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Technical Evaluation and Clinical Feasibility

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A Robot based Hybrid Lower-Limb System for Assist-As-Needed Rehabilitation of Stroke Patients: Technical Evaluation and Clinical Feasibility

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ABSTRACT

Background: Although early rehabilitation is important following a stroke, severely affected patients have limited options for intensive rehabilitation as they are often bedridden. To create a system for early rehabilitation of lower extremities in severely affected patients, we have combined the robotic manipulator ROBERT® and EMG-triggered FES and developed a novel user-driven Assist-As-Needed (AAN) control approach. The method is based on a state machine that can detect user movement capability and provide different levels of assistance, as required by the patient (no support, FES only, and simultaneous FES and mechanical support). **Methods:** To technically validate the system, we tested 10 able-bodied participants who were instructed to perform specific behaviors to trigger the desired system states while conducting knee extension and ankle dorsal flexion exercise. In addition, the system was tested on two stroke patients to establish the clinical feasibility. **Results:** The technical validation showed that the state machine correctly detected the participants' behavior and activated the target AAN state in more than 96% of the exercise repetitions. The clinical feasibility test showed that the system successfully recognized the patients' movement capacity and activated assistive states according to their needs, providing the minimal level of support required to perform the exercise successfully. **Conclusions:** The system was technically validated and preliminarily proven clinically feasible. The present study shows that the novel system can be used to deliver exercises with a high number of repetitions while engaging the participants' residual capabilities through an effective AAN strategy.

1. Introduction

Rehabilitation is important to improve motor function for stroke survivors [1–3]. However, despite rehabilitation, approximately 35% of stroke survivors with a degree of leg paresis show no motor recovery [4]. For individuals who are severely affected by stroke and are confined to a bed or wheelchair in the early phase, treatment options for intensive rehabilitation are limited [1]. However, during this period [5], the neural system is especially primed for recovery through neuroplastic mechanisms [5, 6], and therefore, enabling these patients to exercise despite severe limitations could strongly facilitate their rehabilitation [6–8].

Maier et al. 2019 [9] have identified 15 principles of exercise that are important for optimizing the rehabilitative outcome, including massed practice, optimal dosage, progressive increase in difficulty, provision of multisensory stimulation, and explicit and implicit feedback [9]. Based on the work by Maier et al. 2019, an ideal exercise program should incorporate frequent and intensive sessions, with time to rest in-between the sessions [9]. Furthermore, the exercise difficulty should be tailored to the patients'

capabilities, and the exercise should integrate multisensory stimulation, as this appears to facilitate/modulate sensorimotor recovery [9]. Finally, the exercise should incorporate feedback to the patient, both regarding their performance (e.g., accuracy in hitting a target) and how to improve in the next trials (e.g., “lift your foot higher”) [9].

Robotic interventions may provide a suitable exercise paradigm for patients in the early stages of rehabilitation, which encompasses the aforementioned principles for effective exercising [9]. A common approach to delivering robotic training is to repeatedly move the limbs of the patients. This allows performing many repetitions even for individuals with severe disabilities. However, in some cases, the patients do not actively participate in the exercise, which can significantly limit the effectiveness of rehabilitation [10, 11]. Even when patients actively participate during robotic training, they may still exert less effort than during conventional therapy, reducing the effectiveness of the exercise - a behavior commonly called “slacking” [11].

Functional electrical stimulation (FES) is another well-established approach for the rehabilitation of patients with severe mobility impairments [12–14]. FES relies on the delivery of electrical pulses to activate motor nerves, which allows patients to generate forceful muscle contractions, even if they have little to no voluntary muscle control. However,

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FES is associated with early onset of fatigue [12, 15] and poor control of force [16], limiting the quality and amount of exercising that can be provided to the patient using this technology. Additionally, although actively stimulating neuromuscular tissue, FES does not necessarily involve active movement initiation by the patient, although this is one of the key principles promoting the improvement of motor function after stroke [17]. To enable this, triggering of FES could be based on voluntary effort by the patient, and this can be implemented by monitoring and detecting muscle activation.

Importantly, by combining FES and robotics, one can mitigate the drawbacks that characterize these technologies when they are applied individually. For instance, FES can be used to counteract the patients' passivity during robotic exercising, as it can ensure muscle activation. Likewise, a robot can provide precise force control and delay the onset of muscle fatigue [18, 19]. Additionally, both passivity and early fatigue can be reduced further by implementing the so-called assist-as-needed (AAN) paradigm. In this approach, the intervention automatically adapts to the patients' capabilities, supports them only to the degree that is necessary, and allows them to perform the movements by themselves or activate their muscles as much as they can. AAN can be provided using different strategies, for instance, by adjusting the amount of support to complete the exercise [20–22], or by providing corrective forces only when the patient's movement deviates significantly from the reference trajectory (a so-called virtual tunnel) [22–24]. As shown in the present study, an additional advantage of a hybrid system combining FES and robotics is that AAN can also be implemented by changing the support modality, e.g., using either robot or FES or both methods simultaneously to provide assistance.

Previous exercise systems for patients with severe limitations in their lower extremities include a resistive exercise device using a flywheel [25], and a robot providing cyclic movements comparable to natural gait (NEUROBike) [26]. Both devices may be used by patients while in a bed, but neither is hybrid and thus do not profit from the benefits of combining robotics and FES [25, 26]. Additionally, since these devices do not incorporate AAN, they do not actively and continuously consider the patient's current capabilities [25, 26].

In this study, we show that by combining robotics, FES, and AAN strategies, it is possible to create a system for early, intensive rehabilitation of severely affected patients, usable while the patients lay in a bed or on an examination bench. This work builds upon a previous study where the robotic manipulator ROBERT® (Life Science Robotics ApS) was combined with EMG-triggered FES to provide hybrid support for neurorehabilitation [27]. In the present work, the original system was extended to incorporate a novel AAN strategy that combines support modalities to extend the duration and scope of the training. The novel system was developed as a hybrid solution to limit the slacking effect of pure robotic interventions, ensure active and voluntary involvement of the patients and their muscles in the exercise, delay the onset of fatigue, and apply mechanical

and/or electrical assistance according to the patient's own capability. Here we describe the overall system, present its technical validation in able-bodied participants, and preliminarily assess its clinical feasibility by testing the system on two stroke patients.

