Cardiorespiratory and Muscle Metabolic Responses During Conventional Versus Motion Sensor-Assisted Strategies for Functional Electrical Stimulation Standing After Spinal Cord Injury

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Abstract: This is a case series study with the objective of comparing two motion sensor automated strategies to avert knee buckle during functional electrical stimulation (FES)—standing against a conventional hand-controlled (HC) FES approach. The research was conducted in a clinical exercise laboratory gymnasium at the University of Sydney, Australia. The automated strategies, Aut-A and Aut-B, applied fixed and variable changes of neurostimulation, respectively, in quadriceps amplitude to precisely control knee extension during standing. HC was an “on-demand” increase of stimulation amplitude to maintain stance. Finally, maximal FES amplitude (MA) was used as a control condition, whereby knee buckle was prevented by maximal isometric muscle recruitment. Four AIS-A paraplegics undertook 4 days of testing each, and each assessment day comprised three FES standing trials using the same strategy. Cardiorespiratory responses were recorded, and quadriceps muscle oxygenation was quantified using near-infrared spectroscopy. For all subjects, the longest standing times were observed during Aut-A, followed by Aut-B, and then HC and MA. The standing times of the automated strategies were superior to HC by 9–64%. Apart from a lower heart rates during standing (P = 0.034), the automation of knee extension did not promote different cardiorespiratory responses compared with HC. The standing times during MA were significantly shorter than during the automated or “on-demand” strategies (by 80–250%). In fact, the higher isometric-evoked quadriceps contraction during MA resulted in a greater oxygen demand (P < 0.0001) and wider arteriovenous oxygen extraction (P = 0.08) when compared with the other strategies. In conclusion, even though increased standing times were demonstrated using automated control of knee extension, physiological benefits compared with HC were not evident. Key Words: Spinal cord injury—Standing—Functional electrical stimulation—Exercise physiology—Muscle metabolism.

For patients with acquired spinal cord injury (SCI), electrical stimulation is a suitable means to elicit purposeful contractions of paralyzed muscles and promote increases of leg muscle mass (1,2). Among several types of functional electrical stimulation (FES) exercises, standing is one modality that has been investigated for many years. In a lifestyle limited to wheelchair confinement, the benefits of FES standing for SCI individuals are not just restricted to positive psychosocial outcomes (3). Physiologically, standing has also been reported to prevent orthostatic hypotension and circulatory hypokinesis (4–6). FES-evoked stance can be primarily achieved by stimulating the bilateral quadriceps muscles to produce knee extension. Glutei muscles can also be recruited to promote full hip extension and thereby improve posture (7). However, progressive quadriceps fatigue resulting in knee buckle often

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limits standing times. This phenomena of accelerated muscle fatigue during FES-evoked contraction require intensive muscle strength training. Without the use of orthotic devices, FES-evoked standing can be sustained for only a few minutes (8).

In general, subjects tend to apply more stimulation current than required during FES standing because they feel safer with “stiffer” legs, but this further accelerates muscle fatigue. Computer modeling and simulation strategies have been adopted to control FES-evoked standing using external sensors or through optimization of the input current. Several stimulation strategies have been deployed to maximize standing times before fatigue and subsequent knee buckle. The Parastep system (Sigmedics, Inc., Fairborn, OH, USA) utilizes a strategy whereby the user is required to press buttons mounted on a walking frame to increase the stimulation amplitude to the muscles (9). Mulder and colleagues used a strategy where once knee buckle had been detected, quadriceps stimulation was increased to the neurostimulator’s maximal amplitude (MA) and then ramped down until the next knee buckle event (10).

Following these early approaches, this study investigated two novel strategies to control quadriceps stimulation current based on kinematic feedback from four miniaturized motion sensors. These automated strategies were assessed against conventional hand-controlled (HC) operation of a neuromuscular stimulator and continuous supramaximal stimulation of leg muscles. The main outcomes of standing times to knee buckle, and underlying cardiorespiratory and metabolic responses were investigated.

**MATERIALS AND METHODS**

**Control strategies**

The first automated strategy (Aut-A) applied a step increment of 10 mA to quadriceps bilaterally when a knee flexion angle ($\theta_k$) higher than 10° (knee unlock) was detected. If $\theta_k$ was between 5° and 10° (knee extension), the stimulation amplitude was maintained. If $\theta_k$ returned/decreased below 5° (knee lock), the stimulation amplitude was ramped down by 5 mA over 2 s (2.5 mA/s) and then maintained. The second automated strategy (Aut-B) applied an identical criterion to define the state of knee flexion, but with a wider range of bilateral stimulation amplitude increases or decreases. At first knee unlock, the increment was 5 mA. If this increment was not sufficient to re-establish knee-locking, the subsequent increments were 10 mA. If this 10 mA increase was also unable re-establish knee lock, the next increment was 15 mA and so on. During knee lock, the stimulation was ramped down at the same rate as Aut-A (2.5 mA/s), but with a total amplitude decrease of half the value of the previous increment (Table 1). For both Aut-A and Aut-B strategies, following a change of stimulation amplitude, any increments were disabled for 1 s even if the knee remained unlocked. This interval of 1 s could only be shorter if the rate of knee buckle exceeded 10°/s and collapse appeared imminent. After standing up, the sensors were autocalibrated within the first 8 s of stable stance to determine the initial knee lock position (0° of flexion).

