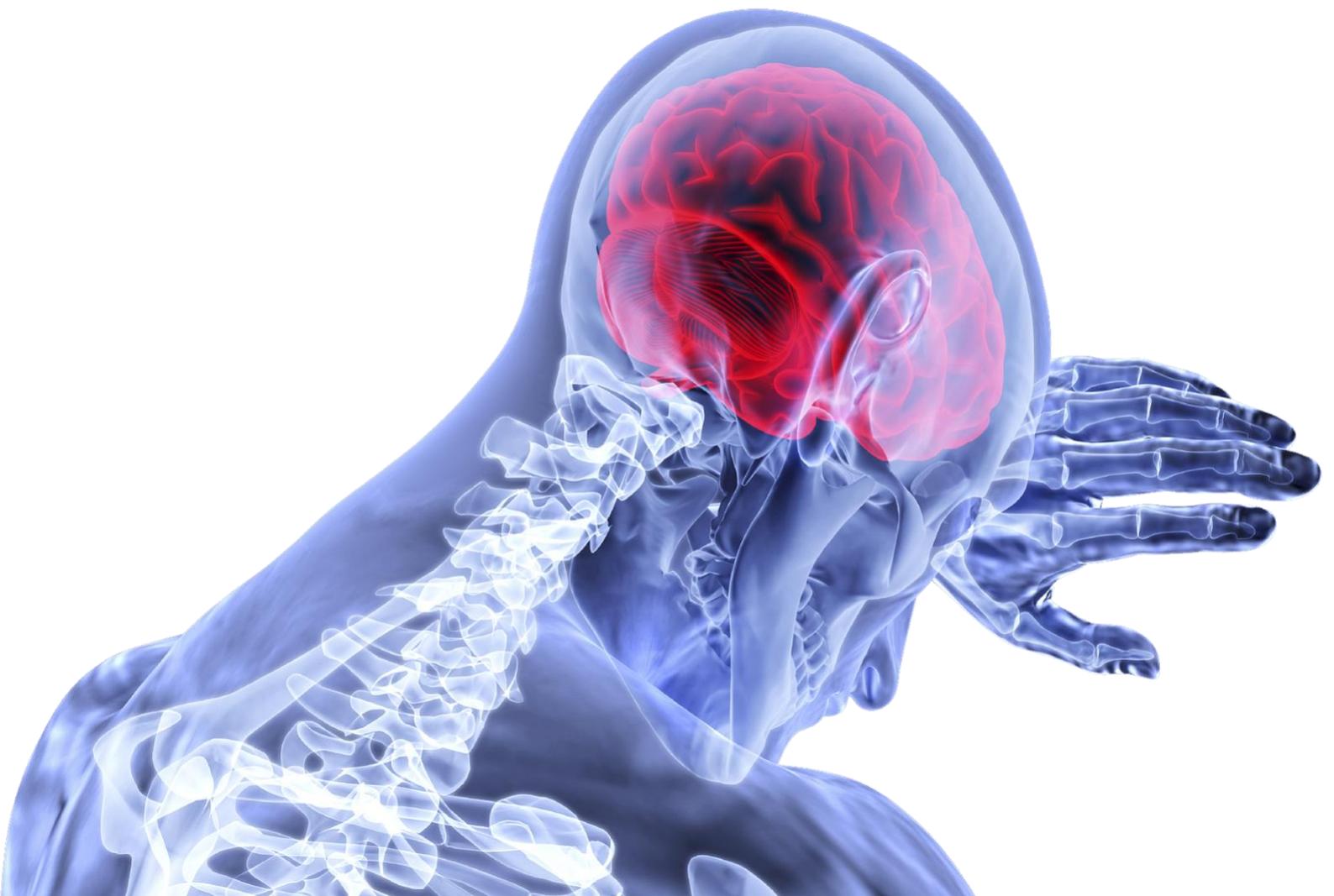


# FLEX CEUs



## Stroke: Developments in Upper Extremity Devices



# Hybrid Assistive Neuromuscular Dynamic Stimulation Therapy: A New Strategy for Improving Upper Extremity Function in Patients with Hemiparesis following Stroke

Hybrid Assistive Neuromuscular Dynamic Stimulation (HANDS) therapy is one of the neurorehabilitation therapeutic approaches that facilitates the use of the paretic upper extremity (UE) in daily life by combining closed-loop electromyography- (EMG-) controlled neuromuscular electrical stimulation (NMES) with a wrist-hand splint. This closed-loop EMG-controlled NMES can change its stimulation intensity in direct proportion to the changes in voluntary generated EMG amplitudes recorded with surface electrodes placed on the target muscle. The stimulation was applied to the paretic finger extensors. Patients wore a wrist-hand splint and carried a portable stimulator in an arm holder for 8 hours during the daytime. The system was active for 8 hours, and patients were instructed to use their paretic hand as much as possible. HANDS therapy was conducted for 3 weeks. The patients were also instructed to practice bimanual activities in their daily lives. Paretic upper extremity motor function improved after 3 weeks of HANDS therapy. Functional improvement of upper extremity motor function and spasticity with HANDS therapy is based on the disinhibition of the affected hemisphere and modulation of reciprocal inhibition. HANDS therapy may offer a promising option for the management of the paretic UE in patients with stroke.

## 1. Functional Recovery of Upper Extremity Motor Function following Stroke

Stroke is a common health-care problem that causes physical impairment, disability, and problems in social participation. The most common impairment caused by stroke is motor impairment. Motor impairment affects the control of the unilateral upper and lower extremities. Recovery of function in the hemiparetic upper extremity is noted in fewer than 15% of patients after stroke [1].

Patients often compensate for their paretic upper extremity by using their intact upper extremity in the performance of everyday tasks [2]. It is supposed that strong reliance on

compensatory overuse of the intact upper extremity inhibits functional recovery of the impaired upper extremity. This may explain the limited improvement of the functional capability of the paretic upper extremity in activities of daily living (ADL).

Principles of motor rehabilitation following stroke have been described as being dose-dependent and task-specific [3]. High-intensity practice and task-specific training are recommended for functional recovery. Several systematic reviews [4, 5] have explored whether high-intensity therapy improves recovery, and the principle that increased intensive training is helpful is widely accepted. Task-specific training is a well-accepted principle in motor rehabilitation. Training

should target the goals that are relevant for the needs of the patients and preferably be given in the patient's own environment.

The goal of upper extremity rehabilitation is to improve the capability of the paretic upper extremity for ADL. Constraint-induced movement therapy (CIMT) has been developed to enhance the forced use of the paretic hand in ADL with reduction of the compensatory overuse of the intact upper extremity. However, to participate in CIMT, the candidates must be able to voluntarily extend their fingers and wrist at least 10 degrees, practice for 6 hours daily in a 2-week course, and spend waking hours with their nonparetic hand in a mitt [6].

To counter potential problems inherent in the intensive services needed for CIMT, we developed an alternative therapeutic approach that provides high-intensity training to facilitate the use of the paretic upper extremity in daily living by combining closed-loop electromyography- (EMG-) controlled neuromuscular electrical stimulation (NMES) with a wrist-hand splint for patients with moderate to severe hemiparesis. Fujiwara et al. called this hybrid assistive neuromuscular dynamic stimulation (HANDS) therapy [7].

## 2. HANDS Therapy

A PubMed literature search was conducted using the MeSH terms stroke, rehabilitation, upper extremity function, and neuromuscular electrical stimulation, and 71 articles were identified. A further search of PubMed with the terms stroke, rehabilitation, upper extremity function, neuromuscular electrical stimulation, and splint identified 4 articles, all regarding HANDS therapy.

HANDS therapy facilitates the use of the paretic upper extremity in daily living by combining closed-loop EMG-controlled NMES with a wrist-hand splint for patients with moderate to severe hemiparesis. This HANDS system is active for 8 hours, and patients are instructed to use their paretic hand as much as possible while wearing the HANDS system. Their nonparetic upper extremity is not restrained. The patients are also instructed to practice bimanual activities in their ADL. All participants in HANDS therapy are admitted, and the length of the intervention is 21 days. They receive 90 minutes of occupational therapy per day, 5 days a week. Each session of occupational therapy consists of gentle stretching exercise of the paretic upper extremity and active muscle reeducation exercise. All participants are instructed how to use their paretic hand in ADL with the HANDS system. Occupational therapists are directed toward participants' goals and focused on their particular impairments and disabilities; thus, the specific therapy that each patient receives varies [7, 8].

Fujiwara et al. [7, 8] reported the indications for HANDS therapy as follows: (1) no cognitive deficits; (2) no pain in the paretic upper extremity; (3) passive extension range of motion (ROM) greater than 0 degrees of the affected wrist and -10 degrees of the metacarpophalangeal joints; (4) detectable surface EMG signals in the affected extensor digitorum communis (EDC) or extensor pollicis longus

(EPL) when the patient intends to extend their fingers; (5) ability to raise the paretic hand to the height of the nipple; (6) scores of Fugl-Meyer test position sense of joints in the glenohumeral joint, elbow, wrist, and thumb of 1 or more; and (7) the ability to walk without physical assistance in daily life (e.g., including patients who can walk independently with a cane and/or an orthosis). The exclusion criteria were (1) history of major psychiatric or previous neurological disease, including seizures; (2) cognitive impairment precluding appropriately giving informed consent or the patient's Mini Mental Examination Scale score was below 25; (3) patients with severe pain in the paretic upper extremity; (4) patients with a pacemaker or other implanted stimulator; and (5) patients with visuospatial neglect or apraxia.

Previous reports showed that none of the patients experienced any discomfort or significant disability with the HANDS therapy.

*2.1. Closed-Loop Electromyography- (EMG-) Controlled Neuromuscular Electrical Stimulation (NMES).* Twenty-nine articles were found in PubMed using the terms stroke, electromyography, neuromuscular electrical stimulation, and upper extremity. Thirteen of 29 articles were on EMG-triggered NMES. Six of 29 articles were on EMG-controlled NMES. Two involved contralaterally controlled electrical stimulation.

EMG-triggered NMES applies preset electrical stimulation when EMG activity reaches a target threshold. The stimulus intensity and duration are determined and not changeable. EMG-controlled NMES applies electrical stimulation during voluntary contraction and changes the stimulation intensity in proportion to the changes in EMG amplitude.

For assistive stimulation, HANDS therapy used closed-loop EMG-controlled NMES, which was developed by Muraoka [9] and commercially available with MURO stimulation (Pacific Supply, Osaka, Japan). This closed-loop EMG-controlled NMES is portable and attaches to the arm (Figure 1). The surface electrodes pick up EMG signals at the target muscle and simultaneously stimulate it in direct proportion to the picked-up EMG signal, with the exception of the 25 ms after delivering each stimulation pulse, in which stimulation artifacts and M wave are observed. The external adjustment unit sets (1) range of stimulus intensity; (2) sensitivity of the EMG; (3) threshold of EMG amplitude that starts stimulation; and (4) gradient of stimulus intensity change to the change of EMG amplitude. Once these parameters were set with the external adjustment unit, the stimulator memorized these parameters.

It is difficult for patients with severe to moderate hemiparesis to extend their paretic fingers. As for hand function to perform ADL, pinch and release, and grip and release, are key functions. It is necessary to restore finger extension to perform ADL with the paretic upper extremity in patients with severe to moderate hemiparesis. To restore finger extension, electrical stimulation is applied to finger extensors in HANDS therapy. A pair of electrodes for EMG detection and stimulation (10 mm diameter) placed 20 mm apart on the

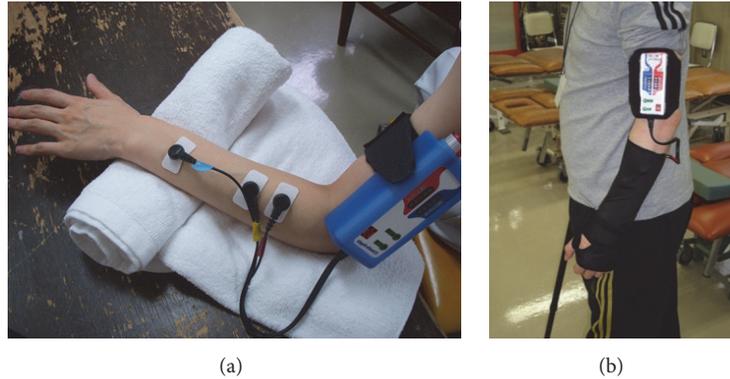


FIGURE 1: (a) Closed-loop electromyography- (EMG-) controlled neuromuscular electrical stimulation (NMES). A pair of electrodes for EMG detection and stimulation are placed on the affected extensor digitorum communis muscle, and one electrode for stimulation is placed on the affected extensor indicis muscle. (b) Participants wear a wrist-hand splint and carry a closed-loop EMG-controlled NMES with arm holder for 8 hours during the daytime.

affected EDC and one electrode (10 mm) for stimulation are placed on the affected EI.

The EMG data and amount of stimulation were recorded with an attached data-logger system of the MURO device while the participants wore the MURO device. The participant's compliance with wearing the device for 8 hours during the daytime can be monitored using this data-logger system in HANDS therapy.

**2.2. Splint.** The patients wear a wrist-hand splint (Wrist Support, Pacific Supply Co.) and carry a portable closed-loop EMG-controlled NMES with arm holder for 8 hours during the daytime. The rationale for combining the stimulation system with a wrist-hand splint was derived from the work of Fujiwara et al. [10]. They showed that wearing a wrist-hand splint reduced spinal motoneuron excitability and flexor muscle overactivity during voluntary finger extension. During finger extension, muscle activities of the finger flexors, wrist flexors, and elbow flexors were reduced with the wrist-hand splint. The wrist-hand splint effect on the elbow flexors was supposed to be mediated by secondary afferent inhibition [11].

The wrist-hand splint also makes the hand shape functional. Hand shape is important for hand function. The hand has longitudinal and transverse arches. These arches are important for holding, and thumb opposition and the web space are important for pinching. A wrist-hand splint helps to form the longitudinal and transverse arches, thumb opposition, and the web space in the hand [10].

### 3. The Effect of HANDS Therapy

Shindo et al. [12] performed a randomized, controlled study among subacute patients (time from stroke onset within 60 days) with hemiparesis following stroke. They explored the effectiveness of HANDS therapy added to conventional rehabilitation as compared with splint therapy in addition to standard inpatient rehabilitation treatment for patients who could not fully extend their paretic fingers and could not

perform pinch and release in their daily life, in a randomized, controlled trial design. Compared with the control group, the HANDS group showed significantly greater gains in the distal (hand/wrist) part of the Fugl-Myer Assessment (FMA) [13] and improvement of the Action Research Arm Test [14]. HANDS therapy is an intervention that resulted in improved hand function following stroke, while a systematic review [3] showed that none of the interventions identified showed a consistent pattern of improvement in hand function.