2. Methods

The objective of this work was to develop a rehabilitation framework which provides lower limb movement assistance to severely affected stroke patients while utilizing the patients' own volition and effort to promote recovery. The system was therefore designed to deliver only the level of assistance that the patient needed to complete the exercise. This was achieved by assessing the patients' own effort at each repetition of the exercise to determine which assistance level to provide. The assistance levels were implemented by activating and/or combining the available support modalities, namely, no support (patients' volitional effort), FES delivery, mechanical assistance, or both (as described in the section AAN state machine). Finally, the system was designed to provide exercises of varying difficulty and help the patients adhere to a specific movement trajectory to promote motor learning [9].

2.1. System components

The developed system comprised the components listed below. Note that different EMG and FES systems were used during the technical validation in able-bodied participants and the clinical feasibility tests in patients, but the system setup, calibration, and functioning were identical during both assessments. The system was composed of:

1. The rehabilitation robot ROBERT®.
2. An FES system with disposable electrodes (Durastick Premium, CefarCompex).
 - (a) Technical validation: NoxiSTIM, JNi Biomedical, Denmark.
 - (b) Clinical feasibility: RehaStim, Hasomed, Germany.
3. An EMG amplifier with Ambu® Neuroline 720 electrodes.
 - (a) Technical validation: Custom-made EMG amplifier, Aalborg University, Denmark.
 - (b) Clinical feasibility: RehaIngest, Hasomed, Germany.
4. A PC running the control state machine and communicating with ROBERT®, the EMG amplifier and the FES device.

Note: In the clinical feasibility test, the stimulator and EMG-recorder differed from the ones used in the technical validation. During the technical validation, the system overall was a prototype whereas the system used in the clinical feasibility test, was a matured version of the system.

ROBERT® is a seven-degree-of-freedom robotic manipulator that can move the lower limbs of a patient in a lying position [27–29] (see figure 1). In the present work,



Figure 1: ROBERT® is a seven-degree-of-freedom robotic manipulator that can move the lower limb of a patient in a lying position. The participant's leg was attached to the end effector of ROBERT® through a foot brace.

the robot produced a resistive force opposing the movement of the participant to impose an active and engaging resistive exercise, while compensating for the pull of gravity on the participant's leg by providing vertical assistive force. In addition, the robot enforced a virtual tunnel, which prevented excessive radial deviation from the defined trajectory, by applying a corrective force proportional to that deviation. Furthermore, in the novel system, the robot was also programmed to provide mechanical assistance to produce the movement when needed, as explained later. Finally, the system recorded the position of the end effector at a sampling frequency of 50 Hz, to estimate the velocity of the movement.

The electrical stimulation frequency and pulse duration were fixed at 30 Hz and 300 μ s [12], respectively, while the pulse amplitude was adjusted individually for each muscle and participant as described in the section System calibration.

The recorded EMG was used to detect the patient's voluntary effort (intention to move) and was implemented as a "trigger" in the AAN state machine. The EMG was recorded in a differential configuration at 1000 Hz and digitally filtered using a 4th order Butterworth bandpass filter (f_L : 20 Hz, f_H : 40 Hz), and a 2nd order Butterworth notch filter (f_L : 48 Hz, f_H : 52 Hz).

ROBERT®, EMG and FES systems were controlled by a state machine described in the section AAN state machine and implemented on a host PC. The PC was connected to ROBERT® through a LAN connection, and to the FES system and the EMG amplifier through a data-acquisition and signal generation device (National Instruments USB-6212) during the technical validation. In the clinical feasibility

tests, the PC was connected to the EMG amplifier and the FES system directly through a USB connection.

The system setup required attaching the participant's foot to the end effector of ROBERT® through a foot brace, mounting two stimulation electrodes and three EMG recording electrodes, and connecting them to the stimulator and the EMG amplifier, respectively.

2.2. System calibration

The system requires several calibration steps. Firstly, the exercise to be administered must be defined by manually guiding the end effector of ROBERT® through the desired trajectory, while the lower leg of the participant is attached to the robot's end effector through the custom brace. A team of physiotherapists and doctors determined that knee extension (KE) and ankle dorsal flexion (ADF) were the two most relevant exercises to focus on during the first tests of the system, due to their relevance to standing and walking abilities.

Secondly, the resistance of ROBERT® and the amplitude of FES were calibrated according to the procedure defined in Leerskov et al. 2022 [28]. In brief, the resistance of ROBERT® was set to a level that was enough to compensate for gravity, i.e., to avoid the participants' leg falling downwards during the KE exercise. Then, the amplitude of FES was set high enough to allow completing the exercise trajectory at this resistance level. If the participant could not tolerate this stimulation amplitude due to discomfort, the resistance of ROBERT® was lowered, and the stimulation intensity recalibrated.

Finally, a threshold for the EMG-trigger was determined. The threshold methods developed for the system, referred to as 'SDx2' and 'SDx3', were tested in stroke patients and presented previously by Rikhof et al. 2022 [29]. In summary, the thresholds were calculated based on three seconds of resting EMG, recorded while the participants relaxed their leg while supported by the robot, in the starting position of the exercise to be performed. The thresholds were then set to the mean of the three seconds of resting EMG, plus two (SDx2) or three (SDx3) times the standard deviation of the resting EMG [29]. In the present work, the 'SDx3' was used by able-bodied participants during the technical validation while 'SDx2' was used by stroke patients during the clinical feasibility test. The calculation of the EMG-trigger threshold switched from the 'SDx3' to the 'SDx2' method in the clinical feasibility test, partly due to the results of the technical validation, and partly due to the results obtained by Rikhof et al. 2022 [29].

During system operation, an EMG-trigger was generated if the mean of the rectified EMG in two out of three consecutive 50-ms windows was above the adopted threshold, and this indicated the participants' intention to move. Additionally, the movement velocity was estimated by differentiating the position of the end effector, recorded by ROBERT®, and then smoothing the obtained signal using a 10-sample moving average filter as in Leerskov et al. 2022 [28].