For the conventional HC strategy, the stimulation amplitude over the quadriceps muscle was increased via button presses in steps of 10 mA by the therapist using visual inspection of the state of knee lock. An MA stimulation strategy was also trialled as a nonfeedback “control” condition, whereby the quadriceps were continuously stimulated at 180 mA, enforcing constant isometric knee lock until fatigue-failure.

For Aut-A, Aut-B, HC, and MA stimulation strategies, FES over the glutei muscles was maintained at 80% of the amplitude of the quadriceps muscles. In this study, neurostimulation strategies were considered bilateral, and a single-leg change of knee flexion was considered as the trigger for both limbs.

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**FES system**

The FES system used in this study stimulated quadriceps and glutei muscles via self-adhesive surface electrodes (33 Hz, 150 µs) (11). Four compact motion sensors (12) were strapped onto the subject’s thighs and shanks. The sensors were sampled at 10 Hz and provided absolute joint angles in the

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**TABLE 1. Modulation of quadriceps stimulation amplitude using the automated strategies**

<table>
<thead>
<tr>
<th>State</th>
<th>Knee angle ($\theta_k$)</th>
<th>Aut-A</th>
<th>Aut-B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee unlock</td>
<td>$\theta_k \geq 10^\circ$</td>
<td>↑ Step up of 10 mA</td>
<td>↑ Step up of 5, 10, 15, 20 mA</td>
</tr>
<tr>
<td>Knee extension</td>
<td>$5^\circ &gt; \theta_k &gt; 10^\circ$</td>
<td>No change</td>
<td>No change</td>
</tr>
<tr>
<td>Knee lock</td>
<td>$\theta_k \leq 5^\circ$</td>
<td>↓ Ramp down 5 mA at 2.5 mA/s</td>
<td>↓ Ramp down 50% of previous increment at 2.5 mA/s</td>
</tr>
</tbody>
</table>

Described in greater detail in the text.
sagittal plane with respect to the direction of gravity. Knee angles were defined as the difference in the angular data between shank and thigh segments. A hand-held PC (Cassiopeia EG-800, Casio, Inc., Tokyo, Japan) was utilized to control the neuromuscular stimulator and to collect data from the sensors.

Study participants
Four AIS-A thoracic paraplegics (lesion level: T4–T11; age: 54 ± 10 years; body mass: 65 ± 13 kg; postinjury duration: 9 ± 5 years) participated in this study. They were all experienced FES users, with at least 24 weeks of quadriceps strength training by means of FES-evoked exercise. Being sensorimotor “complete” SCI, none could evoke voluntary muscle contractions sufficient to promote standing. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research.

Testing protocol
Each subject undertook 4 days of assessments with three trials per day and recovery intervals of 5 min between trials. Based on pilot studies that we conducted, the 5-min recovery period was considered sufficiently long to enable reasonable standing times on second and third trials, with a sensible approximation to possible occupational or home environment tasks. The tests consisted of 1 day for each of the four strategies: Aut-A, Aut-B, and HC were performed in a randomized order, and MA was undertaken on last day due to its high fatigue rate. Tests were not carried out on consecutive days, but inter-test intervals no longer than 2 days were adhered to. Each trial was terminated when one of the knees buckled greater than 30°.

Subjects S1 and S2 used a walking frame for balancing, while S3 and S4 used an elbow frame due to their poorer abdominal strength. This was chosen to help them keep their hips stabilized during upright posture. As a safety measure, all subjects wore a harness system to avert injury in case of a severe knee buckle and collapse. We acknowledge a limitation in contrasting Aut-A, Aut-B, HC, and MA, as we did not measure upper limb loading forces among the subjects, and this could have affected our findings.

Measurements
During stance, heart rate (HR, beats/min) was measured via three-lead electrocardiogram (Portoscope CR55, Cardiac Recorders Ltd., London, UK). During standing, breath-by-breath expired gases were collected via open-circuit spirometry (MedGraphics CPX-D system, Medical Graphics Corp., St Paul, MN, USA). Both HR and oxygen uptake (VO₂, mL/min) were smoothed using an eight-breath rolling average, and the resultant values were obtained from the average of 30 s of measurement, at rest, and at the end of the third standing trial. In addition, cardiac output (Qc, L/min) was assessed at rest and at the end of the third standing trial via the Defares CO₂-rebreathing technique (13). Left ventricular stroke volume (SV, mL/beat) and arteriovenous oxygen extraction [C(a-v)O₂, mLO₂/ mL] were calculated from HR and Qc, and the Fick equation, respectively. Cardiorespiratory data were presented herein as “net values” (i.e., the differences between exercise responses at the end of third standing trial and rest) to account for disparate intersubject differences in resting responses.