HANDS therapy improved upper extremity function even in patients with chronic stroke [7, 8]. Fujwara et al. [8] applied HANDS therapy to 61 patients with chronic hemiparetic stroke. Their mean time since stroke onset was 28.4 months. Three weeks of HANDS therapy improved FMA, the motor activity log 14 (MAL) amount of use score [15], and the modified Ashworth scale (MAS) [16]. Improvement of the FMA, MAL, and MAS lasted for 3 months after the end of HANDS therapy. In the study of Fujiwara et al. [7], arm and finger functions were assessed with the Stroke Impairment Assessment Set (SIAS) motor function score [17]. They found that both arm and hand function had been improved by HANDS therapy, and these improvements were maintained until 3 months after the end of HANDS therapy. They also showed improved capability of the paretic hand in ADL.

These studies showed that HANDS therapy improved arm and hand motor functions, increased the amount of use of the paretic upper extremity in ADL, and reduced finger and wrist spasticity, not only in subacute, but also in chronic stroke. The mean FMA gains with HANDS therapy were 12.2 in subacute patients [12] and 7.7 in chronic patients [8]. These gains surpassed the minimal clinically important difference for treatment-induced gains of 4.25 on the FMA [18].

### 4. The Mechanism of Functional Recovery and Neural Plasticity Induced with HANDS Therapy

Dose-dependent, task-specific, and use-dependent plasticity are principles of rehabilitation for functional recovery.

HANDS therapy improved motor function and increased the amount of paretic hand use. These improvements were maintained until 3 months after the end of HANDS therapy. These long-lasting effects of HANDS therapy can be explained by the concept of the threshold of effective rehabilitation, which was proposed by Han et al. [19]. If spontaneous arm use is above a certain threshold, then training can be stopped, as repeated spontaneous use provides a form of motor learning that further improves performance and spontaneous use. Below this threshold, training is in vain, and compensatory movements with the less affected hand are reinforced. In HANDS therapy, participants were trained to use their paretic hand for 8 hours in 3 weeks using closed-loop EMG-controlled NMES and a hand splint. Such an amount of training may be above the threshold of effective rehabilitation.

The effect of training is task-specific [20]. The aim of HANDS therapy is to make the paretic hand useful for ADL and to have the paretic hand participate in ADL. The key functions of the hand in ADL are grip and release and pinch and release. It is difficult for patients with moderate or severe hemiparesis to extend their fingers. The closed-loop EMG-controlled NMES, therefore, helps to extend the paretic fingers, and the splint helps the patient pinch and hold the objects with paretic fingers. Using this HANDS system, participants were trained to use their paretic hand in their ADL, producing proximal and distal coordinated movements, such as reach, grip and release, and pinch and release.

One of the mechanisms of functional recovery of stroke is use-dependent plasticity. Functional recovery involves changes in neuronal excitability that alter the brain's representation of motor and sensory functions. The inhibitory neurotransmitter GABA is critical for cortical plasticity. In animal studies, reducing GABA<sub>A</sub>ergic inhibition proved beneficial for functional recovery [21, 22]. In humans, this GABA<sub>A</sub>ergic inhibitory system can be assessed with a paired-pulse transcranial magnetic stimulation (TMS) technique, in which a conditioning TMS pulse below the threshold for eliciting a motor-evoked potential (MEP) inhibits a suprathreshold test stimulus at short intervals (1–5 ms) (short intracortical inhibition (SICI)) [23]. Fujiwara et al. [8] showed that HANDS therapy induced disinhibition of SICI in the affected hemisphere, and there was a direct correlation between the change of SICI in the affected hemisphere and the change of FMA. Patients who showed more disinhibition of SICI showed longer lasting improvement of motor impairment. It has been supposed that long-lasting functional reorganization of the brain may be mediated by disinhibition of intracortical inhibitory interneurons in severely hemiparetic patients. In moderate to severe hemiparesis, compensatory brain responses include increased activation in the surrounding damaged zone and masked network [24]. HANDS therapy strengthened disinhibition of the affected SICI. It is thought that compensatory disinhibition occurred in moderate to severe chronic stroke during functional recovery induced with HANDS therapy. The mechanism of functional recovery of the upper extremity is not able to be explained by the

disinhibition of SICI alone. More is necessary to induce functional recovery.

HANDS therapy improved the spasticity of the fingers and wrist. Spasticity is often blamed for poor function in patients with minimal finger extension but some preservation of flexion [20]. The mechanisms underlying spasticity poststroke have not been fully elucidated, but decreased reciprocal inhibition may contribute to motor impairment in spastic hemiparesis [7]. In healthy subjects, group I-mediated reciprocal inhibition contributes to the suppression of antagonist muscle activity during movement [25, 26]. This reciprocal inhibition is disrupted among patients with spastic hemiparesis [7, 27]. HANDS therapy reduced cocontraction of finger flexors during finger extension movement. This may be due to the restoration of reciprocal inhibition with HANDS therapy. Fujiwara et al. [8] studied reciprocal inhibition with the flexor carpi radialis H reflex conditioning-test paradigm [28] before and after HANDS therapy. HANDS therapy increased the magnitude of presynaptic inhibition and long loop presynaptic inhibition. They found a significant correlation between restoration of RI and improvement of wrist spasticity.

Disinhibition of affected intracortical interneurons increases the activity of the descending projection from the affected hemisphere to the spinal cord. Increased activities of the descending projection to the spinal cord modulate the activities of reciprocal inhibitory interneurons [29, 30].

More evidence is needed to investigate the neural plasticity changes underlying functional improvement after HANDS therapy by using brain imaging techniques such as fMRI.

HANDS therapy was applied in subacute and chronic stroke patients. There was no report of adverse effects. We consider that HANDS therapy is suitable for subacute and chronic phase of stroke and patients with synergy level, who cannot extend their paretic finger enough to use their paretic hand in their ADL.

## 5. Conclusion

HANDS therapy is one of the neurorehabilitation therapeutic approaches that facilitates the use of the paretic upper extremity in daily life by combining closed-loop EMG-controlled NMES with a wrist splint. Functional recovery from stroke has been induced with HANDS therapy even in chronic and moderate to severe hemiparesis. The improvements of motor function and spasticity induced by HANDS therapy are based on cortical and spinal plastic changes.

As the other NMES, HANDS therapy may offer a promising option for the management of the paretic upper extremity in patients with stroke. Further development and clinical application of HANDS therapy are needed.

## Competing Interests

There is no conflict of interests regarding the publication of this paper.

# Development of portable elbow joint device for stroke patient rehabilitation

## Abstract

Stroke is a brain disease occurs when blood stops flowing to any part of the brain, damaging brain cells and causes joint stiffness. By doing continuous passive motion (CPM) exercise, the joint stiffness can be reduced and it helps maintaining the range of motion (ROM) of the joint. Portable Elbow Joint Device (PEJD) will provide CPM exercise to patients with Neurological problems such as stroke and traumatic brain injuries that affected the arm. Existing devices of the elbow rehabilitation therapy are large, complex and difficult to be carried anywhere. The upgrading of PEJD focuses on reducing cost, ensuring comfort, and making it portable and light in weight. Besides, PEJD will assist stroke patients in involuntary progressive muscles weakness. A Gear Motor w/Encoder, model No. GB37Y3530-12V-83R is used to move the arm/elbow joint and its angle in controllable speed, timer by using Arduino Nano (microcontroller). The Arduino Nano is a small, complete, and breadboard-friendly board based on the ATmega328 (Arduino Nano 3.0). A rechargeable battery is added on the device to enable the device to operate using DC power supply. The innovation of PEJD will benefit the stroke and elbow injury patients during rehabilitation process as the angle is adjustable, count and speed buttons are also available for such therapy treatment.

**Keywords:** Stroke, joint stiffness, continuous passive motion (CPM), elbow joint rehabilitation device, Arduino Nano

## Introduction

The elbow is the joint connecting the proper arm to the forearm. The elbow joint structure is shown in **Figure 1**. It is marked on the upper limb by the medial and lateral epicondyles and the olecranon process. Structurally, the joint is classed as a synovial joint and functions as a hinge joint. The elbow joint is a compound synovial joint, which means that it is a large working structure that is made up of several smaller moving parts or separate articulations. A synovial joint, otherwise known as a diarthrosis, is the most flexible type of joint [5], seeing as it achieves its range of movement at the point of contact between the articulating bones. This mechanical area forms the meeting point between the radius and ulna of the forearm with the humerus of the brachial region [5]. It is deemed a compound joint because the joint cavity is continuous with the radioulnar joint, as well as the contact points between these bones and

the humerus respectively.

Every joint in the human body has its own range of motion. The orientation of the bones forming the elbow joint produces a hinge type synovial joint, which allows for extended 180° (straighten out lower arm) and flexion 150° (bring lower arm to the biceps) of the forearm [1].

## Continuous passive motion

Portable Elbow Joint Device (PEJD) provides continuous passive motion (CPM) exercises to the patients with neurological problems such as stroke and traumatic brain injuries which affected the arm [2]. Besides, it is used during the first phase of rehabilitation process following an elbow injury or elbow that has undergone surgical procedure. Rehabilitation program supports the findings of Gates et al (1992) that post-use of CPM improves total range of motion and therefore function. Thus,

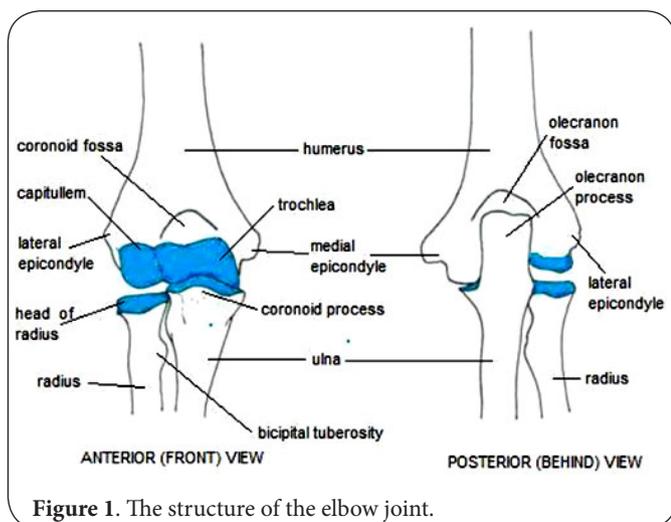


Figure 1. The structure of the elbow joint.

continuous passive motion exercises are important to the patient's elbow recovery from stroke, traumatic brain injuries and also from elbow injury.

A CPM machine or elbow joint rehabilitation device is an electrical, motor-driven device that helps support the injured limbs. It is used to move a joint at variable rates through a progressively increasing range of motion (ROM) [4]; no muscular exertion is required of the patient. CPM acts to reduce blood and fluid accumulation in and around traumatized joints or that have undergone surgery. In this way, CPM is useful in avoiding the development of subsequent joint stiffness in the first few hours or days.

CPM Elbow (Model 3142), a Micro-Computer controlled unit, represents the latest breakthrough in CPM technology. Solid state circuitry control panel with highly visual LED Digital readouts allows Flexion and Extension of Elbow joint through a prefixed Range of Motion and Time.

The existing devices of the elbow rehabilitation device are large, expensive and too heavy, complex and difficult to be carried anywhere due to the size attached to the chair. Patients should be hospitalized for the elbow rehabilitation therapy frequently. The current device which comes together with a wheel stand is not stable and it causes trouble to patients while undergoing treatment. It is also hard for patients to move around because they must stay at one place during the elbow rehabilitation therapy. As the device may move, patients need to sit down during rehabilitation process to ensure the treatment runs smoothly. Furthermore, current devices need to operate on AC power supply.

The therapy process takes place in a comfortable state anywhere. PEJD also facilitates the movement of patient's elbow during treatment. It can reduce the patients' burden when they bend their arm. Furthermore, it can also provide continuous passive motion exercises to help the patient's recovering from stroke, ulnar nerve and elbow injury. The device can be controlled as the count, speed and angle are

adjustable during the treatment process.

## Methodology

### Technical Design

The feature of basic mechanical design is conglutinated wilfully and supported with high strength of the aluminium alloy holder as shown in Figure 2. It provides immobilization by fixing the elbow in every 10-15° with padded shoulder strap to release the pressure around the shoulder. PEJD can simply press and rotate hinge with lock. In addition, it can extend limitation from 0° ~ 90° and flexion limitation from 0° ~ 120°. From this mechanical, additional design of brace for support the movement of motor.

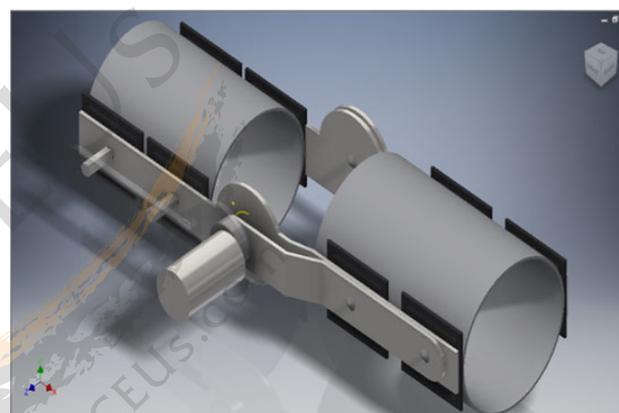


Figure 2. The basic mechanical design of PEJD.

This model is designed by inventors using 3D CAD software. The DC motor is providing the elbow movement. The material used includes adjustable strap which is lightweight, and it is made from breathable fabric and easy to wear. In addition, the design is suitable for both men and women. The casing is designed for extra protection to the hardware. This mechanical design provides fully adjustable tightened impact and better compression to the elbow.

### Electronic Hardware and Software Interface Design

The electronic hardware is shown in Figure 3, consists of Arduino Nano (ATmega328), Arduino Software, DC Motor with encoder, Encoder, Nokia 5110 LCD and Motor Driver L298N. Arduino is a computer hardware and software company, project and user community that designs and manufactures microcontroller kits for building digital devices and interactive objects that can sense and control objects in the physical world [8]. The project's products are distributed as open-source hardware and software. The controller of PEJD, Arduino Nano, is a small, complete, and breadboard-friendly board based on the ATmega328 (Arduino Nano 3.0) or ATmega168 (Arduino Nano 2.x) as shown in Figure 4.