2.3. AAN state machine

The level of support to be provided to the user was determined by an AAN state machine (figure 2) and assessed during each repetition of the exercise, as explained below.

If the participant could complete the exercise repetitions voluntarily, they were not assisted (AAN state: *Vol*) in order to maximize the use of their own resources. If a participant could not complete the exercise, FES was administered (AAN state: *Trig* and *Auto*) to produce the required force to complete the repetition. The *Trig* state was activated when the participant could initiate a movement but was unable to complete it, while the *Auto* state was activated when the participant was too weak to even initiate a movement. FES was chosen as the first level of assistance because it engages actively the participant's own muscles while also producing substantial afferent input, both directly by stimulating the sensory fibers and indirectly through the induced movements. If FES alone was insufficient to complete the exercise repetition, mechanical assistance was provided by the robot in addition to FES (AAN state: *Mech*), as the second level of support. The mechanical assistance was provided by disabling the resistance of ROBERT® opposing the movement and then activating the position controller that moved the participants' limb towards the end of the desired trajectory. Using such progressive assistance, from no support to FES only and then combined FES and mechanical support, the participants were guaranteed to accomplish the exercise, while being encouraged to use as much remaining capacity as possible to initiate and/or perform the movement actively. When the participant's leg reached the end of the exercise trajectory, the assistance was deactivated, and the

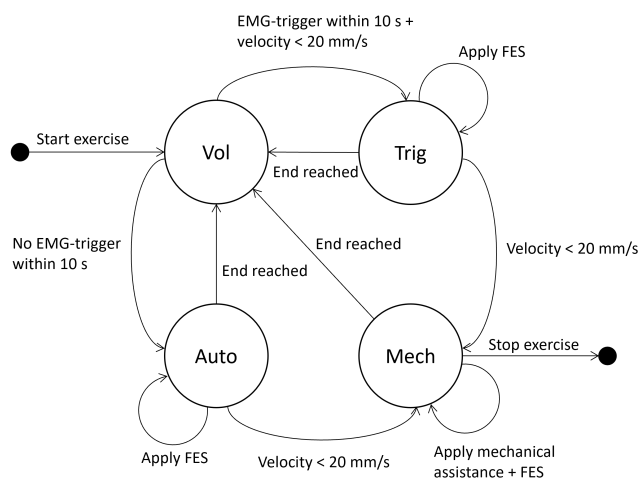


Figure 2: The state machine for the control of the assist-as-needed training protocol implemented in the system. The circles indicate the four different states. 'End reached' refers to the end of the exercise trajectory. Note that once the end of the exercise trajectory has been reached, FES is turned off and the robot moves the leg to the start position of the exercise, unless the exercise is ended. *Vol*: Voluntary, *Trig*: EMG-triggered FES, *Auto*: Auto-triggered FES, and *Mech*: Mechanical assistance.

robot moved the leg to the starting point of the trajectory. A new repetition was then administered, unless the preset number of repetitions was reached (end of exercise).

To determine the level of assistance required by the participant, the state machine monitored the EMG-trigger and the velocity of the end effector (see section 2.2). The EMG indicated if the participant actively contributed to the exercise or at least attempted to move, and the movement velocity was used to determine if the participant could move the leg along the trajectory at a given assistance level. During technical validation, a successful movement was defined as the ability to maintain an average velocity equal to or higher than 20 mm/s. In the clinical feasibility test, the minimum velocity was lowered to 5 mm/s and 1 mm/s, for KE and ADF, respectively, to reflect the reduced motor capabilities of the patients, as an initial test on stroke patients revealed that the velocity thresholds were unnecessarily high, and the *Auto* state wait time was assessed as being inappropriately long for clinical application. Hereafter, these values will be referred to as the velocity thresholds.

Vol was the default state for each new exercise repetition, and it was active as long as the participant could perform the exercises voluntarily by their own effort. In this state, the system monitored both the EMG-trigger and the movement velocity. If the average movement velocity of the participant decreased below the velocity threshold consistently during a 2-s interval, this was considered as an indication that the participant could not move using their own effort. If this coincided with the detection of an EMG-trigger, the state machine progressed to the *Trig* state, and FES was administered. If, while in the *Vol* state, the participant could not generate an EMG-trigger within a 10-s interval (5-s interval in the clinical feasibility test), this was interpreted as a sign of excessive weakness or fatigue, and the state machine transitioned to the *Auto* state and applied FES.

If the average movement velocity was below the velocity threshold consistently for more than 2 s while FES was being administered (*Auto* or *Trig* states active, see figure 2), the state machine transitioned into *Mech* state, and the robot provided mechanical assistance in addition to FES.

2.4. Experimental procedure

Two experiments were conducted, namely, a technical validation performed on able-bodied participants at Life Science Robotics ApS, Aalborg, Denmark, and a preliminary clinical feasibility test conducted on two stroke patients, at Roessingh Research and Development, Enschede, the Netherlands. Both experiments were conducted according to the Helsinki Declaration and the experiments were approved by the local ethical committees, as explained below.

2.4.1. Participants

Ten able-bodied volunteers were recruited to participate in the technical validation (five males, mean age: 28.3 ± 5.5 years). The inclusion criteria were that they had no known neurological or muscular disease. Volunteers were excluded if they (1) were pregnant, (2) had implanted devices e.g., a pacemaker, (3) lacked the ability to cooperate, or

Table 1

Overview of patient characteristics. LE: Lower Extremity.

	Time since stroke (days)	Fugl-Meyer Assessment LE Score	Motricity index LE
Patient 1	29	3	0
Patient 2	39	16	39

(4) were diagnosed with cognitive deficits. The study was approved by The North Denmark Region Committee on Health Research Ethics (N-20210015) and all participants signed informed consent forms before inclusion.