Quadriceps muscle oxygenation was measured via near-infrared spectroscopy (NIRS) using a spatially resolved time domain NIRS system (ISS 96208 Oximeter, ISS, Inc., Champaign, IL, USA). With the NIRS probe placed over the middle section of the subject’s left quadriceps muscle, the ratio of oxyhemoglobin (HbO₂) to the total hemoglobin (THb) (% oxygen saturation, O₂Sat) was estimated. The NIRS data were normalized among subjects via arterial occlusion of the upper thigh using an inflatable pressure cuff (E20 & AG101, D.E. Hokanson, Inc., Bellevue, WA, USA) set to 270 mm Hg. This super-systolic arterial occlusion was maintained for approximately 10 min or until any further decrease in O₂Sat had ceased. The normalized 100% O₂Sat was considered the mean value of O₂Sat obtained at rest prior to the arterial occlusion. The nadir of muscle oxygen saturation during occlusion was normalized as % O₂Sat, representing the lowest value of muscle hypoxia (14).

Statistical analysis
Due to the small sample size employed in this case series design, nonparametric analyses were employed to determine whether there were differences between standing times or physiological responses among the proposed strategies. To transform the data from continuous to discreet before nonparametric analyses, outcomes were coded as “true” or “false.” For each comparison, chi-squared analysis was employed to ascertain the probability of a nonrandom outcome (i.e., not 50–50) above the 99% confidence limit (P < 0.01) for statistical significance. In the text, we have reported direct probabilities of our primary outcome measurements (e.g., P = 0.0005).
RESULTS

For all four subjects, Aut-A promoted the longest standing times followed by Aut-B, HC, and then MA ($P = 0.0005$) (Fig. 1). In relation to HC, standing times were longer employing Aut-A than for Aut-B (Table 2). Furthermore, standing times were significantly longer for Aut-A, Aut-B, and HC compared with MA.

To better understand why Aut-A promoted longer standing times than Aut-B, the patterns of Aut-B’s variable stimulation increases were investigated. In relation to Aut-A which produced fixed stimulation increases of 10 mA, the incremental steps of Aut-B were progressively higher than 10 mA toward the end of standing for all subjects ($P = 0.004$), suggesting greater muscle recruitment and fatigue generation with that automated strategy (Fig. 2).

Despite the fact that longer standing times were evoked using Aut-A and Aut-B, the subjects’ HRs remained lower during these strategies compared with HC ($P = 0.03$) (Fig. 3). However, the shortest standing times associated with MA did not necessarily imply the highest HRs in relation to the remaining strategies ($P = 1.0$). In contrast, net cardiac outputs were lower for MA ($P = 0.004$), although differences between the automated strategies and HC were not significant ($P = 0.48$). There were no differences of oxygen uptake between automated and nonautomated strategies (i.e., Aut-A, Aut-B vs. HC, $P = 1.0$; Aut-A, Aut-B, HC vs. MA, $P = 0.56$).

**TABLE 2. Percentage differences of standing times in relation to nonautomated strategies**

<table>
<thead>
<tr>
<th></th>
<th>Gain in standing times compared with HC (%)</th>
<th>Total standing time in relation to MA (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Aut-A</td>
<td>Aut-B</td>
</tr>
<tr>
<td>S1</td>
<td>29</td>
<td>17</td>
</tr>
<tr>
<td>S2</td>
<td>49</td>
<td>25</td>
</tr>
<tr>
<td>S3</td>
<td>64</td>
<td>9</td>
</tr>
<tr>
<td>S4</td>
<td>39</td>
<td>10</td>
</tr>
</tbody>
</table>

**FIG. 1.** Total standing times for automated and nonautomated strategies. All four subjects stood for longer periods with Aut-A, followed by Aut-B, HC, and then MA. Data comprise the sum of the three standing trials.

**FIG. 2.** Aut-B’s stimulation increases after a knee buckle ($\theta_k \geq 10^\circ$).
SV revealed greater differences between the subjects who stood with a walking frame (S1 and S2) compared with those subjects who stood with an elbow frame (S3 and S4) (Fig. 4). There were no apparent differences of SV among the standing strategies (Aut-A, Aut-B vs. HC, P = 0.48; Aut-A, Aut-B, HC vs. MA P = 1.0). Systemic arteriovenous oxygen extractions were higher during MA (P = 0.08) than for all the other strategies suggesting greater leg metabolism, but were not different between Aut-A, Aut-B, or HC (P = 0.48).