Figure 5 shows the gear motor with encoder, model No

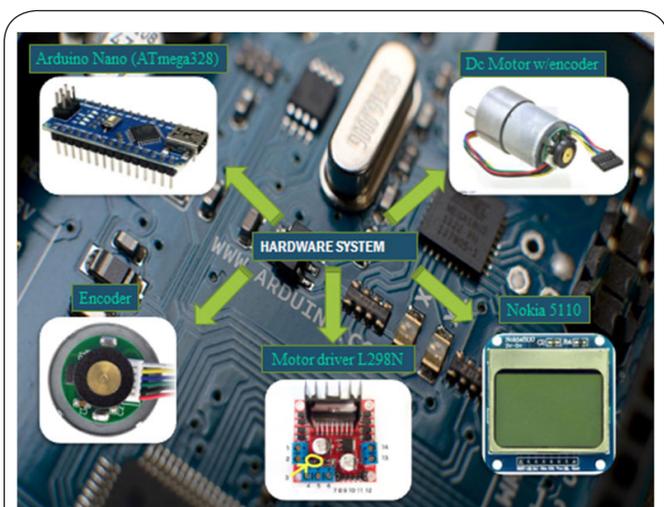


Figure 3. Electronic hardware.

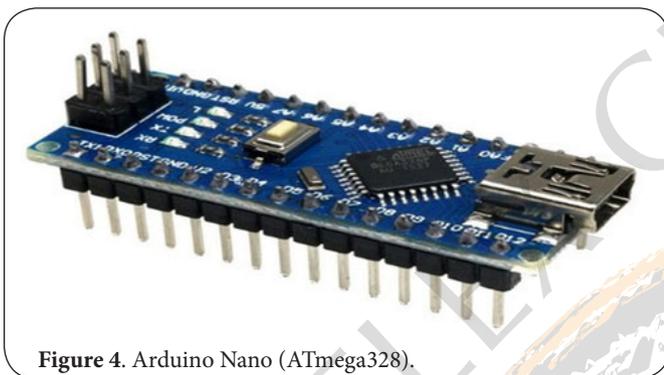


Figure 4. Arduino Nano (ATmega328).

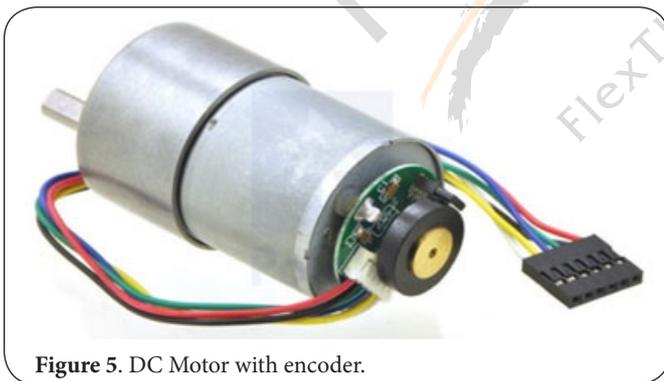


Figure 5. DC Motor with encoder.

GB37Y3530-12V-83R. It is a powerful 12V motor with a 131:1 metal gearbox and an integrated quadrature encoder that provides a resolution of 16 counts per revolution of the motor shaft, which corresponds to 2096 counts per revolution of the gearbox's output shaft. These units have a 0.61" long, 6 mm-diameter D-shaped output shaft. This motor is intended for use at 12V, though the motor can begin rotating at voltages as low as 1V.

The function of PEJD is summarized in **Figure 6**. From power

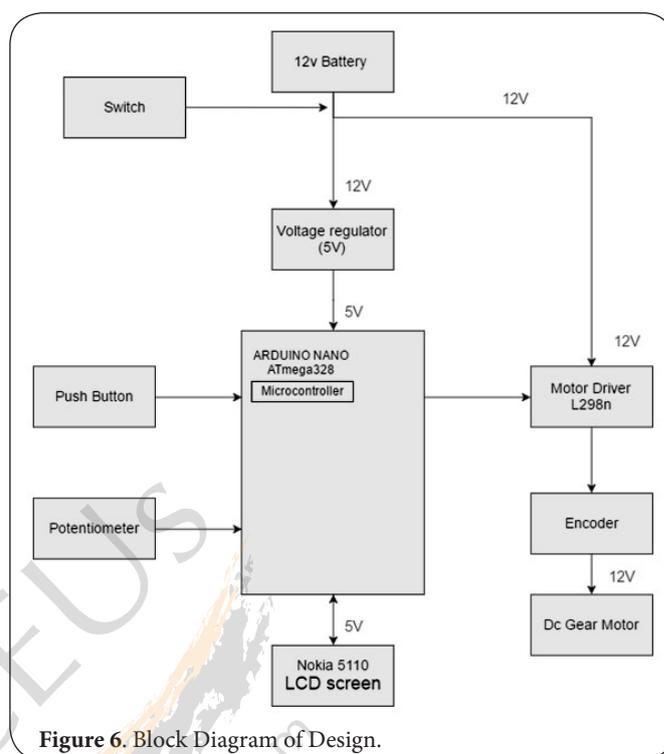


Figure 6. Block Diagram of Design.

supply 12V battery, this device uses voltage regulator (5V) and motor driver L298n. From voltage regulator (5V), power will be enter the microcontroller (Arduino Nano ATmega328) [8]. The microcontroller (Arduino Nano ATmega328) controls the entire system. The mode can be selected from the potentiometer for speed, angle and count setting. The signal from potentiometer goes into microcontroller (Arduino Nano ATmega328). The motor driver L298N will receive a signal from the microcontroller (Arduino Nano ATmega328) to submit to the DC gear motor. The push button is used to run the operation of the device. Nokia 5110 LCD screen will display the speed, angle and count while the device is running. PEJD runs using rechargeable battery. A rechargeable battery can be charged, discharged into a load, and recharged many times, while a non-rechargeable or primary battery is supplied fully charged and discarded once discharged. It is composed of one or more electrochemical cells.

### User's satisfaction survey

Thirty stroke patients volunteered to participate in the survey for user's satisfaction survey. The survey involves interview and observation after the trial test of the device. The respondents are from various levels of age, jobs, qualification and family background. Age ranges from 20 to 50 years and average height and body mass are  $1.50 \pm 0.2$  m and  $50 \pm 5$  kg, respectively. The inclusion criterion is that the patient should only use the device after surgical procedure or consultation by physiotherapist so it couldn't interfere with the user's study performance. The PEJD device is categorized as first phase of

rehabilitation following a soft tissue surgical or trauma. The exclusion criterion is the morbidity of any direct use before any consultation. The trial was carried out with cooperation of patients, doctors and physiotherapists.

### Procedures

Each patient completed trials within a single day. Subjects operate the device following the steps indicated. The simple procedure starts with ON button. After that, a few settings will be adjusted depending on the patients' condition and comfort. Settings include motor speed, angle and counting times. The trials were performed in range of high and low for speed, angle of 15°, 30°, 45°, 60° and 90° and counting times

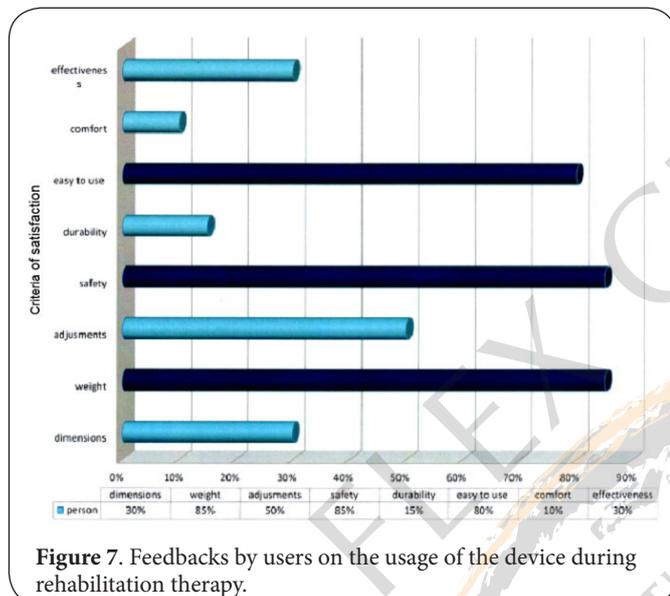
of 10, 20, 30 and so on. The result from all those parameters will be indicated as performance of patient ability in joint movement and were used for further analysis.

### Result and discussion

The result in **Figure 7** shows that safety is one of the criteria that are given priority, followed by its weight and easy to use. Patients also indicated that using the device is comfortable as it fits well to their paretic arm. They felt that device did not make any physical strain due to its light weight in nature. The device must in safety condition when a device in running time. In addition, being user friendly is also one of the appealing criteria. The effectiveness of the product and its weight also need to be considered in upgrading the design. A clinical trial was conducted on post stroke patients to evaluate the performance of the Portable Elbow Joint Device, how it saves manpower and to evaluate the usage of device for active assistive therapy.

### Conclusion

The elbow joint is a compound synovial joint, with several smaller moving parts, or separate articulations. Joint stiffness will occur after joint trauma problem and with the Continuous passive motion (CPM) exercise, the joint stiffness can be reduced and helps to maintain the range of motion (ROM) of the joint. The Portable Elbow Joint Device will provide continuous passive motion exercises with controllable speed, timer and the angle of movement by using Arduino Nano (microcontroller) [7]. Furthermore, a rechargeable battery is added to the device which enables the device to operate on DC power supply. Besides, as this product is portable and provides comfort, it allows the patients to move around during elbow therapy.



**Figure 7.** Feedbacks by users on the usage of the device during rehabilitation therapy.

### Competing interests

The authors declare that they have no competing interests.

### Authors' contributions

Authors' contributions	KLC	MR	AZ1	AZ2	NM1	NM2	MI
Research concept and design	✓	✓	✓	✓	--	--	--
Collection and/or assembly of data	--	--	✓	✓	✓	✓	✓
Data analysis and interpretation	✓	✓	--	✓	--	--	--
Writing the article	✓	✓	--	--	--	--	--
Critical revision of the article	✓	✓	--	--	--	--	--
Final approval of article	✓	✓	--	--	--	--	--
Statistical analysis	✓	✓	--	✓	--	--	--

# Feasibility and clinical experience of implementing a myoelectric upper limb orthosis in the rehabilitation of chronic stroke patients: A clinical case series report

## Abstract

Individuals with stroke are often left with persistent upper limb dysfunction, even after treatment with traditional rehabilitation methods. The purpose of this retrospective study is to demonstrate feasibility of the implementation of an upper limb myoelectric orthosis for the treatment of persistent moderate upper limb impairment following stroke (>6 months). **Methods:** Nine patients (>6 months post stroke) participated in treatment at an outpatient Occupational Therapy department utilizing the MyoPro myoelectric orthotic device. Group therapy was provided at a frequency of 1–2 sessions per week (60–90 minutes per session). Patients were instructed to perform training with the device at home on non-therapy days and to continue with use of the device after completion of the group training period. Outcome measures included Fugl-Meyer Upper Limb Assessment (FM) and modified Ashworth Scale (MAS). **Results:** Patients demonstrated clinically important and statistically significant improvement of  $9.0 \pm 4.8$  points ( $p = 0.0005$ ) on a measure of motor control impairment (FM) during participation in group training. It was feasible to administer the training in a group setting with the MyoPro, using a 1:4 ratio (therapist to patients). Muscle tone improved for muscles with MAS >1.5 at baseline. **Discussion:** Myoelectric orthosis use is feasible in a group clinic setting and in home-use structure for chronic stroke survivors. Clinically important motor control gains were observed on FM in 7 of 9 patients who participated in training.

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## Introduction

Stroke is a leading cause of long term disability in the United States[1]. Traditional rehabilitation does not restore normal motor control for all stroke survivors, and upwards of 50% live with persistent upper limb dysfunction[2]. This leads to diminished functional independence

and quality of life[3]. Motor learning-based interventions have shown promise[4]. However in today's health care milieu, for those with chronic motor deficits, provision of the intensive rehabilitation necessary to provide motor learning-based interventions is challenging. Therefore, new treatment methods are needed under these constraints.

An emerging technology that warrants further investigation is myoelectric control which harnesses the user's EMG signal to power a custom fabricated orthotic device. When the user activates a target muscle, the EMG signal from that muscle signals a motor to produce a desired movement. Myoelectric control has been studied in different populations[5], but its study in stroke has been limited. One commercially available upper limb myoelectric device is the MyoPro motion-G (Cambridge, MA). The MyoPro motion-G provides assistance to the weak upper limb and allows the patient to perform movement they otherwise are unable to complete. Preliminary evidence suggests it may be effective in improving motor control[6-9] and one study showed improvement in self-reported function and perception of recovery[10]. This device has been utilized in the occupational therapy (OT) clinic at our medical center for 5 years. The purpose of this study is to demonstrate feasibility of administering treatment with the MyoPro using a group therapy design in a cohort of patients with chronic stroke whose progress with standard OT had plateaued.

## Methods

This is a retrospective analysis of data collected longitudinally while chronic stroke patients participated in group training with a MyoPro in our clinic. Training was provided by OT staff. This study was approved by the IRB of the Louis Stokes Cleveland Department of Veterans Affairs Medical Center (IRB #17030-H23). Approval was obtained to review and analyze patient data.

## MyoPro treatment candidate selection criteria

Patients were assessed for eligibility to receive a MyoPro once they reached a plateau in functional performance following traditional OT. Inclusion criteria included: regular/consistent therapy attendance; trace muscle contraction in major upper limb muscle groups; adequate passive ROM to don/doff device; intact cognition; active shoulder flexion  $\geq 40^\circ$  and shoulder abduction  $\geq 20^\circ$ ; ability to don/doff device with/without a reliable caregiver. Nine patients were prescribed a MyoPro at the conclusion of their regular OT.

## Technology

The MyoPro Motion-G is a custom fabricated, myoelectric upper limb orthosis worn on the paretic upper limb (Fig 1). It supports the affected limb and assists the user to perform flexion/extension of the elbow and opening/closing of the hand. Sensors within the device detect the patient's EMG signal during volitional muscle contraction. When an EMG signal is sensed, motors within the device provide assistance to complete the desired movement (i.e. hand opening/closing). Using computer software, the therapist adjusts the EMG level at which device movement is triggered. The degree of movement produced by the device is proportional to the recorded EMG level produced by the patient's volitional effort. Patients interface with the device through a push button control panel and via software on a computer. Users can switch between 4 individual SINGLE modes (BICEP mode, TRICEP mode, hand CLOSE mode, and hand OPEN mode), and are able to train multi-joint movement by practicing combinations of these modes (i.e. BICEP+hand CLOSE modes). Additionally, users can combine both EMG sensors simultaneously at a given joint (i.e. DUAL mode elbow, which combines the biceps and triceps EMG sensors; DUAL mode hand, which combines the finger flexor and extensor EMG sensors) or all 4 EMG sensors can be used simultaneously (DUAL mode elbow + DUAL mode hand). To practice joint movement in a SINGLE mode, the patient is required

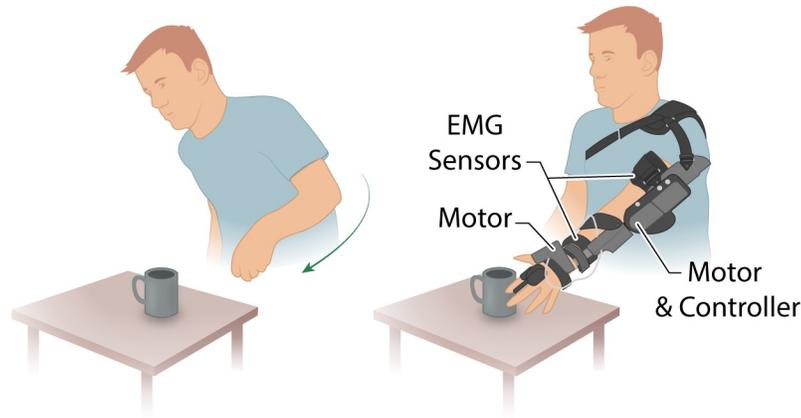


Illustration by Cleveland FES Center

**Fig 1. Schematic drawing of an individual reaching for an object without and with the device donned.** With assist of the device, the goal directed movement of reaching for the object can be completed. The Cleveland FES Center created this illustration and has granted the authors permission to publish it in this manuscript.