Data from two patients (two males, mean age: 47.5 ± 2.1 years) related to AAN-state progression and fatigue scores were taken from a more comprehensive clinical feasibility study with additional participants (to be reported separately), to assess the initial feasibility of the AAN approach in stroke patients. Their characteristics and their performance during the clinical feasibility test are shown in table 1. Stroke survivors were recruited if they (1) had a (sub)acute stroke, and (2) hemiparetic lower extremity. Stroke survivors were excluded from the clinical feasibility study if they (1) had pre-morbid disability of the lower extremity, (2) skin lesions at the hemiparetic leg, (3) a pacemaker, (4) contraindications for mobilization, (5) severe cognitive impairments, or (6) were pregnant. The clinical study was approved by the METC East-Netherlands (NL76919.091.21), and the patients signed informed consent forms before inclusion.

2.4.2. Participant preparation

The participants were lying on a medical bed and their lower leg was attached to the end effector of ROBERT® through a foot brace (see figure 1). In able-bodied participants, the right leg was attached to the robot, regardless of their dominant side. Patients used their most affected leg.

To obtain KE using FES, the anode (8 x 13 cm) was placed at approximately 3 cm from the patella and centered on the mediolateral aspect of the thigh [30, 31]. The cathode (8 x 13 cm) was placed as proximal as possible on the thigh, with the electrode's medial side, aligned with the center of the anode to activate the rectus femoris and vastus lateralis muscles (figure 3A) [30, 31]. To generate ADF, the cathode (3.2 cm diameter) was placed on the muscle belly of the tibialis anterior, approximately 5 cm distal to the head of the fibula and close to the tibia [31, 32]. The anode (4 x 6 cm) was placed halfway between the head of the fibula and the lateral malleolus, with the shorter medial side close to the tibia (figure 3B) [31, 32]. For both KE and ADF, the oval electrodes were positioned with the shorter side parallel to the muscle fibers.

Three EMG electrodes were placed in sequence approximately in the middle between the stimulation electrodes relevant to the exercise, with the center electrode serving as the reference in able-bodied participants (figure 3A and 3B). In stroke patients, however, the reference electrode was placed on the patella.

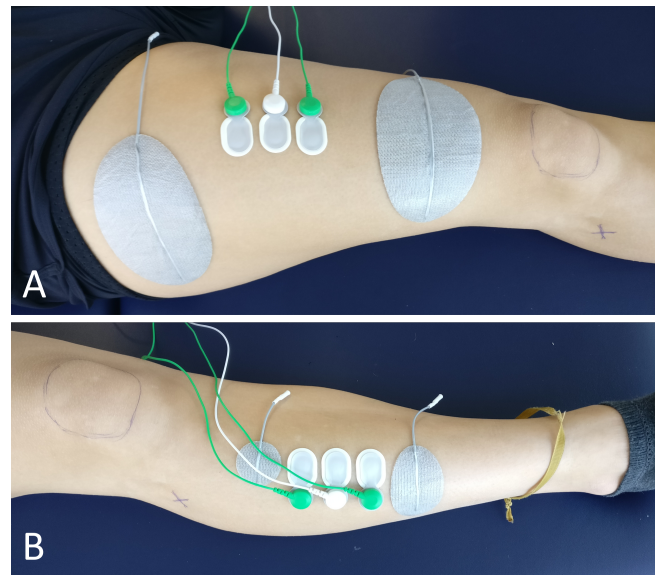


Figure 3: An overview of the two electrode configurations used for KE and ADF, respectively. A – For KE, the electrodes were placed medio-laterally on the thigh near the patella, and proximolaterally. B - For ADF, the electrodes were placed on the muscle belly of the tibialis anterior, and halfway down the shank. For both KE and ADF three EMG electrodes were placed on a line between the stimulation electrodes. The patella is outlined with a circle, and the head of the fibula is marked with a cross.

After mounting all electrodes, the calibration steps described in the section 2.2 were performed. For KE, the desired trajectory started with the participant's or patient's leg at roughly 90 degrees hip and knee flexion and ended with a fully extended leg. For ADF, the desired trajectory started with the participant's or patient's ankle as extended as comfortably possible and ended with their ankle as flexed as comfortably possible.

2.4.3. Technical validation

The experiment consisted of a single session lasting approximately two hours per participant. The able-bodied participants were informed that the four different states (*Vol*, *Trig*, *Auto*, and *Mech*) would be tested and in which order. The participants were asked to adopt a behavior that would trigger the state transitions necessary to end in the target state. Each state was tested a total of 20 times in bouts of five repetitions, across four trials in a randomized order (see randomisation scheme in figure 4), using the following procedure:

- *Vol*: Participants exercised using their own voluntary effort, as they felt natural.
- *Trig*: Participants were asked to produce a small movement (KE / ADF) or contraction to generate sufficient EMG to activate the EMG-trigger and then relax. Such behavior activated the transition from *Vol* to *Trig* state, which resulted in the administration of FES.

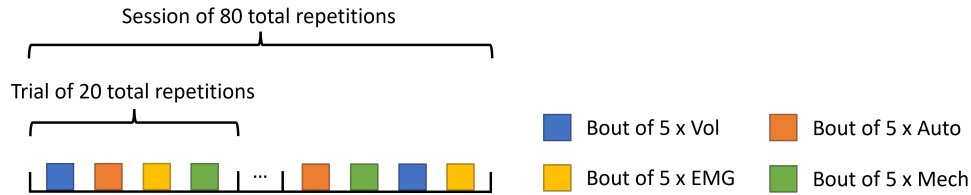


Figure 4: Overview of randomization of state targets during the technical validation. Each colored block corresponds to five repetitions of a specific state. Each trial consisted of four blocks (20 repetitions), and the whole session consisted of four trials for KE and four for ADF (80 repetitions each, 20 per state).

- *Auto*: Participants were instructed to relax. Eventually, the 10-s time limit for detecting the EMG-trigger was exceeded, triggering the *Auto* state and the administration of FES.
- *Mech*: Participants were asked to relax (same as *Auto*). The stimulator was turned off, and therefore although the FES was “activated” when the system progressed into *Auto* state, the stimulation was not delivered, and no movement was generated. This eventually led to the triggering of mechanical assistance.

After completing 20 repetitions of each state for KE, the same procedure was repeated for the ADF exercise.

