerosis. *J Rehabil Med* 2014;46:698-702.
17. Ratchford JN, Shore W, Hammond ER, et al. A pilot study of functional electrical stimulation cycling in progressive multiple sclerosis. *NeuroRehabilitation* 2010;27:121-8.
18. Reynolds M, McCully K, Burdett B, Manella C, Hawkins L, Backus D. Pilot study: evaluation of the effect of functional electrical stimulation cycling on muscle metabolism in non-ambulatory people with multiple sclerosis. *Arch Phys Med Rehabil* 2015;96:627-32.
19. Edwards T, Motl R, Sebastião E, Pilutti L. Pilot randomized controlled trial of functional electrical stimulation cycling exercise in people with multiple sclerosis with mobility disability. *Mult Scler Relat Disord* 2018;26:103-11.
20. Bowen J, Gibbons L, Ganas A, Kraft GH. Self-administered Expanded Disability Status Scale with functional system scores correlates well with a physician-administered test. *Mult Scler* 2001;7:201-6.
21. McCormack H, Horne D, Sheather S. Clinical applications of visual analogue scales: a critical review. *Psychol Med* 1988;18:1007-19.
22. McGuigan C, Hutchinson M. The multiple sclerosis impact scale (MSIS-29) is a reliable and sensitive measure. *J Neurol Neurosurg Psychiatry* 2004;75:266-9.
23. Costelloe L, O'Rourke K, Kearney H, et al. The patient knows best: significant change in the physical component of the Multiple Sclerosis Impact Scale (MSIS-29 physical). *J Neurol Neurosurg Psychiatry* 2007;78:841-4.
24. Cella DF, Dineen K, Arnason B, et al. Validation of the functional assessment of multiple sclerosis quality of life instrument. *Neurology* 1996;47:129-39.
25. Kroll T, Kehn M, Ho P, et al. The SCI Exercise Self-Efficacy Scale (ESES): development and psychometric properties. *Int J Behav Nutr Phys Act* 2007;4:34.
26. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Int Med* 2001;16:606-13.
27. Zarit SH, Reever KE, Bach-Peterson J. Relatives of the impaired elderly: correlated of feelings of burden. *Gerontologist* 1980;20:649-55.
28. Academy of Neurologic Physical Therapy. ANPT outcome measures recommendations (EDGE) – multiple sclerosis. Available at: <http://www.neuropt.org/practice-resources/neurology-section-outcome-measures-recommendations/multiple-sclerosis>. Accessed July 10, 2019.
29. Nooijen CF, Post MW, Spooren AL, et al. Exercise self-efficacy and the relation with physical behavior and physical capacity in wheelchair-dependent persons with subacute spinal cord injury. *J Neuroeng Rehabil* 2015;12:103.
30. Krause JS, Saunders LL, Reed KS, Coker J, Zhai Y, Johnson E. Comparison of the Patient Health Questionnaire and the Older Adult Health and Mood Questionnaire for self-reported depressive symptoms after spinal cord injury. *Rehabil Psychol* 2009;54:440-8.
31. Sakakibara BM, Miller WC, Orenczuk SG, Wolfe DL. A systematic review of depression and anxiety measures used with individuals with spinal cord injury. *Spinal Cord* 2009;47:841-51.
32. Scholten EW, Hillebregt CF, Keteaar M, Visser-Meily JM, Post MW. Measures used to assess impact of providing care among informal caregivers of persons with stroke, spinal cord injury, or amputation: a systematic review. *Disabil Rehabil* 2019;1-27.
33. Bailey R. Examining daily physical activity in community-dwelling adults with stroke using social cognitive theory: an exploratory, qualitative study. *Disabil Rehabil* 2019;33:1-9.
34. Anens E, Zetterberg L, Urell C, Emtner M, Hellström K. Self-reported physical activity correlates in Swedish adults with multiple sclerosis: a cross-sectional study. *BMC Neurol* 2017;17:204.

35. Katsavos S, Artemiadis AK, Zacharis M, et al. Predicting caregiving status and caregivers' burden in multiple sclerosis. A short report. *Neurol Res* 2017;39: 13-5.
36. Cohen J. *Statistical power analysis for the behavioral sciences*. New York: Academic Press; 1988.
37. Durlak J. How to select, calculate, and interpret effect sizes. *J Pediatr Psychol* 2009;34:917-28.
38. Cheng EM, Hays RD, Myers LW, Ellison GW, Beckstrand M, Vickrey BG. Factors related to agreement between self-reported and conventional Expanded Disability Status Scale (EDSS) scores. *Mult Scler J* 2001;7:405-10.