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to produce an adequate EMG signal to reach the therapist-adjusted threshold. To return to the starting position their EMG must drop below this threshold (i.e. the patient must learn to relax the muscle). To trigger movement in DUAL mode, both flexor and extensor EMG signals are taken into account. The motor is activated after a corresponding muscle's EMG exceeds its threshold and is greater than the EMG in the antagonist muscle. For example, elbow extension is achieved when triceps EMG exceeds its threshold and biceps EMG is less than triceps EMG. This practice facilitates relearning coordinated control of agonist/antagonist muscles across the joint as opposed to abnormal co-activation of both muscles which precludes practice of such movement.

## Intervention

An orthotist performed custom fabrication of each patient's device along with initial fitting and setting of device parameters for training. A group training paradigm was employed where patients were scheduled for 1–2 weekly group sessions (60–90 minutes/session). Patients unable to attend the group sessions received individualized MyoPro training (n = 2).

**Patient selection.** Patients entered the group when they were deemed plateaued in their traditional therapies. The group accepted new patients using a rolling enrollment schedule-i.e. an individual was offered entry into the group when they were plateaued with their traditional OT. Because of this, patients joined the group at different time points and therefore some have data that spans a longer duration. Upon discontinuation of group therapy, patients were issued a home exercise program to complete with their MyoPro and encouraged to use the device in performing everyday activity. In this data analysis, we labeled the first phase (i.e. when they attended group therapy training) as the Supervised phase and the following phase as the Unsupervised phase (when group therapy was discontinued). For the Unsupervised phase, all patients had access to their device as it was purchased for their personal use. However, 5/9 patients did not attend any further therapy sessions after the group training ended and therefore received no further evaluation. Four patients had sought out additional visits with OT (1 session every 5–10 weeks) after the conclusion of the group therapy and were subsequently re-evaluated. It is notable that some patients did not have a device for some period of time during this Unsupervised period as it was being upgraded to the most current model.

**Intervention: Training progression.** At each session, patients donned the device. Then, a training progression was employed (Table 1). First, patients performed preparatory exercises using SINGLE modes (i.e. BICEP mode or hand CLOSE mode). During BICEP mode training, patients were instructed to bend their elbow and then relax back to the start position. For hand CLOSE mode, they practiced closing their hand and relaxing back to the start position. After preparatory activities, therapeutic exercises were performed in either the seated or standing position. These exercises were designed to prepare patients for activities that required sustained contraction or contraction across multiple joints in preparation for function. For example, patients performed multiple repetitions of BICEP mode with instruction to bend their elbow, sustain a position for a fixed time, and then relax the elbow followed by completing hand CLOSE mode, holding for a period of time and relaxing. Depending on individual ability, exercises also included combined hand and elbow motions to work on separate and simultaneous elbow and hand motions. As patients progressed, they would also perform functional task training with the device including sorting laundry, placing utensils away, sorting tools, holding a pot while stirring with unaffected hand, and sweeping.

**Outcomes.** Outcome measures were the Fugl Meyer Upper Limb Assessment (FM) and modified Ashworth Scale (MAS). FM is an impairment measure of motor control, [11] with good validity, [12] intra-rater and inter-rater reliability, [13] and is recommended for use in chronic stroke trials [14] (0–66 points; a higher score equals less impairment). MAS is a commonly used clinical test of muscle tone with high interrater reliability (kappa = 0.92 or percent of agreement = 97.4%) [15]. It consists of a six-point scale (0, 1, 1.5, 2, 3 and 4) used to grade tone elicited during passive movement [16]. A score of 0 corresponds to normal tone while a rating of 4 corresponds to rigidity. The timing of data collection varied among patients. However, they were all evaluated at around the 12-week time point of the device use. Outcomes were collected without the device donned.

**Statistical analysis.** Data analysis included descriptive statistics and use of paired t-tests. Two-sided Type I error level of 0.05 was adopted for hypothesis testing.

## Results

Table 2 provides patient characteristics (n = 9). Fig 2 provides information regarding the change in FM score over time along with individual patient participation patterns in the group training sessions. Patients were moderately impaired at initial data collection according to FM

**Table 1. Summary of group training protocol.**

1. Don on Device
2. Warm Ups/Preparatory Activities (Sitting &/or Standing)
  - a. Bend elbow, relax/extend– 25 reps (BICEP or DUAL MODE)
  - b. Extend elbow, relax/flex– 25 reps (TRICEP or DUAL MODE)
  - c. Close hand, relax/open– 25 reps (CLOSE or DUAL MODE)
  - d. Open hand, relax/close– 25 reps (OPEN or DUAL MODE)
3. Therapeutic Exercises (Seated &/or Standing)
  - a. Bend elbow and Hold 10+ seconds, then Relax– 25 reps
  - b. Close Hand and Hold 10+ seconds, then Relax– 25 reps
  - c. Yo-yos: Bend elbow low, middle, full (~45°, 90°, full range)– 25 reps\*\*relax and extend elbow between each rep
  - d. Combined motions:
    - i. Close hand>Bend Elbow>Open Hand>Extend Elbow– 25 reps
    - ii. Open hand>Bend Elbow>Close Hand> Extend Elbow>Open Hand– 25 reps
4. Functional Tasks
  - a. Sorting tools, laundry, utensils
5. Turn off/doff Device

**Table 2. Patients' Characteristics (N = 9).**

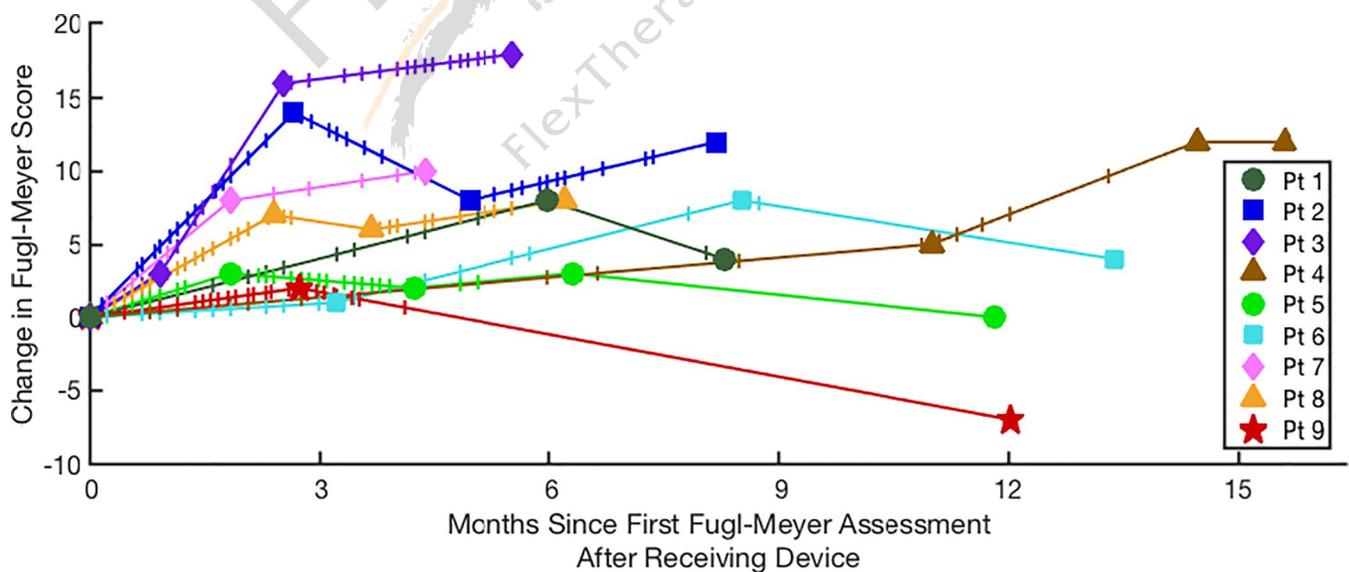
Age in years, mean (SD)	62 (9.5)
Female, %	11%
Years since stroke, mean (SD)	4.3 (3.7)
Stroke Hemisphere, % Left	67%
Stroke Type, % ischemic	78%

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(Table 3). Four of 9 patients had their dominant arm affected by stroke (patients 1,2,3 and 9, Table 3).

### Supervised phase: change in FM score

There was variability in the length of time patients trained with the device during the Supervised phase (11.9–62 weeks), however, the majority of patients (7/9) had testing completed around the 12-week point of using the device (Table 3 and Fig 2). Two patients were not re-tested until the 26<sup>th</sup> (patient#1) and 62<sup>nd</sup> (patient#4) weeks of participation in the MyoPro group therapy. For those who were evaluated at about 12 weeks of working in the Supervised phase, there were significant changes in FM (7.3 (5.9) points;  $p = 0.017$ ; Table 3). The timing of 12-week testing varied from 8 to 14 weeks. At the conclusion of the Supervised phase, patients had participated in group training an average of 32.16(12.8) hours and a statistically significant change from the initial FM score was observed (9.0(4.8) points;  $p = 0.00053$ ; Table 3). Sixty percent of patients improved FM between the 12-week testing and the end of the Supervised phase (mean length of Supervised phase was 30 weeks). Seven out of nine patients demonstrated a FM change score  $\geq 5$  points at the end of the Supervised phase which is within or above the minimal clinically important difference (MCID) range of 4.25–7.25 points[17]. Patient#7 had non-device OT sessions twice per week in addition to the group device visits.



**Fig 2. Change in Fugl-Meyer score over time for each group therapy participant.** The change in FM score from the initial evaluation is shown with different symbols for each patient. Vertical tick marks correspond to therapy sessions using the device for each individual of the group.

<https://doi.org/10.1371/journal.pone.0215311.g002>

Table 3. Device use and change in Fugl-Meyer scores.

Patient	Initial FM	Supervised Phase				Unsupervised phase		
		12-week testing (actual week #)	FM change @ 12-week testing	Supervised phase duration (weeks)	FM change during Supervised phase	Unsupervised phase duration (weeks)	FM change post Supervised phase	FM change from initial test
1	24			26.0	+8	10.0	-4	+4
2	24	11.6	+14	35.6	+12	na		+12
3	29	11.0	+16	24.0	+18	na		+18
4	41			62.9	+12	na		+12
5	53	8.0	+3	27.4	+3	24.0	-3	0
6	29	14.0	+1	37.0	+8	21.1	-4	+4
7	42	8.0	+8	19.0	+10	na		+10
8	14	10.4	+7	27.0	+8	na		+8
9	45	11.9	+2	11.9	+2	40.4	-9	-7
Mean (SD)	33.4 (12.5)	10.7 (2.1)	7.3 (5.9)*	30.1 (14.5)	+9.0 (4.8)†	24.0 (12.6)	-5.0 (2.7)	+6.8 (7.4)‡

\* t-test p = 0.017

† t-test p = 0.00053

‡ t-test p = 0.026

na—not applicable as these patients did not have re-evaluation following an Unsupervised phase

<https://doi.org/10.1371/journal.pone.0215311.t003>

### Unsupervised phase: FM score

Only 4 patients had FM scores obtained following the Unsupervised phase (Table 3 and Fig 2). These 4 patients demonstrated some worsening, although most were still improved compared with the initial score. Patient#1 had initial FM = 24, gained 8 points during the Supervised phase, but lost 4 FM points during the Unsupervised period even though they were still attending near-weekly standard OT sessions without the device. Patient#5 had initial FM = 53, gained 3 and then lost 3 FM points. However, patient#5 had additional twice weekly OT sessions without the device for the 1<sup>st</sup> half the Supervised phase and weekly sessions for the 2<sup>nd</sup> half. During the Unsupervised phase this patient did not use the device half the time due to device upgrading and participation in a research study. Patient#6 had initial FM = 29, gained 8 and then lost 4 FM points during the Unsupervised phase; this patient also had biceps, forearm and hand botulinum toxin treatments for spasticity during the Unsupervised phase. Patient#9 had initial FM = 45, gained 2, but lost 9; the patient did not have the device for 2 months prior to the final evaluation.

### Change in MAS score

At the initial testing, abnormal muscle tone (MAS>0) was detected in elbow flexors of 6 patients and in wrist flexors of all tested patients (Table 4). Data is missing for patient#7 (initial test) and patient#4 (after device use). Although there was no statistically significant pre to post change observed with a group-wise comparison (p>0.05), improvements were observed for some patients. For elbow flexor tone, there was an improvement of MAS score for 3 patients and worsening in 1 patient. The improvement for patient#6 from 1.0 to 0 was made approximately 4 months after receiving the device and 9 months prior to reporting initiation of botulinum toxin treatments. Worsening of MAS score occurred in patient#5 who had very mild MAS of 1 at the initial test. For wrist flexors, there was an improvement in MAS score for 4 patients and worsening in one. Importantly, for 3 patients with MAS > 1.5 at initial testing, there was a consistent improvement in MAS score during the Supervised phase.