2.4.4. Clinical feasibility test

The clinical feasibility test consisted of a single session per patient, which lasted approximately 2.5 hours.

During the session, the patients performed up to 20 repetitions (depending on their capability) of active movements without any assistance, to assess their status. Thereafter, two trials of up to 30 repetitions of both KE and ADF were administered, with the state machine active. The patients were instructed to exercise using their own efforts, without advising them to adopt any specific behavior – and thus, every change in the state of the system was due to the changes in the patients’ capability.

Following each trial of 30 repetitions, the patients were asked to rate how fatigued they were after exercising with the system. They used a VAS scale from 0-10, with “0” corresponded to “not fatigued at all”, and “10” to “the most fatigued imaginable”.

2.4.5. Outcome measures

During the two experiments, data were continuously recorded by the system. The collected data comprised the AAN state transitions for each repetition, the EMG signals, the velocity of the end effector, and the timestamps for state transitions.

The main outcome of the technical validation was the accuracy of the AAN state machine in correctly transitioning to the target state. The accuracy of the AAN state machine was obtained by comparing the target state instructed to the participants with the final state achieved by the system at the end of the repetition and calculating the percentage of matches. As the AAN state machine was programmed to be

progressive in terms of support, as explained in the section *AAN state machine*, only the final state was considered when calculating the accuracy. For each state, the sensitivity and precision of transitions were additionally calculated. The sensitivity was calculated as: $TP/(TP + FN)$, where TP indicates true positives and FN false negatives of a given state. The precision was calculated as: $TP/(TP + FP)$, where FP denotes false positives of a given state.

In the clinical feasibility test, the main outcome was the progression of AAN states. The values 1 to 4 were assigned to *Vol*, *Trig*, *Auto*, and *Mech* states, respectively, and a line was fitted to these values in order of exercise repetitions. Therefore, the fitted line would have a positive slope, if the states with increasing levels of assistance would be activated more often as time progressed. This, in turn, indicated that the patients were increasingly fatigued while the system correctly responded to their decreased motor capacity by providing more assistance.

The secondary outcomes during the technical validation were the number of identified EMG-triggers in each state, the onset of FES and mechanical assistance relative to the expected onsets (as defined in figure 2), and the completion time of a repetition in each state.

The detection of EMG-triggers was investigated in offline analysis by applying the EMG-trigger detection algorithm to all EMG data recorded at each exercise repetition. A percentage of completed exercise repetitions containing detected EMG-triggers could then be calculated for each AAN state. EMG-triggers were expected during all *Vol* and prior to all *Trig* state repetitions, as these involved complete or partial voluntary effort. No triggers were expected prior to or during the *Auto* and *Mech* states, as participants should be relaxing according to the instructions to participants in the section *Technical validation*.

The onset of FES was calculated as the time when the system started the delivery of FES, relative to the last time the velocity was larger or equal to the velocity threshold. If an EMG-trigger was detected, only the velocity samples after the EMG-trigger counted towards the onset of FES. The onset of mechanical assistance was calculated as the time elapsed between the FES onset and the time when the mechanical assistance was provided. Ideally, the onset of FES would be 2 or 10 s (in the *Trig* or *Auto* state respectively), while the onset of mechanical assistance would be 2 s.

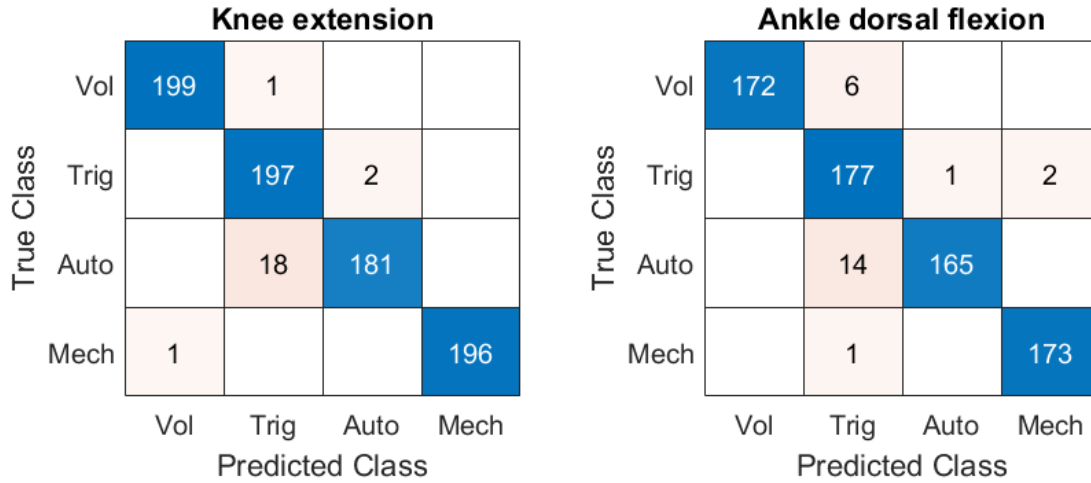


Figure 5: Confusion matrix for transitioning between the different AAN states during KE and ADF exercises (healthy participants).

The completion time of each exercise repetition was calculated as the time from the start of one exercise repetition, to the start of the next repetition.

In the clinical feasibility test, the secondary outcome was the average fatigue score.

The aforementioned analyses were completed for both KE and ADF exercises, using MATLAB version R2022b.

All outcome measures are reported as mean \pm standard deviation across participants.

3. Results

3.1. Technical validation

3.1.1. Knee extension

On average, able-bodied participants completed 19.9 ± 0.3 repetitions of each state (see table 2). The state machine accuracy for transitioning between the states was $97.2 \pm 2.2\%$ during the KE exercise. The specific state transition rates are shown in figure 5, and the sensitivity and precision of each state transition are shown in table 2.

The sensitivity and precision of transitions into each state was more than 90%. *Mech* had the overall highest sensitivity and precision, and *Auto* had the lowest. The most common error was the activation of the *Trig* state instead of *Auto*, which happened 18 times (9.0%), while other misclassifications were rare, i.e., ≤ 2 times (1%).