Among the standing strategies, MA demonstrated the largest decline of quadriceps oxygen saturation (P < 0.0001) compared with the others, supporting the C(a-v)O₂ data (Fig. 5). For the automated strategies, Aut-A and Aut-B did not promote differences of O₂Sat when compared with HC (P = 0.41).

Notably, a poor correlation was observed between mean O₂Sat values and C(a-v)O₂ at the end of third standing trials (r = −0.36), even including MA.

**DISCUSSION**

The feasibility of automating the control of knee extension was clearly demonstrated as superior to the conventional HC approach. For Aut-A and Aut-B, the modulation (i.e., automated increase or decrease) of quadriceps neurostimulation amplitude to avert knee buckle or knee hyperextension significantly improved standing times compared with HC and MA (by 80%–250%; Table 2). The shorter standing times of Aut-B in relation to Aut-A could have been caused by the numerous stimulation increments greater than 10 mA observed during the latter approach, which likely increased muscle fatigue late in standing. Even though MA may be considered the most practical strategy as it required neither sensors nor user operation to maintain upright mobility, its physiological drawbacks were translated into functional shortcomings, due to very short observed standing times when compared with Aut-A, Aut-B, and HC.

The shortest standing times during MA were probably due to the greater isometric quadriceps contraction forces evoked by continuous stimulation at very high (180 mA) current amplitudes. Supporting this view, the MA strategy demonstrated the highest arteriovenous oxygen extractions at the lowest oxygen saturations in the stimulated quadriceps muscles. The physiological explanation for this outcome might be that more muscle fibers were recruited (and recruited earlier) by MA, thereby increasing quadriceps oxygen demand. A degree of anaerobiosis can also not be ruled out as high muscle contraction forces reduce arterial blood flow, resulting in greater muscle hypoxia and earlier fatigue.

In contrast, oxygen saturation levels during the automated strategies and HC were higher than during MA. The slower quadriceps stimulation increases during Aut-A, Aut-B, and HC certainly recruited muscle fibers more gradually compared with MA, probably allowing a greater blood supply...
to working muscles in relation to the oxygen requirement of standing. Also, it is important to consider that the fatigue of the electrically stimulated quadriceps may have occurred due to the accommodation of motor nerve thresholds, regardless of available oxygen supply via arterial blood inflow (15).

Interestingly, a poor correlation was noted between mean O2Sat and C(a-v)O2 at the end of third standing trials even including the purported strong association between the two variables for MA. Quadriceps O2Sat may not always reflect systemic arteriovenous oxygen extraction because (i) the former is a highly localized measure of muscle oxygenation while the latter is a measure of systemic oxygen extraction including circuits in other parts of the body, including upper limbs, and (ii) NIRS reflects light absorbency of Hb chromophores, not strictly metabolic events in muscle.

Unlike HR, which is a fast-response cardiorespiratory variable (response in seconds under parasympathetic neural control), cardiac output is a relatively time-dependent variable because it is a product of fast-responding HR and more slowly accommodating SV. Accordingly, S1’s high HR did not necessarily result in greater cardiac outputs in relation to other subjects. Most likely, S1’s high HR occurred as compensation for his decreased SV due to venous pooling. Also, it is important to consider that the lowest cardiac outputs during MA could be related to the shorter standing times and, these, to the lower inflow of arterial blood due to the quadriceps isometries (16,17). Even with the longer standing times during the automated strategies, these did not promote different cardiorespiratory responses (VO2, Qc) when compared with the HC strategy.

With regard to the amplitude values of the incremental steps of Aut-A and Aut-B, we could have applied step increments based on a percentage of the stimulation amplitude required to generate the subject’s maximal quadriceps force. However, because it was known that the relationship of muscle force versus stimulation dosage loses a significant portion of its linearity after SCI (18,19), predetermined values for incrementing stimulation amplitude were applied in this study. This was a practical measure as well, as Aut-A and Aut-B could be applied to different subjects without any previous setup of stimulation parameters.

**CONCLUSION**

In the research or clinical environment, widely accepted and fail-safe control strategies for functional electrical stimulation standing are yet to be devised. The event-driven strategies proposed in this study may be of relevance for future efforts in the creation of FES systems with sufficiently high standards of safety and performance. This will be a fundamental step for the greater acceptance of the FES devices within the spinal cord-injured community.

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**Conflict of Interest:** The authors declare that they do not have any financial or personal relationships with other people or organizations that could have inappropriately influenced this manuscript.
REFERENCES


**FIG. 5.** Quadriceps oxygen saturation across different stimulation strategies during first, second, and third standing trials. Although MA provided the lowest O2Sat values ($P < 0.0001$), the automated strategies did not promote greater O2Sat values in relation to HC ($P = 0.41$).