**Table 4. Modified Ashworth scale scores before and after device use.**

Patient	Elbow Flexors			Wrist Flexors			Time with MyoPro (weeks) <sup>†</sup>
	Pre*	Post	Change	Pre	Post	Change	
1	0.0	0.0	0.0	1.0	1.0	0.0	46.0
2	4.0	1.5	-2.5	4.0	1.5	-2.5	47.0
3	0.0	0.0	0.0	1.5	1.0	-0.5	27.1
4	1.0	NC		1.0	NC		
5	1.0	1.5	0.5	2.0	1.5	-0.5	4.3
6	1.0	0.0	-1.0	1.0	1.0	0.0	17.0
7	NC	1.0		NC	0.0		40.1
8	1.5	1.5	0.0	1.0	1.5	0.5	39.0
9	2.0	1.0	-1.0	3.0	2.0	-1.0	19.4
Mean (SD)	1.3 (1.3)	0.8 (0.7)	-0.6 (1.0)	1.8 (1.1)	1.2 (0.6)	-0.6 (1.0)	30.0 (15.5)

NC = not collected

\* MAS prior to receiving the MyoPro

<sup>†</sup> Time elapsed after receiving the MyoPro

<https://doi.org/10.1371/journal.pone.0215311.t004>

## Discussion

This study provides evidence that it is feasible to utilize a myoelectric upper limb orthosis using a group training paradigm for the rehabilitation of moderately impaired chronic stroke survivors. The main finding is that clinically important changes on a motor control performance measure were observed in individuals with chronic stroke who participated in group training. Of note, these patients were deemed plateaued with traditional OT services and were being discharged from standard care. There was a trend toward decreased flexor tone in individuals presenting with elevated flexor tone.

The gains on FM in our clinical practice setting study are comparable to many studies conducted in the research setting with subjects who were less impaired. For example, in research studies of less impaired individuals (baseline FM 39–55 points), patients demonstrated gains ranging from 6–9 points on FM [18–26]. For studies with similar impairment level to our cohort (baseline FM 27–36 points), treatment gains on FM ranged from 2–14 points [27–35]. Participants across these research studies trained an average of 24.9 hours (range of 7–48 hours), similar to the number of face to face hours for our patient cohort. It is encouraging that our results are comparable to many of these studies even though they were obtained in a clinical treatment setting under the constraints of current health care delivery where patient selection and therapy administration is less strictly controlled than in the rehabilitation administered within the research setting. Translation of research into actual clinical practice is an area of great interest and significant challenge in rehabilitation science [36,37]. Within the research setting, rehabilitation typically has strict subject inclusion/exclusion criteria, duration, intensity and content of care. Our patient cohort reflects real world variability in impairment levels and the care that is specifically tailored to meet the needs of the individual receiving the care (as opposed to a standardized research intervention). Our observation, therefore, presents a novel training paradigm that would be feasible within our current clinical practice setting using a group therapy approach and motor learning as the basis for intervention.

The MyoPro allows practice of three important motor learning principles. First, it encourages coordinated, volitional muscle activation. With EMG-biofeedback the patient learns to

selectively contract a desired muscle in a coordinated manner that would be difficult to accomplish without the device. Often when a patient attempts a movement (i.e. grasp preparation), involuntary co-contraction of the antagonist occurs. This abnormal co-contraction limits opening of the hand in preparation for grasp. Furthermore, due to disparity of muscle strength between the agonist/antagonist pairings (i.e. greater strength in the finger flexors versus the extensors), the ability to selectively practice finger extension is precluded. Others have studied whether myoelectric control can address pathological co-contraction with some promising findings[38,39]. In one study, EMG biofeedback training was used to decouple the anterior deltoid and bicep muscles, and patients demonstrated more selective muscle activation with modest improvement on FM[38]. Improved coordination of agonist/antagonist pairs was also demonstrated with a hybrid EMG-driven robotic/neuromuscular electrical stimulation system and there was a clinically significant improvement on FM[39]. The Myopro employs biofeedback in a targeted manner to allow for very consistent, incremental practice of individual muscle activation as well as coordination training of agonist/antagonist pairings. The second principle is motivation for repeated practice which is encouraged by the reward of movement the device delivers. Moderately/severely impaired patients are usually discouraged in their repeated task practice because they do not experience the product of their hard labor. This device compensates for patients' physical disabilities and produces a desired joint movement which motivates additional practice. Furthermore, the training is ultimately aimed at completion of meaningful functional tasks which provides further motivation. Finally, the device allows for incremental progression of training. Both single and multi-joint movement exercises can be performed; exercise can be fragmented; device settings (i.e. EMG threshold) can be adjusted to introduce additional challenge; and practice can be done in different body postures. Overall, the combination of EMG biofeedback with a wearable powered upper limb orthosis presents a powerful therapeutic tool that fits well within the framework of motor learning.

Patients were scheduled for 1–2 weekly sessions. However, high attendance variability was noted with some patients (i.e. patient#4; Fig 2) while others attended a greater number of sessions within a shorter time frame (i.e. patient# 3; Fig 2). Despite this variability, patients improved individually on the main study outcome measure. It is reasonable to suggest that consistent gains across all participants may have occurred because patients had access and were encouraged to practice with their device in the home setting.

Our study results were obtained in a clinical setting using a group therapy training paradigm. This is important for a few reasons. First, our study demonstrates that clinically important treatment gains can be made in chronic stroke patients with persistent motor control deficits in an actual clinical setting, as opposed to a controlled research laboratory. Furthermore, training was implemented efficiently in a group training paradigm (4:1 patient to therapist ratio). Delivery of care in a group setting allows more patients to benefit from limited rehabilitation resources and evidence suggests it can be as effective as individual therapy in stroke[40]. Additionally with group therapy training, patients were given the opportunity to train over several months. This may have allowed sufficient time to address persistent motor control impairments and allow for consolidation of gains. Of note, patients in our cohort had plateaued in traditional OT, and with exception of a few were being discharged from therapy. However, they were given the opportunity to try this novel training approach. Clinically important and statistically significant gains were made on the FM after therapists assessed the patients to be plateaued with traditional services. Though efficacy of group training with the device cannot be determined due to small sample size and variability of training parameters, our results provide groundwork for further examination of this training paradigm to be considered in addressing persistent deficits following stroke.

Mitigation of elevated flexor muscle tone was demonstrated in several patients. Three patients showed a decrease in elbow flexor tone and 4 patients showed a decrease in wrist flexor tone by the end of the study. The variability in the muscle tone data is likely due to small sample size and/or inclusion of patients who did not initially present with tone or presented with mildly increased tone. Furthermore, muscle tone management may require regular use of the device. Future research will be needed to evaluate the effect of myoelectric orthotics on management of spasticity.

Data for the Unsupervised phase is limited in two ways. First, only 4 of 9 patients were re-evaluated. Second, there were long periods when patients did not have full access to their device as it was being upgraded. As a result, much of the time participants were without their device and could not continue their independent training. During the Unsupervised phase, we observed degradation in motor control performance according to FM for all patients. Non-use of the device may result in deterioration of motor performance, although this conclusion is preliminary. Our results suggest that further study is warranted to determine whether regular home use of the device is needed to maintain gains made during supervised training.

Several limitations of the current study constrain interpretation of our findings. Two main limitations were the inconsistent timing with which testing was completed and variability in treatment doses across different patients. Additionally, this was a retrospective analysis of clinical care delivered to a small, heterogeneous group of stroke survivors and data was not available on patients' adherence with the home exercise program. However, given that this was an actual clinical setting and not a designed clinical trial, our data may be more representative of clinical practice patterns in chronic stroke. Finally, we report only measures of impairment, thus limiting our interpretation of findings in terms of function and quality of life. More robust measurement across multiple domains is necessary to further elucidate how the device impacts patient care and functional performance.

## **Conclusions**

In a group clinical setting, it was feasible to implement a myoelectric upper limb orthosis with chronic stroke survivors. Clinically important and statistically significant gains were made on a measure of upper limb motor control. The results may be explained by the motor learning based functionality of the device. Further study is warranted in a larger cohort.

# Home rehabilitation supported by a wearable soft-robotic device for improving hand function in older adults: A pilot randomized controlled trial

## Abstract

### Background

New developments, based on the concept of wearable soft-robotic devices, make it possible to support impaired hand function during the performance of daily activities and intensive task-specific training. The wearable soft-robotic ironHand glove is such a system that supports grip strength during the performance of daily activities and hand training exercises at home.

### Design

This pilot randomized controlled clinical study explored the effect of prolonged use of the assistive ironHand glove during daily activities at home, in comparison to its use as a training tool at home, on functional performance of the hand.

### Methods

In total, 91 older adults with self-perceived decline of hand function participated in this study. They were randomly assigned to a 4-weeks intervention of either assistive or therapeutic ironHand use, or control group (received no additional exercise or treatment). All participants performed a maximal pinch grip test, Box and Blocks test (BBT), Jebsen-Taylor Hand Function Test (JTHFT) at baseline and after 4-weeks of intervention. Only participants of the assistive and therapeutic group completed the System Usability Scale (SUS) after the intervention period.

**Competing interests:** The authors have declared that no competing interests exist. Potential conflict of interests: Our project partners Bioservo Technologies AB and Hocoma AG were involved in the ironHand project (grant AAL-2013-6-134), and interested in commercializing the ironHand system. Alejandro Melendez- Calderon was with Hocoma AG at the time of the study, but is now with Cereneo AG, Switzerland. He does not receive any financial or personal benefits from Hocoma AG or any other source for the publication of this study. This does not alter our adherence to PLOS ONE policies on sharing data and materials.

## Results

Participants of the assistive and therapeutic group reported high scores on the SUS (mean = 73, SEM = 2). The therapeutic group showed improvements in unsupported handgrip strength (mean  $\Delta = 3$ ) and pinch strength (mean  $\Delta = 0.5$ ) after 4 weeks of ironHand use ( $p \leq 0.039$ ). Scores on the BBT and JTHFT improved not only after 4 weeks of ironHand use (assistive and therapeutic), but also in the control group. Only handgrip strength improved more in the therapeutic group compared to the assistive and control group. No significant correlations were found between changes in performance and assistive or therapeutic iron-Hand use ( $p \geq 0.062$ ).

## Conclusion

This study showed that support of the wearable soft-robotic ironHand system either as assistive device or as training tool may be a promising way to counter functional hand function decline associated with ageing.

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## Introduction

Hand function predominantly determines the quality of performance in activities of daily living (ADL) and work-related functioning. Older adults with age-related loss of muscle mass (i.e. sarcopenia) [1] and/or age-related diseases (e.g. stroke, arthritis) [2, 3] suffer from loss of hand function. As a consequence, they experience functional limitations, which affects independence in performing ADL [3–5].

An effective intervention for improving hand function of (stroke) patients should consist of several key aspects of motor learning, such as high-intensity and task-specificity in repetitive and functional exercises that are actively initiated by the patient him/herself [6, 7]. In a traditional rehabilitation setting, those kinds of interventions are performed with one-on-one attention from the healthcare professional for each patient. This might become problematic in the near future when the population of older adults with age-related diseases (e.g. stroke, rheumatoid arthritis) with hand function decline will rise, resulting in an increased need for healthcare professionals and a rise of healthcare costs [8]. Therefore, new alternatives to provide intensive therapy for all patients are needed in the future.

New technological developments, such as robot-assisted hand training, have the potential to provide such intensive, repetitive and task-specific therapy. Several reviews [9–11] already showed positive results on motor function after robot-assisted training of the upper extremity. However, limiting factors of robot-assisted therapy are the need for supervision of a healthcare professional, the high costs of the devices and the limited availability of wearable devices for training at home [12]. Furthermore, it is often not efficient in transferring the trained movements into daily situations [6]. Therefore, the next generation robotic training approaches should pay substantial attention towards home-based rehabilitation and the functional nature of the exercise involved.

A new way of providing functional, intensive and task-specific hand training would involve using new technological innovations that enable support of the affected hand directly during the performance of ADL, based on the concept of a wearable robotic glove [13–18]. In this way, the affected hand can be used repeatedly and for prolonged periods of time during functional daily activities. These robotic gloves can use different human-robot interfaces to provide

assistance for the affected hand, such as an EMG-controlled glove, a tendon driven glove, a glove controlled by force sensors etc. [13, 14, 16, 18, 19]. All these robotic gloves use soft and flexible materials to make such devices more lightweight and easy to use, accommodating wearable applications. This concept of a wearable soft-robotic glove allows persons with reduced hand function to use their hand(s) during a large variety of functional activities and may even turn performing daily activities into extensive training, independent from the availability of healthcare professionals. This is thought to improve hand function and patient's independence in performing ADL.

Therefore, an easy to use and wearable soft-robotic glove (ironHand system), supporting grip strength and hand training exercises at home, was developed within the ironHand project [20]. Previous studies have examined feasibility [20] and the orthotic effect of the ironHand system [21]. In a first randomized controlled clinical study, the effect of prolonged use of such an assisting glove during ADL at home on functional performance of the hand was explored, in comparison to its use as a training tool at home.