The EMG-trigger detection rate, the onset of FES and mechanical assistance, and the completion time of exercise repetitions in all states during KE exercise, are reported in table 2.

As shown in table 2, EMG-triggers were detected during $62.0 \pm 39.9\%$ of the *Vol* state repetitions, indicating a high variability between subjects. On the other hand, $100.0 \pm 0.0\%$ of *Trig* state repetitions were preceded by an EMG-trigger. During $0.5 \pm 1.7\%$ of the *Auto* state repetitions (a single occurrence) an EMG-trigger was produced, while

$3.0 \pm 4.2\%$ of the *Mech* repetitions (six occurrences) were preceded by an EMG-trigger.

The onset of FES was 2.05 ± 0.02 s for *Trig*, and 10.02 ± 0.00 s for *Auto*, while the onset of mechanical support was 2.10 ± 0.01 s. These were consistent with the completion times for a repetition in each state during KE, ranging from 7.09 s during *Vol* to 19.48 during *Mech* preceded by *Auto*. The completion time increased across the states in the following order: *Vol*, *Trig*, *Mech* preceded by *Trig*, *Auto*, and *Mech* preceded by *Auto*. This correctly reflects the onset time for FES and mechanical support, and how these relate to each state.

3.1.2. Ankle dorsal flexion

One subject did not complete the ADF exercise due to discomfort during electrical stimulation. The remaining subjects completed 19.8 ± 0.7 repetitions of each state (see table 3). The accuracy of the state machine for transitioning between states was $96.6 \pm 5.3\%$. The specific state transition rates for each state are shown in figure 5 and the sensitivity and precision characterizing each state are shown in table 3.

The achieved sensitivity and precision were higher than 90%. As in KE, the highest sensitivity and precision were obtained for *Mech* and the lowest for *Trig*. Likewise, the most common error was the transition into *Trig* instead of *Auto*, which occurred 14 times (7.8%). Other misclassifications were rare, i.e., ≤ 6 times (3.5%).

The EMG-trigger detection rate, the onset of FES and mechanical assistance, and the completion time of exercise repetitions in all states during ADF exercise, are reported in table 3.

EMG-triggers were detected in all *Vol* and *Trig* repetitions, none was detected in *Auto* and $12.4 \pm 23.2\%$ were detected in *Mech* (20 occurrences).

The onset of FES was 2.01 ± 0.01 s for *Trig*, 10.02 ± 0.00 s for *Auto*, and 2.10 ± 0.02 for *Mech*. These were also

Table 2

The system outcome measures during KE per state. Repetitions: the number of completed repetitions, per participant. EMG-trigger: the percentage of repetitions during which EMG-triggers were detected. Onset: The onset of FES or mechanical assistance. Time: The time to complete an entire exercise repetition.

	Repetitions	Sensitivity (%)	Precision (%)	EMG-trigger (%)	Onset (s)	Time (s)
<i>Vol</i>	20.0 ± 0.0	99.5 ± 1.6	99.5 ± 1.6	62.0 ± 39.9	-	7.09 ± 0.39
<i>Trig</i>	19.9 ± 0.3	99.0 ± 3.2	91.3 ± 4.9	100.0 ± 0.0	2.05 ± 0.02 ^F	11.25 ± 0.94
<i>Auto</i>	19.9 ± 0.3	91.0 ± 5.2	99.0 ± 3.3	0.5 ± 1.7	10.02 ± 0.00 ^F	15.59 ± 0.52
<i>Mech</i>	19.7 ± 0.5	99.5 ± 1.7	100.0 ± 0.0	3.0 ± 4.2	2.10 ± 0.01 ^M	15.25 ± 2.05 ^{PT} 19.48 ± 0.74 ^{PA}

F - Onset of FES administration.

M - Onset of mechanical assistance.

PT - Cases where *Mech* was preceded by *Trig* (190 cases).

PA - Cases where *Mech* was preceded by *Auto* (6 cases).

Table 3

The system outcome measures during ADF per state. Repetitions: the number of completed repetitions, per participant. EMG-trigger: the percentage of repetitions during which EMG-triggers were detected. Onset: The onset of FES or mechanical assistance. Time: The time to complete an entire exercise repetition.

	Repetitions	Sensitivity (%)	Precision (%)	EMG-trigger (%)	Onset (s)	Time (s)
<i>Vol</i>	19.8 ± 0.7	96.5 ± 6.0	100.0 ± 0.0	100.0 ± 0.0	-	3.60 ± 0.62
<i>Trig</i>	20.0 ± 0.0	98.3 ± 2.5	91.1 ± 12.2	100.0 ± 0.0	2.01 ± 0.01 ^F	6.43 ± 0.93
<i>Auto</i>	19.9 ± 0.3	92.2 ± 12.5	99.5 ± 1.6	0.0 ± 0.0	10.02 ± 0.00 ^F	12.44 ± 0.40
<i>Mech</i>	19.3 ± 1.1	99.4 ± 1.9	98.9 ± 2.3	12.4 ± 23.2	2.10 ± 0.02 ^M	9.35 ± 1.87 ^{PT} 16.18 ± 1.27 ^{PA}

F - Onset of FES administration.

M - Onset of mechanical assistance.

PT - Cases where *Mech* was preceded by *Trig* (153 cases).

PA - Cases where *Mech* was preceded by *Auto* (20 cases).

consistent with the completion times of a repetition in each state during ADF, ranging from 3.6 s during *Vol* to 16.18 s during *Mech* when preceded by *Auto*. The order of the states with respect to completion time was the same as for KE.

3.2. Clinical feasibility test

3.2.1. Progression of states

The number of repetitions in each state for each patient during KE and ADF is shown in table 4, and the progression of states across repetitions of KE and ADF exercise for the two stroke patients is shown in figure 6.

The states of the AAN system, and thereby the support provided by the system, varied between the two patients and between the two exercises. All states but *Mech* were triggered by patient 1, whereas all states were triggered during ADF by patient 2. The physical capability was quite stable (magnitude of the slope of the fitted line < 0.01) during both exercises for patient 1, and during KE for patient 2. Both patients could perform KE exercises using voluntary efforts and the system did not need to provide assistance, as the state machine was in the *Vol* state consistently across repetitions. ADF was, however, more challenging and *Trig* was the most prevalent state for patient 1. Furthermore, patient 1 exhibited a slight increase in the prevalence of the *Auto* state during ADF (one occurrence in the first 30 repetitions versus six in the final 30 repetitions). The pattern of triggered states

for patient 2 during ADF (line slope ≈ -0.032) indicated a decreasing need for support during the exercise. Initially, the patient triggered all assistance levels, whereas after approx. 20 repetitions, the state machine consistently remained in the *Vol* state and the system did not need to deliver assistance.

3.2.2. Fatigue

The fatigue scores reported by the patients following KE and ADF exercises are reported in table 4.

For KE, both patients rated the fatigue score at 2.0 ± 0.0 , while ADF was rated at 4.0 ± 0.0 by patient 1, and 5.5 ± 0.7 by patient 2. Thus, patient 2 reported a fatigue score 1.5 higher than patient 1 during ADF. Note that patient 1 received three times more support compared to patient 2 (56 repetitions vs 17 repetitions, as seen in table 4 and figure 6).

4. Discussion

In this study, we presented a novel hybrid system for the rehabilitation of the lower limbs which further expands the framework introduced by Petersen et al. 2020 [27]. The novel system presented in this study was comprised of the robotic manipulator ROBERT®, an EMG-triggered FES system, and a state machine implementing AAN control. The system used in this study differs from that used by Petersen et al. 2020, which relied on an EMG-trigger to administered FES,

Table 4

Overview of patient characteristics and their performance during the clinical feasibility test. Rep: Repetitions of exercise in KE/ADF. *Vol*, *Trig*, *Auto*, *Mech*: Number of repetitions completed in the *Vol*, *Trig*, *Auto*, *Mech* state during KE/ADF, respectively. Fat. KE, Fat. ADF: Ratings of fatigue in trial 1/trial 2 of KE and ADF, respectively.

	Rep.	<i>Vol</i>	<i>Trig</i>	<i>Auto</i>	<i>Mech</i>	Fat. KE	Fat. ADF
Patient 1	60/60	57/4	2/49	1/7	0/0	2/2	4/4
Patient 2	60/60	60/43	0/5	0/9	0/3	2/2	5/6

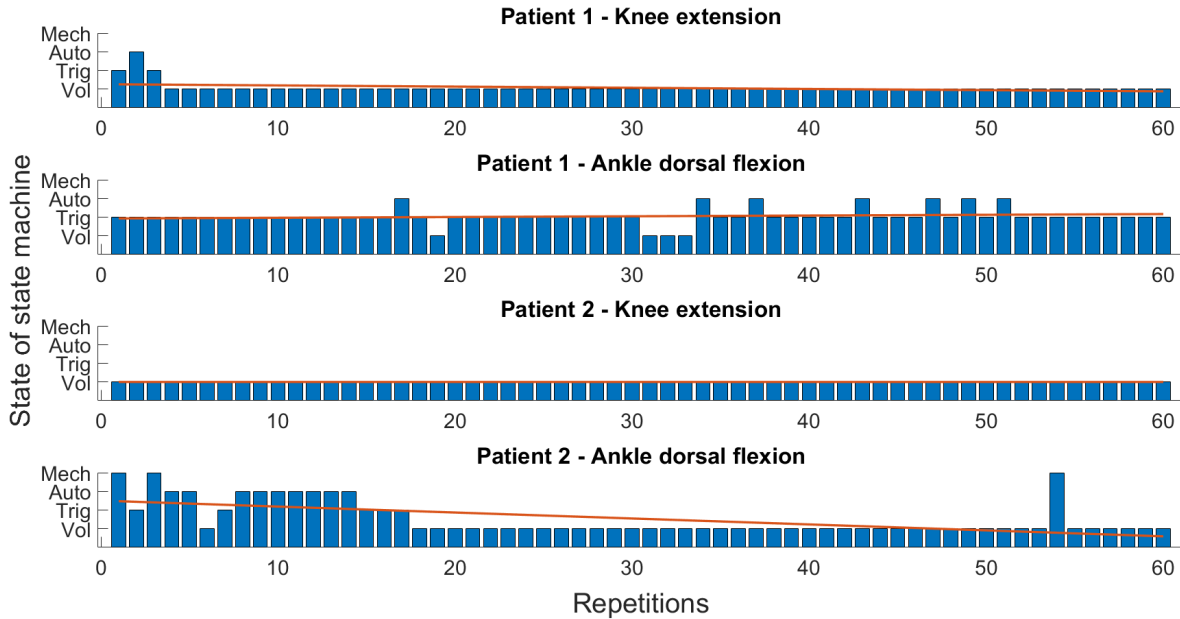


Figure 6: The support provided by the system during each repetition of KE and ADF, for the two stroke patients. The red line illustrates a fitted line describing the progression of support; an ascending line would indicate increasing support as time progresses; a descending line would indicate decreasing support. The slopes of the lines are -0.006, 0.004, 0.000, and -0.032, respectively.

without further consideration of whether the patient was expectedly able to exercise on their own or not [27]. The developed AAN paradigm combined different assistance modalities to allow patients to exercise by exploiting their own capabilities and without unnecessary external support, which is suggested to facilitate motor learning and lead to greater rehabilitative outcomes [20, 24]. The present study established the technical and preliminary clinical feasibility of the system while its rehabilitative potential will be investigated in future clinical studies.

The results of the technical validation suggested that the system correctly identified the behavior executed by able-bodied volunteers to generate the transition into the target state of the system, with a high accuracy of 96.6-97.3%. This suggests that the system has been properly implemented to detect the desired behaviors and thereby apply the appropriate level of support (no support, FES only, or FES and mechanical assistance).