## Methods

### Participants

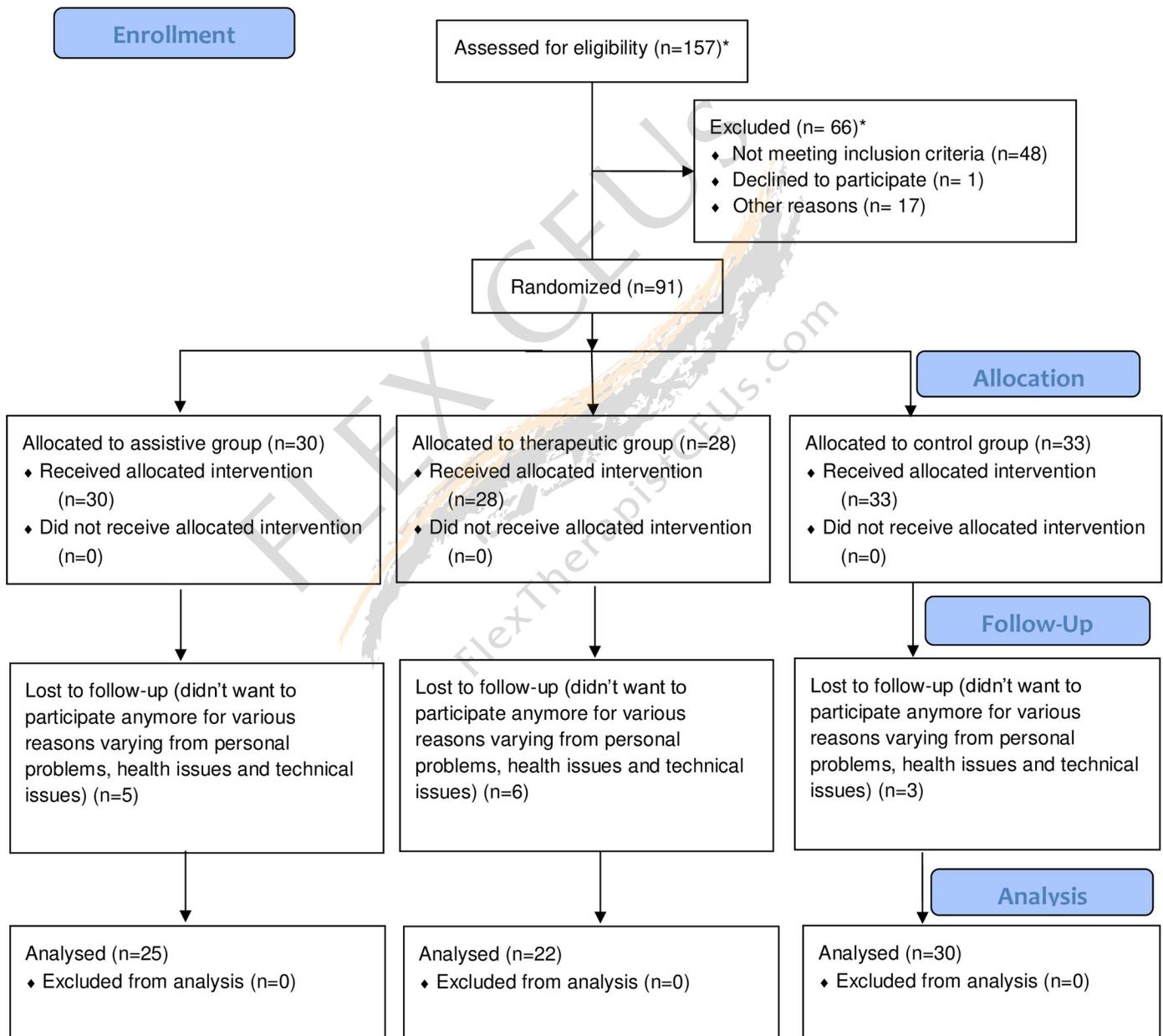
Four sites (1) Roessingh Research and Development (RRD), Enschede, (2) National Foundation for the Elderly (NFE), Bunnik in the Netherlands, (3) Eskilstuna Kommun Vård- och omsorgsförvaltningen (ESK), Eskilstuna in Sweden and (4) terzStiftung (TERZ), Berlingen in Switzerland were involved in the recruitment of the participants. Inclusion criteria for participation into this study were: older adults over the age of 55; self-reported difficulties in performing daily activities, related to hand function decline; at least 10 degrees of active flexion and extension movement of the fingers; able to don/doff the glove by themselves; discharged from specific arm/hand therapy; sufficient cognitive status to understand two-step instructions; (corrected to) normal vision; and living at home. Potential participants were excluded if they had: severe sensory problems, acute pain or wounds on their hands that may create problems when wearing the glove; severe contractures limiting passive range of motion; insufficient knowledge of the Dutch, Swedish or German language to understand the purpose or methods of the study; and participation in other studies that can affect functional performance of upper limb. A power calculation wasn't applicable for defining the sample size due to the explorative and innovative nature of the study, so the sample size was based on pragmatic grounds. The current findings will serve as input for power calculations for future clinical trials.

An informed consent form was signed by both the participating individuals and the researchers before the study started. The study was approved by the local Medical Ethical Committees in the Netherlands (registration number: NL56746.044.16), Switzerland (registration number: KEKTGOV2015/16) and Sweden (registration numbers: 2016/923-31/2 and 2017/466-32). For this study, recruitment of participants started June 14, 2016 and ended April 11, 2017. The authors confirm that all ongoing and related trials for this drug/intervention are registered.

### Design

In this multicentre, longitudinal, pilot randomized controlled trial, participants were randomly assigned (using a pre-defined block randomization list, allocating 6 participants per block per center) into three different groups (assistive, therapeutic or control group) (Fig 1). The assistive group used the ironHand system independently during the performance of ADL at home or at work. The therapeutic group performed hand exercises with the ironHand system

**CONSORT 2010 Flow Diagram**



\* Information about enrollment only available of 1 site. After randomization information is available of all 4 sites.

independently at home and the control group did not receive the ironHand system nor followed any arm/hand therapy. The duration of the treatment was 4 weeks for all groups.

During evaluation sessions within one week before the start of the study and within one week post training, the participants performed various hand function tests to assess the therapeutic effect of the different modes of the ironHand system. All tests were performed in a controlled environment across the four sites: RRD, NFE, ESK and TERZ.

The researchers involved in the study received instructions about how to handle, operate and explain use of the ironHand system to participants by personnel from the technical project partners (Bioservo Technologies AB, Hocoma AG) prior to the start of the study. Also, they were instructed on how to execute the hand function tests by researchers from RRD (coordinator of the study), following a standard procedure.

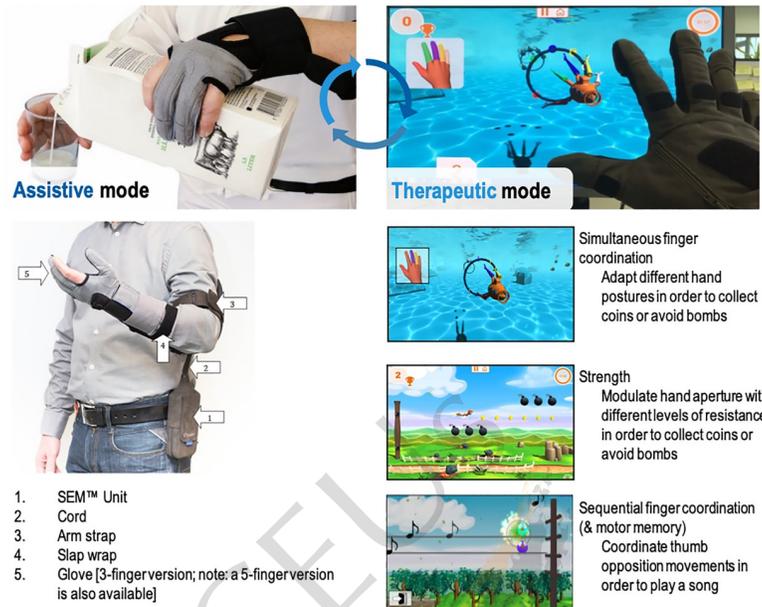
## Intervention

**The ironHand assistive group.** Participants assigned to the ironHand assistive group received the wearable soft-robotic glove for independent use as an assistive tool during daily activities at home or work for 4 weeks. It was recommended to use the assistive ironHand glove at least 180 min/week during the most common ADL, such as dressing/undressing, eating/drinking, functional transfers and personal hygiene. Nevertheless, they were free to choose for which activities, when and for how long they used the glove. The participants were asked to register the amount of use and activities in which they used the ironHand system in a diary.

**The ironHand therapeutic group.** Participants assigned to the ironHand therapeutic group used the soft-robotic glove only in combination with a laptop with the therapeutic ironHand software, as a training tool, independently at home for 4 weeks. They were instructed to only use the glove during training exercises with the laptop, they were not allowed to use the glove as an assistive tool during daily tasks. These participants were recommended to perform the hand exercises (games) with the ironHand system for (a minimum of) 180 minutes a week. These exercises were controlled by active arm and hand movements, recorded from flex and force sensors in the glove. Therefore, a calibration procedure presented as a game was performed, to assess participants' current active range of motion of the hand and fingers at the end of the baseline session. After the calibration game, the therapist made a therapy plan (in which the exercises and starting levels were defined) based on the limitations and treatment goals of the participants. The therapist could choose three different games designed to train hand strength, simultaneous finger coordination and sequential finger coordination (see Fig 2) and three difficulty levels (easy, medium and high). During the exercises, participants received feedback about points collected during the game and corresponding scores. The participants were asked to register the amount of use and games that were played in a diary.

**The control group.** Participants assigned to the control group did not follow a specific intervention during the intervention period. They continued their normal activity pattern of their most-affected hand.

Participants of the assistive and therapeutic group received an ironHand system for their most-affected hand. Before the participants took the ironHand system home, researchers gave instructions about all relevant aspects of the ironHand system, demonstrated it to and practiced with the participant, until the researchers were confident that the participant knew how to use the system at home properly, according to their group allocation (assistive vs. training tool). Additionally, participants received a manual with most important information about the



**Fig 2.** Overview of the ironHand system with assistive functionality (left panel) and therapeutic functionality (right panel). \* Reprinted from Bioservo Technologies under a CC BY license, with permission from Bioservo Technologies, original copyright 2017.

<https://doi.org/10.1371/journal.pone.0220544.g002>

system and a phone number that they could call in case of problems. Furthermore, participants of all three groups were contacted weekly during these 4 weeks of intervention to make sure the participant was doing well and to investigate the progress of the participant. If the games or difficulty level was too easy or too difficult for the participants of the therapeutic group, it was possible to change the order of games and difficulty levels via remote access during their weekly contact.

## Device

The ironHand system was developed to support older adults and patients with self-reported hand function limitations during the performance of daily activities (the assistive functionality) or hand training exercises (therapeutic functionality). The assistive functionality of the ironHand system (see Fig 2, left panel) provides extra strength to the grip of the thumb, middle finger and ring finger of persons with reduced hand function. The grip support is applied by artificial tendons in the wearable soft-robotic glove (placed along the length of the fingers), actuated via motors in the control unit of the system. The extra grip strength is modulated by pressure sensors (Interlink Electronics) in the finger tips. An intention detection logic ensures that the extra strength to the grip is activated in a natural and intuitive way and only after an active contribution by the user. Furthermore, the actuators of the system provide extra force to the grip in proportion to the grip force applied by the user.

The therapeutic functionality of the ironHand system (see Fig 2, right panel) provides a motivating game-like environment to train specific aspects of hand function, such as hand/finger strength, finger coordination or finger independence. The system consists of a therapeutic platform referring to a computing system (e.g. PC or laptop) to which a soft-robotic glove can

be connected. The flex sensors along the dorsal side of the 5-finger glove control the hand training exercises played on the PC or laptop. The hand training exercises, assessments, connectivity to other devices, patient database, additional safety mechanisms and user interface are embedded in the therapeutic software.

## Evaluation

For both evaluation sessions, the same order of tests was applied, as follows. First, maximal handgrip strength of the most-affected hand was assessed as primary outcome measure. Subsequently, secondary outcome measures were assessed, starting with pinch strength of the most-affected hand were measured with a dynamometer. Next, hand function performance of the most-affected hand was measured with the Jebsen-Taylor Hand Function Test (JTHFT) and the Box and Blocks Test (BBT). The System Usability Scale (SUS), that measures subjective experience of usability of the ironHand system, was completed at the end of the post-evaluation session, only by the participants of the assistive and therapeutic intervention groups.

## Assessments

**Maximal handgrip strength.** Maximal handgrip strength was measured with the Jamar hydraulic hand dynamometer, Patterson Medical Ltd., Warrenville, IL, USA, with the handle position set at 4 for all attempts for all subjects. The positioning of each participant was standardized as described by the American Society of Hand Therapists [22]. The participant had to squeeze the handgrip of the dynamometer maximally for 5 seconds. Handgrip strength was expressed in kilogram-force (kgf). Each participant had three attempts, with at least 60 seconds of rest between subsequent attempts. The best of three consistent attempts was used for analysis.

**Maximal pinch strength.** Maximal pinch strength was measured with the BaselineLite Hydraulic Pinch Gauge dynamometer (Fabrication Enterprises, White Plains, New York, USA), following the same positioning procedure as described for the maximal handgrip strength test. The pinch strength was measured between the thumb and index finger and thumb and middle finger. The participant was instructed to grasp the pinch dynamometer with the distal segment and ventral side of the thumb and finger. The other fingers were not allowed to give any support. The subject had 3 attempts for each combination and between all the attempts was at least 60 seconds rest. The highest value of the three consistent attempts was used for further analysis.

**Jebsen-Taylor Hand Function Test (JTHFT).** The JTHFT assesses functional performance and consists of 7 different unilateral hand skill tasks related to ADL: (1) writing 1 sentence of 24 letters (2) turning over 7.6- x 12.7-cm cards (3) picking up small, common objects (i.e., paper clips, coins and bottle caps) and move these to a box (4) simulated feeding (i.e., teaspoon with beans) (5) stacking checkers (test of eye-hand coordination) (6) picking up large empty cans (7) moving weighted (450 g) cans [23, 24]. The subject performed each task with the most-affected hand while sitting comfortably close to the table. The duration of each task from start (lifting hand from table) to completion of the task was recorded in seconds with a stopwatch (maximal duration is 120 seconds per task) and summated as the total score.

**Box and Blocks Test (BBT).** The BBT evaluates unilateral gross manual dexterity. The subject had to grasp and transport as many blocks as possible within one minute from one compartment to the other, one by one, over a partition. The number of blocks counted after one minute serves as the outcome measure [25, 26].

**System Usability Scale (SUS).** Subjective experiences of system usability were measured with the SUS. The 10 questions of the SUS were scored on a 5-point Likert scale ranging from

1-strongly disagree till 5-strongly agree. The total score of the SUS ranges from 0–100 and is calculated as described in [27]. A higher score indicates better usability of the system. A system that scores below 50 on the SUS can be almost certain of usability difficulties in the field and is not acceptable, a SUS score between 50–70 indicates marginal acceptability, a SUS score above 70 indicates a good probability of acceptance, a SUS score above 85 indicates excellent usability and a SUS score above 90 indicates best imaginable [28, 29].

Only participants of the assistive and therapeutic group completed the SUS, because the control group did not have sufficient experience with the ironHand system to validly answer questions about its usability.

**Use time.** Use time was recorded using a diary in both assistive and therapeutic intervention groups.

## Statistical analysis

Statistical analyses were performed with the software package IBM SPSS statistics version 23.0 for Windows. First, histogram plots of all outcome measures were checked for normal distribution by visual inspection. Descriptive statistics, using mean  $\pm$  standard error of the mean (SEM) or the median (interquartile range), were used to describe the participants' characteristics, outcome measures and use time. To confirm equality of characteristics across groups after randomization, an One-Way ANOVA was performed for ratio/interval data and a Chi-squared test or the Fisher exact test for nominal/ordinal data.

To investigate the training effect of ironHand system use, a mixed-model analysis was performed for each outcome measure (handgrip strength, pinch strength, BBT, JTHFT), with time of measurement as within-subject factor and group as between-subject factor, including its interaction (time  $\times$  group) to assess whether there is a difference in treatment effect over time between groups. For the JTHFT, first a log-transformation was performed before the mixed-model analysis was performed, to normalize the data, which was successful for all groups on the following subtasks of the JTHFT: 'card turning', 'checkers', 'large, heavy objects', and total performance time JTHFT. For the JTHFT subtasks of the groups that did not follow a normal distribution, even after a log-transformation, ('writing' therapeutic group, 'small, common objects' assistive group, 'simulated feeding' assistive and control group, 'large, light objects' assistive group, 'total performance time JTHFT–without subtask writing' assistive and control group), a Wilcoxon signed rank test was performed to compare pre-post evaluation. Thereafter, the individual differences between pre-post evaluation for these JTHFT subtasks were calculated for each group, which did follow a normal distribution. Subsequently, a one-way ANOVA was performed for these subtasks to investigate the difference between groups for training effect of ironHand system use. The difference in amount of ironHand use between the assistive and therapeutic group was analysed with the Mann-Whitney U test. Additionally, correlation analyses were performed for ironHand use time with differences between pre-post evaluations of all clinical assessments using the Spearman's correlation coefficient. The overall significance level was set at  $\alpha \leq 0.05$ .

## Results

A total of 91 participants (Table 1) were included in the study, of which 14 participants dropped out (for various reasons varying from personal problems, health issues and technical issues). Of the 91 included participants, 74 (81%) were older adults with self-perceived hand function limitations due to various age-related problems (of which the most prominent were rheumatoid arthritis and osteoarthritis), and 17 (19%) were stroke patients with hand function limitations. Of those 91 participants, 30 were allocated to the assistive group (5 dropped out),

**Table 1. Descriptive characteristics of participants (N = 91)<sup>a</sup>.**

Characteristic	Total (n = 91)	Assistive group (n = 30)	Therapeutic group (n = 28)	Control group (n = 33)
Age (years) <sup>b</sup>	73 (±1)	74 (±2)	71 (±2)	73 (±1)
Gender (M/F) <sup>b</sup>	28 (31%) / 63 (69%)	10 (33%) / 20 (67%)	5 (18%) / 23 (82%)	13 (39%) / 20 (61%)
Dominant hand (R/L) <sup>b</sup>	83 (91%) / 8 (9%)	27 (90%) / 3 (10%)	24 (86%) / 4 (14%)	32 (97%) / 1 (3%)
Most-affected hand (R/L/both) <sup>b</sup>	59 (65%) / 18 (20%) / 14 (15%)	20 (67%) / 6 (20%) / 4 (13%)	15 (54%) / 7 (25%) / 6 (21%)	24 (73%) / 5 (15%) / 4 (12%)
Baseline Handgrip strength (kgf) <sup>b</sup>	15.3 (±0.8)	16.3 (±1.4)	12.4 (±1.5)	16.9 (±1.3)

<sup>a</sup>Mean (±SEM) or Count (%)<sup>b</sup>no significant difference between groups (p≥0.053)<https://doi.org/10.1371/journal.pone.0220544.t001>

28 to the therapeutic group (6 dropped out) and 33 to the control group (3 dropped out) (see Fig 1). When using baseline handgrip strength as indicator for self-reported mobility difficulties (<37 kg (men) and <21 kg (women) [30]), the current participants comprised largely people classified with weak grip (95%).

### Therapeutic effect of the ironHand system

Overall, inspection of Table 2 showed that participants of the assistive, therapeutic and control group improved performance on almost all outcome measures after 4 weeks, which is most pronounced in the therapeutic group.

Handgrip strength and pinch strength (of thumb with index finger) only increased significantly (p<0.039) in the therapeutic group by respectively 3.0 kgf (24.9%) and 0.4 kgf (14.4%) from pre- to post-evaluation (see Table 2). The number of blocks transferred during the BBT only increased significantly in the assistive (3.6 blocks, 8.5%, p = 0.007) and control group (2.6 blocks, 5.9%, p = 0.025) from pre- to post-evaluation, indicating better performance (see Table 2).

Results (mean ± SEM) of the different subtasks of the JTHFT are presented in Table 3. Lower performance time on any subtask indicates better performance. The assistive group improved performance (p<0.015) in 5 subtasks of the JTHFT ('card turning', 'small, common objects', 'simulated feeding', 'large, light objects', 'large, heavy objects'), the therapeutic group improved performance (p<0.029) in 4 subtasks of the JTHFT ('card turning', 'small, common objects', 'checkers' and 'large, heavy objects') and the control group improved performance (p<0.017) in 5 subtasks of the JTHFT ('writing', 'card turning', 'small, common objects', 'large, light objects' and 'large, heavy objects') after 4 weeks intervention.

In most outcome measures (handgrip and pinch strength, BBT and JTHFT), the improvement over time did not differ significantly between groups (p≥0.221). For handgrip strength an interaction effect for group and time (p = 0.009) was present, with improvements from pre-

**Table 2. Scores for all intervention groups of handgrip strength, pinch strength and BBT<sup>a</sup>.**

	Assistive group		Therapeutic group		Control group	
	Pre	Post	Pre	Post	Pre	Post
Handgrip strength	16.3 ± 1.5	18.1 ± 1.5	12.4 ± 1.1	15.4 ± 1.2	16.9 ± 1.5	16.6 ± 1.5
Pinch strength—thumb and index finger	3.5 ± 0.3	3.7 ± 0.3	3.0 ± 0.3	3.4 ± 0.3	3.3 ± 0.3	3.5 ± 0.3
Pinch strength—thumb and middle finger	3.1 ± 0.3	3.1 ± 0.3	2.5 ± 0.3	2.9 ± 0.3	2.5 ± 0.3	2.8 ± 0.3
BBT	43.2 ± 2.8	46.8 ± 2.9	42.9 ± 2.9	45.4 ± 3.0	43.9 ± 2.7	46.5 ± 2.7

<sup>a</sup>Data is represented as mean ± SEM<https://doi.org/10.1371/journal.pone.0220544.t002>

**Table 3. Subtasks scores for all intervention groups on the JTHFT<sup>a</sup>.**

Subtask	Assistive group		Therapeutic group		Control group	
	Pre	Post	Pre	Post	Pre	Post
Writing <sup>b</sup>	23.1 ± 1.1	22.2 ± 1.1	18.9 (14.5–38.0)	15.7 (12.3–32.8)	21.3 ± 1.1	18.7 ± 1.1*
Card turning	11.3 ± 1.1	8.8 ± 1.1*	12.2 ± 1.1	9.3 ± 1.1*	10.3 ± 1.1	8.4 ± 1.1*
Small, common objects	10.5 (8.4–21.0)	9.6 (7.3–12.5)*	13.2 ± 1.1	11.4 ± 1.1*	12.1 ± 1.1	10.8 ± 1.1*
Simulated feeding	11.9 (8.8–16.5)	10.0 (8.5–14.5)*	12.7 ± 1.1	11.7 ± 1.1	10.2 (7.7–15.0) <sup>b</sup>	10.2 (7.8–14.1)
Checkers	10.1 ± 1.2	9.7 ± 1.2	10.0 ± 1.1	8.3 ± 1.1*	8.0 ± 1.1	7.6 ± 1.1
Large, light objects	6.6 (5.2–8.7)	5.4 (3.9–7.1)*	7.2 ± 1.1	6.4 ± 1.1	6.9 ± 1.1	6.2 ± 1.1*
Large, heavy objects	7.9 ± 1.1	6.1 ± 1.1*	7.7 ± 1.1	6.2 ± 1.1*	7.6 ± 1.1	6.6 ± 1.1*
Total performance time <sup>b</sup>	80.7 ± 1.1	70.0 ± 1.1*	82.9 ± 1.1	71.8 ± 1.1*	73.6 ± 1.1	66.3 ± 1.1*
Total performance time–without subtask writing	55.8 (45.0–94.2)	46.2 (35.3–62.2)*	64.6 ± 1.1	54.6 ± 1.1*	52.0 (39.4–71.8)	47.5 (37.2–67.5)*

<sup>a</sup>Normally distributed data is represented as mean ± SEM and data not following the normal distribution is represented as median (interquartile range)

<sup>b</sup>Missing data of 5 participants in the assistive group, 6 in the therapeutic group and 7 in the control group because they were not able to perform the writing task

\*significant difference from pre-evaluation.

<https://doi.org/10.1371/journal.pone.0220544.t003>

to post evaluations in the therapeutic group ( $p < 0.001$ ), but no change in the assistive group ( $p = 0.135$ ) and control group ( $p = 0.561$ ). When represented as relative change with respect to baseline values, the therapeutic group became 25% stronger after 4 weeks of ironHand system use, in contrast to an improvement in the assistive group of 12% and a decrease of 2% in the control group.

### Use time

Use time was reported through diaries, with complete diaries available from 21 participants (out of 77 participants). Total use time of these participants was on average 879 ( $\pm 194$ ) minutes, or 15 ( $\pm 3$ ) hours. When calculated as average use time per day, this reflects 31 ( $\pm 7$ ) minutes each day for 4 weeks. The mean training duration, averaged per week over 4 weeks, was 220 ( $\pm 49$ ) minutes. When distinguishing between intervention groups (Fig 3), we can observe that the assistive group ( $n = 9$ ) used the system on average about twice as long as the therapeutic group ( $n = 12$ ) (average daily use 45  $\pm$  12 min vs. 21  $\pm$  7 min). This observed group difference was significant ( $p = 0.033$ ). However, it should be noted that the variation between individuals is large, ranging from 18 to 3375 minutes per 4 weeks.

Correlation analyses showed for some outcomes a relation between use time and change scores per group, for the assistive and therapeutic groups. Most pronounced correlations, approaching significance, were observed for the assistive group with pinch strength between thumb and middle finger ( $\rho = 0.67$ ,  $p = 0.071$ ) and the therapeutic group with pinch strength between thumb and index finger ( $\rho = 0.55$ ,  $p = 0.062$ ).

### Experiences of end-users

SUS data were available from participants allocated to the assistive or therapeutic groups (total 58 included, of which 47 completed the post-evaluation and 11 dropped out).

Mean SUS score across both groups was 73 ( $\pm 2$ ), varying on individual level between 48 and 100. When divided per group, mean SUS for the assistive group ( $n = 25$ ) was 77 ( $\pm 3$ ) and for the therapeutic group ( $n = 22$ ) 69 ( $\pm 3$ ). According to adjective ratings scales corresponding with the SUS score [29], the ironHand system used as assistive device is perceived as having good usability and used as training tool to have OK usability (Fig 4).

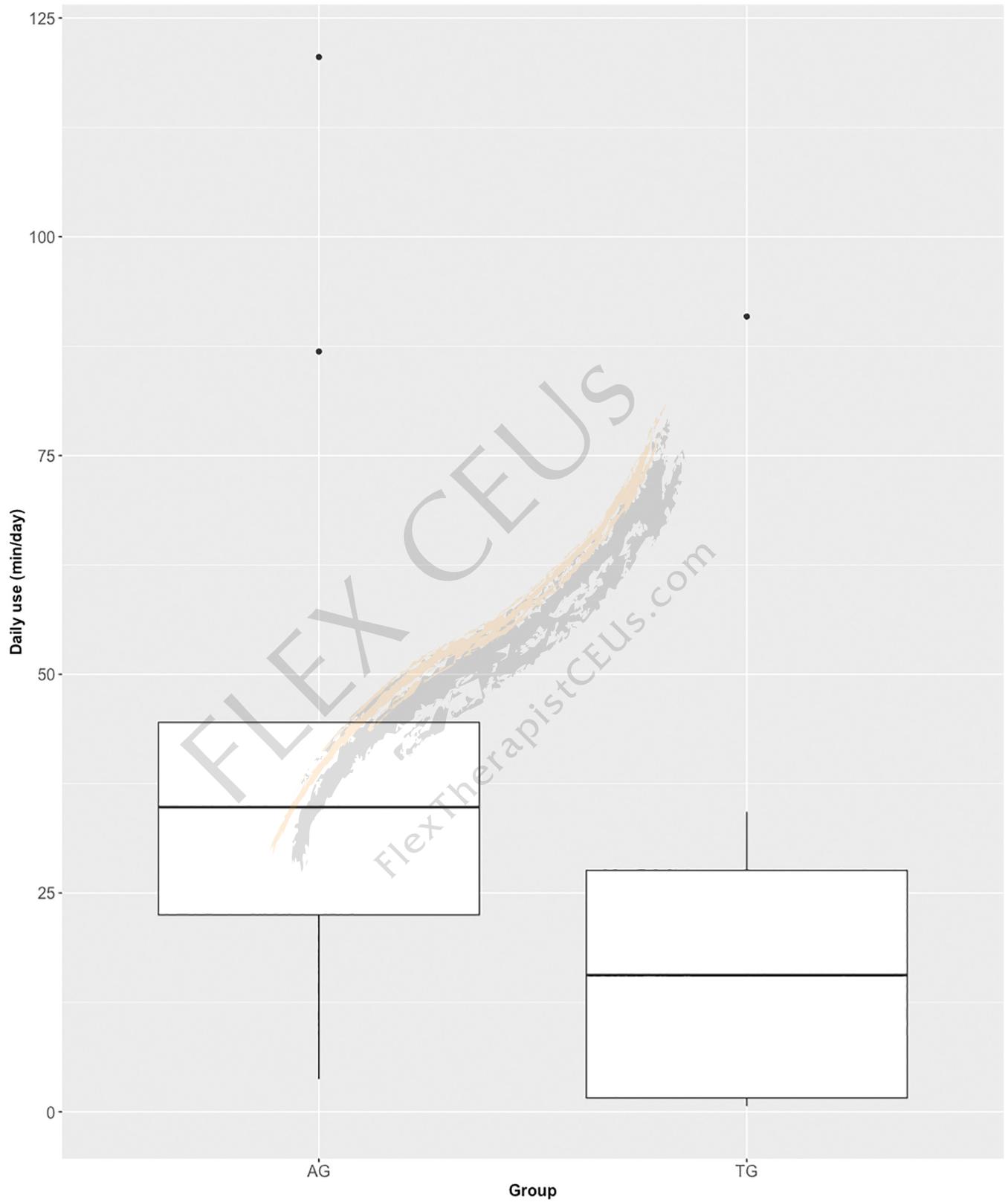


Fig 3. Daily use (min/day), separately for assistive group (AG) and therapeutic group (TG).

<https://doi.org/10.1371/journal.pone.0220544.g003>

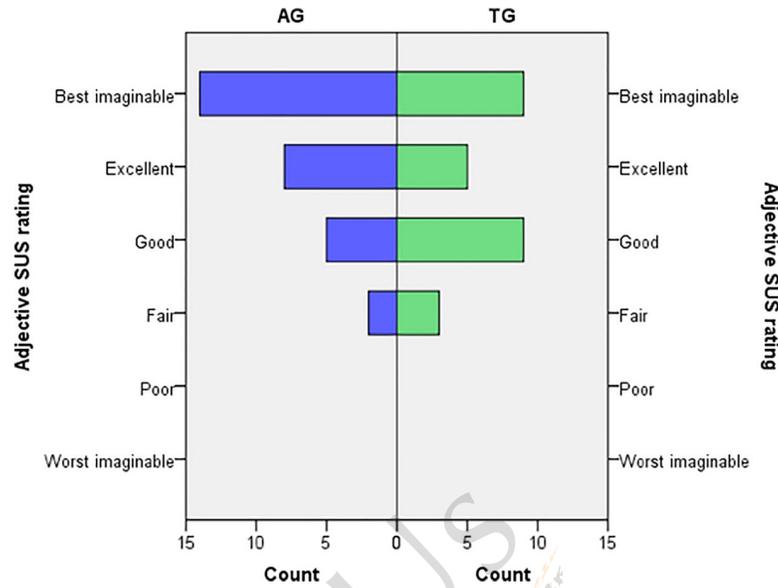


Fig 4. Frequency distribution of SUS score, categorised by adjective ratings [29], separately for assistive group (AG) and therapeutic group (TG).