Overall, the AAN system exhibited high sensitivity and precision (>90%). The most common error was the transition into *Trig*, when the target was *Auto* due to the detection of “false” EMG-triggers. At the end of a repetition, the robot

guided the leg/ankle of the participant back into the starting position. Once there, the position controller was deactivated, while the resistance opposing the exercise trajectory was turned on. This switch occasionally generated sufficient noise to produce an EMG-trigger at the very beginning of an exercise repetition. Petersen et al. 2020 reported that 20.5% and 15.5% of EMG-triggers, for KE and ADF respectively, were premature and produced by noise, suggesting that they may have faced a similar issue [27]. The number of premature triggers in Petersen et al. 2020, is twice the number of errors in the *Auto* state (15.5-20.5% versus 7.8-9.0%), which comprises noise and unintended triggers, suggesting that the issue was smaller in the present study. Additionally, some errors were caused because the participants unintentionally generated EMG activity as they did not relax sufficiently while the robot moved their leg to the start position, thereby producing an EMG-trigger immediately when the next repetition started. Finally, participants occasionally made mistakes and moved when they were supposed to stay still (e.g., during testing of the *Auto* state) due to lack of focus or misunderstanding of instructions. However, such mistakes are not considered an error in the system, as the AAN state

machine acted appropriately to the input provided, although the input was unintended in the test.

In addition, EMG-triggers were occasionally not detected when they were supposed to be generated. For instance, only 62% of *Vol* repetitions during KE resulted in EMG-trigger detection, although 100% was expected, as this state involved the most muscular activity. The subjects were able to complete the exercise repetition while remaining in the *Vol* state, as they completed the repetition before the timer activated the *Auto* state. Further inspection of the data revealed that five participants had difficulties in producing triggers during the testing of the *Vol* state. This was likely caused by the participants not relaxing properly during the calibration, leading to high thresholds. It is also possible that these participants produced the desired trajectory by relying on the gluteus maximus (hip extension), more than the quadriceps [33] thereby generating less EMG-activity in the monitored muscles. The participants were not instructed in how to move during the testing of the *Vol* state but were simply told to produce the movement ‘naturally’. However, when testing the *Trig* state, they were instructed specifically to focus on knee extension, resulting in EMG-triggers being identified in 99% of *Trig* repetitions despite the low detection rate when testing the *Vol* state. Finally, the difference in ability to produce EMG-triggers, could be caused by individual differences in the tissue composition, as the amount of adipose tissue under the recording electrodes affects the amplitude of the recorded EMG [34]. To avoid the challenges in EMG-trigger detection, future versions of the system will include an option to manually adjust the trigger-threshold, in cases where triggers are not produced appropriately. Additionally, a blanking method should be implemented, which would ignore the EMG during the switch in the beginning of an exercise repetition, which could produce false triggers. Finally, a possibility would be to place EMG electrodes on more muscles (e.g., gluteus maximus) but this would increase the system setup and calibration time, which can decrease its clinical applicability.

The onsets of FES and mechanical support obtained in the technical validation, during both KE and ADF, suggest close compliance with the specifications of the AAN state machine (figure 2). Additionally, the completion time of repetitions in each state followed the expected order and allows for a number of repetitions of KE and ADF in the range of 184-507 and 222-1000, respectively, during one hour of uninterrupted exercise. This is within the range required for promoting neural change, although in the low end [35, 36]. However, as the system targets severely affected patients, who may have limited alternatives to exercise, the immediate goal of the system is to enable the patients to receive simple yet demanding training while alternative options are limited.

In the clinical feasibility test, it was expected that the patients exercising with the system would be as actively involved as allowed by their physical capabilities while receiving the minimum required support. This is indeed supported by the states activated during the exercise (figure 6). Patient 1 required consistent FES support during ADF,

and patient 2 required gradually reduced support. This indicates that the system was able to adapt to the support required by the patient, which is in line with the principles identified by Maier et al. 2019 [9], and further supports the potential feasibility of using the system with patients in a rehabilitative setting.

Both patients could perform KE using voluntary efforts, and this was correctly detected by the system, which remained in the *Vol* state and did not provide support. This was however surprising for patient 1 as they had a Motricity Index of 0 at recruitment. We believe that the gravity compensation provided by the system, and the supine exercising position were enough to allow for the emergence of the volitional movement. Although unexpected, this is an encouraging result implying that sometimes even a simple intervention and minimal support can substantially improve the patient’s ability to move and exercise. However, patient 1 still needed active support during ADF, which was expected considering the low motricity index of the patient. Another unexpected result was that Patient 2 decreased the need for support while performing ADF. This may be due to different reasons. The patient might have become more familiar with the system functioning after a few repetitions, the first repetitions could provide the required muscle warm-up [37], or the patient could have become more motivated and engaged [37], and after that could continue without support. Finally, the reduced need for support may be caused by potentiation following repeated administration of FES, similar to what was observed in Leerskov et al. 2022 in able-bodied individuals, who exercised with a comparable rehabilitation system [28].

The patients rated the fatigue due to exercising with the system at 2 and 4.75 out of 10, for KE and ADF, respectively, indicating that both patients were more fatigued during ADF, which is reflected in the increased need for support in ADF relative to KE, for both patients. Additionally, patient 2 rated fatigue during ADF higher than patient 1, which is consistent with the fact that patient 2 exercised mostly using their own efforts (*Vol*), whereas patient 1 primarily received support (*Trig*). Overall, the fatigue scores indicate that exercising with the system has the capacity to provide an exertive exercise that is not too exhaustive. For KE it may be necessary to provide additional repetitions to observe more fatigue, and more repetitions are required in general to reach levels necessary to induce neural changes [38].

4.1. Future direction

Future work should include the assessment of the rehabilitative capability of the system in more stroke patients and over an extended period of time. Previous studies suggest that hybrid robotic-FES rehabilitation is effective [39–41], however, the hypothesis that the AAN state machine may further improve these results, is yet to be proven in a clinical study. If this is true, the system introduced in the present study may be a powerful tool for the early rehabilitation of severely affected stroke patients.

5. Conclusion

The results of the technical validation in able-bodied participants and the preliminary clinical feasibility test in two stroke patients suggested that the novel hybrid rehabilitation system using AAN-control is valid and feasible for use by severely affected stroke patients. The system detects the capability of the user, and adjusts the level of support to the minimum required, while providing an exertive exercise.

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