<https://doi.org/10.1371/journal.pone.0220544.g004>

## Discussion

This study shows first of all that older adults that used the ironHand system as assistive device or as a training tool were capable to use the ironHand system by themselves at home. Both groups used the ironHand system for a substantial amount of time, with the assistive group using the ironHand system twice as long as the therapeutic group. Usability of both systems was perceived acceptable. When comparing pre- and post-evaluations for all groups separately, participants of the therapeutic group showed improved unsupported handgrip strength and pinch strength after 4 weeks of ironHand system use, while the improvement in functional performance in the assistive and therapeutic groups did not differ from that in the control group. Only handgrip strength improvements from pre- to post-evaluations did differ between groups, participants of the therapeutic group improved more compared to the assistive and control group. No significant correlation was found between the total duration of ironHand use and changes in performance, for the assistive and therapeutic groups.

To our knowledge, this is one of the first user trials that applied and tested a fully wearable robotic system to support hand function at home for unsupervised use during an extended period of multiple weeks. Moreover, this was done in a large group of older adults with hand function limitations. It also involved two scenarios that provide a unique approach, where the ironHand system was used as assistive device or as a training tool. The findings emerging from this extensive user trial indicate first of all that the ironHand system was very well accepted by the users. The majority of SUS ratings fell in the higher categories: 'good', 'excellent' and even 'best imaginable', for both assistive and therapeutic systems. The findings regarding user experiences showed an improved usability across the subsequent iterations within the ironHand project, as indicated by a gradual increase of SUS scores of both the assistive system and the therapeutic system across its previous development stages [20, 21, 31]. The present level of usability indicates high probability for acceptance in the field [28].

The usability of the ironHand system regarding SUS scores is similar to that reported for other assistive or rehabilitation technology. A passive orthosis to support wrist and hand

movements of stroke patients during game-like exercises at home received an average SUS score of 69 in its first iteration [32] and 73 in its second iteration [33]. The usability ratings of the ironHand system are comparable to these findings, with an average SUS score of 73. In terms of use time, the ironHand system scored considerably better (220 vs. 105 and 118 minutes a week) than the passive orthosis reported by Nijenhuis et al. [32, 33]. In addition, the study of Wittmann et al. 2016 [34] showed promising results on feasibility of high dose unsupervised arm therapy at home for stroke patients using an inertial measurement unit-based virtual reality system.

The findings from this study showed that unsupported handgrip strength improved in the therapeutic group and functional task performance improved after 4-week use of a soft-robotic glove at home, either as assistive device or as training tool. However, improvement of functional performance in the technology-assisted groups was not different from the improvement observed in the control group. Remarkably, the control group received no exercise programme and still improved their performance. It is possible that participants improved their performance due to a learning effect on the clinical tests. Such a learning effect might be even more pronounced in those participants that used their non-dominant hand. In addition, a role of response bias (in particular, demand characteristics [35]) cannot be excluded either. It is possible that participants allocated to the control group became more aware of their affected arm in daily life due to their participation to the study in itself, and used their affected arm/hand more than they would have done prior to the study, even though they were instructed to continue their normal activity pattern. Unfortunately, we did not measure their normal arm activity in daily life, so we could not control for this. These issues make it difficult to explain the observed improvement in the control group in the current study, which complicates interpretation of the current findings.

Nevertheless, hand strength did improve more after therapeutic use of the ironHand system than in the assistive or control group. In terms of application as a rehabilitation tool in the therapeutic group, improvements in handgrip strength, pinch strength and functional use of the arm/hand have been reported after robotic hand rehabilitation, applying mostly stationary and/or portable systems as training device in clinical settings after stroke [36–38]. The study of Vanogli et al. 2017 [38] showed that improvements after robotic rehabilitation were significantly higher to those after control intervention consisting of a dedicated program of regular exercises. The studies of Nijenhuis et al. [32, 33] examined the effect of a portable, though not wearable, hand training system after stroke, applied at home with offline supervision, and also reported improved hand function. In this case, the system was stationary yet portable, and not suitable for assistance of daily life activities. In comparison to a control group receiving regular home exercises, no difference was found [39], indicating that technology-assisted training results in similar improvements in hand function as regular exercise programmes. Several wearable systems for hand rehabilitation have been developed recently (see [12] for an overview), but no other clinical studies focusing on hand function changes using fully wearable systems intended for home use could be identified at this point, especially in comparison to use of the wearable system as daily support and/or a control group.

Regarding training interventions for reduction of age-related decline in hand function, intensive resistance training has been reported as one of the most efficient interventions to counter or prevent sarcopenia, with improvements of up to >50% in strength after six weeks of training at a rhythm of 2–3 sessions per week [40]. After ironHand therapeutic use, which partially involved resistance training exercises, substantial improvements in handgrip strength were observed, indicating that such application of a soft-robotic glove combined with dedicated (strength) exercises may be a way to provide motivating strength training to address sarcopenia.

Remarkably, a similar effect, although to a smaller degree, was present in older adults using the assistive system to support performance of functional activities during daily life. Moreover, there was no decline in strength and functional performance after using the assistive system. This suggests that using the hands intensively during submaximal yet highly functional activities has a training effect in itself, and could be beneficial in dealing with sarcopenia as well, although the comparable findings in the control group complicate this inference. A review indicating that a multi-component physical exercise programs (involving endurance, flexibility, strength, etc.) showed less functional decline in frail elderly than single-component programs focussing on strength only [41], may indicate support for this. This may also be relevant specifically in case of hand osteoarthritis, where exercise has shown to have a beneficial influence on hand function, pain and finger stiffness [42]. Similarly, functional practice is known as one of the essential elements for motor relearning after stroke [6], suggesting that application of a soft wearable robotic glove may be a dedicated solution to enable highly functional treatment. It is also possible that the support from the assistive glove enabled people to use their arms and hands in more strenuous and/or higher dose activities than would otherwise be possible in their daily life. Considering that low physical activity and low amounts of exercise seem to be the most powerful predictors of ADL disability [43], technological support as proposed with this ironHand system facilitating people to increase their activity level during their daily lives, can be very promising to counter or prevent functional decline associated with ageing.

Recently, development of wearable soft-robotic gloves aimed at supporting people with disabilities in daily life have attained considerable attention [13–18, 44], and the field is growing [45]. To our knowledge, none of these research groups have yet investigated the effect of such assistive robotic devices in daily life among a large sample of people with hand function limitations. One research group has published a study into the direct influence of their soft-robotic glove, pneumatically actuated and controlled by muscle activity [46]. So far, they showed a reduced performance on JTHFT in one healthy subject compared to normative JTHFT data of healthy subjects [13] and increased performance on the BBT with the assistive glove in one patient with muscular dystrophy [47]. The results of the JTHFT are in line with those from the ironHand project (as reported in [21]), but the findings on the BBT are not in line with those from the ironHand project (as reported in [21]). Other wearable systems for hand rehabilitation have been developed as well [14, 44, 46], but these have neither been evaluated during a longitudinal study.

These recent technological developments in the field of wearable robotics are directed towards more unobtrusive support of the arm in a real life setting, which is intended to further facilitate highly functional and intensive training, even enabling more self-administered scenarios [37]. This presents a dual application of soft-robotics: as assistive device in daily life, which is believed to have a direct benefit on functional independence [13, 14] and/or as training tool to improve unsupported functioning. The findings of the orthotic effect of the ironHand assistive system [21, 48] and the training effect of the ironHand therapeutic system (as described in this study) support that both of these approaches can indeed benefit people with hand function limitations. Even more, based on the current findings a third scenario appeared, where users of the assistive system improve unsupported hand function over time. This may be related to a large variety of functional activities being supported in daily life throughout the day, which likely turns everyday activities into highly functional and intensive practice. This underlines the major potential that a soft-robotic wearable glove system can have for increasing functional independence of a very large group of users with varying causes of hand function limitations.

Even though the current study is one of its kind and has generated a large amount of highly valuable information regarding the user acceptance and potential impact on daily lives of the ironHand system, some aspects of the study have given rise to several lessons and recommendations. First, timed performance of functional tasks may not necessarily capture the full potential of the training effect provided by the ironHand system. The JTHFT was specifically selected based on its validity for application in the elderly population, and we anticipated that a timed outcome measure would be more sensitive to change in a relatively high functioning population (participants were living at home independently and were able to perform most ADL tasks, despite perceiving limitations in this respect). Adding an outcome measure that can capture more detailed information about movement or task execution in future research should be considered to better understand how a wearable glove system influences hand function. Second, the population involved in the current trial was rather heterogeneous, as intended to examine the potential of the ironHand system across a broad user population. A more in-depth analysis investigating potential differences between subgroups according to disorder or level of physical limitations could shed more light on the therapeutic potential of the ironHand system, and might distinguish which users would benefit most from assistive or therapeutic application of the ironHand system. Third, not only participants in the assistive and therapeutic group showed improvements in performance but also the participants in the control group showed improvements in performance on some outcome measures, for example on the BBT. This indicates that there is also a learning effect for performing the clinical tests. Fourth, in each center detailed instructions were given about the recruitment and inclusion procedure, explaining carefully that allocation to groups should strictly follow the randomization list in order of inclusion. Nevertheless, potential influence of selection bias due to treatment foreknowledge can't be controlled or ruled out in this study. Fifth, the current study results might be biased due to the awareness of the intervention group by the participant and the assessor or the fact that some variables were only assessed on a very limited proportion of the overall sample size. It is not possible to compare the current results of this study with other studies. Therefore, more research is needed.

## Conclusion

The current pilot randomized controlled trial is one of the first of its kind in investigating the impact of using a wearable soft-robotic device for hand support during multiple weeks at home. Findings of this user trial showed that participants were capable to use both modalities (assistive and therapeutic) of the ironHand system by themselves for a substantial amount of time at home. After 4 weeks of ironHand use in the therapeutic group, participants showed improvements in unsupported handgrip strength and pinch strength. Functional performance improved not only after 4 weeks of ironHand use (assistive and therapeutic), but also in the control group who received no additional exercise or treatment. Only handgrip strength improved more in the therapeutic group compared to the assistive and control group. These results suggest that, even though the findings from the control group complicate interpretation of the results on functional performance from the technology-supported groups, technological support from wearable robotics as provided through the ironHand system may be promising to improve functional performance in persons with hand problems associated with ageing in general, or specific age-related disorders (varying from rheumatoid arthritis and osteoarthritis to stroke).

## Supporting information

**S1 Checklist.** **S1 Dataset.** **S1 Protocol.**  
(DOC) (XLSX) (PDF)

# Effect of a mixed reality-based intervention on arm, hand, and finger function on chronic stroke

## Abstract

**Background:** Virtual and mixed reality systems have been suggested to promote motor recovery after stroke. Basing on the existing evidence on motor learning, we have developed a portable and low-cost mixed reality tabletop system that transforms a conventional table in a virtual environment for upper limb rehabilitation. The system allows intensive and customized training of a wide range of arm, hand, and finger movements and enables interaction with tangible objects, while providing audiovisual feedback of the participants' performance in gamified tasks. This study evaluates the clinical effectiveness and the acceptance of an experimental intervention with the system in chronic stroke survivors.

**Methods:** Thirty individuals with stroke were included in a reversal (A-B-A) study. Phase A consisted of 30 sessions of conventional physical therapy. Phase B consisted of 30 training sessions with the experimental system. Both interventions involved flexion and extension of the elbow, wrist, and fingers, and grasping of different objects. Sessions were 45-min long and were administered three to five days a week. The body structures (Modified Ashworth Scale), functions (Motricity Index, Fugl-Meyer Assessment Scale), activities (Manual Function Test, Wolf Motor Function Test, Box and Blocks Test, Nine Hole Peg Test), and participation (Motor Activity Log) were assessed before and after each phase. Acceptance of the system was also assessed after phase B (System Usability Scale, Intrinsic Motivation Inventory).

**Results:** Significant improvement was detected after the intervention with the system in the activity, both in arm function measured by the Wolf Motor Function Test ( $p < 0.01$ ) and finger dexterity measured by the Box and Blocks Test ( $p < 0.01$ ) and the Nine Hole Peg Test ( $p < 0.01$ ); and participation ( $p < 0.01$ ), which was maintained to the end of the study. The experimental system was reported as highly usable, enjoyable, and motivating.

**Conclusions:** Our results support the clinical effectiveness of mixed reality interventions that satisfy the motor learning principles for upper limb rehabilitation in chronic stroke survivors. This characteristic, together with the low cost of the system, its portability, and its acceptance could promote the integration of these systems in the clinical practice as an alternative to more expensive systems, such as robotic instruments.

**Keywords:** Stroke, Upper limb, Hemiparesis, Physical therapy, Virtual reality, Augmented reality, Tabletop systems

## Background

Motor impairments are a common consequence of stroke and a major cause of disability [1]. Specifically, upper limb paresis is among the most significant deficits and represents an important obstacle for independence [2]. Impairment of upper limb motor function is present in more than 80 % of stroke survivors, and moderate dexterity after six months is only expected in 30 to 40 % of the cases [3].

It is commonly assumed that recovery of motor function after a brain injury involves neural reorganization of spared areas in both hemispheres to take over functions previously driven by the injured areas [4]. In fact, brain plasticity and behavior are interrelated: on one hand, behavior is a result of reorganized brain activity [1, 4]; on the other hand, adaptive neural reorganization is driven by skill-dependent experiences and behavior [4]. Nevertheless, reorganization is not driven by mere repetition. It only occurs when the experience implies learning [4]. Therefore, it can be deduced that motor rehabilitation should focus on driving plasticity by experiences that mean a challenge for the motor skills of the patients. In addition, motor learning principles, such as intensity, repetition, task-orientation, and feedback have proven to modulate the functional improvement after stroke [5–9].

Virtual Reality (VR) is an especially interesting research field since it allows to create computer-generated environments and provide customized experiences involving different sensory channels, commonly sight, hearing, and/or touch [10]. An increasing number of studies report promising results of its application to motor rehabilitation after stroke [10, 11], specifically for upper limb [11–13]. First, movement kinematics when reaching, grasping, transporting, and releasing objects in a virtual environment are comparable to those in the physical world, thus suggesting that the training of arm movements in VR can be a feasible alternative [14]. Second, VR has been shown effective at improving upper limb movements for reaching and grasping tasks involving proximal segments and global arm movements, in individuals with stroke in both acute and chronic stages [11, 13]. Third, distal fine motor control has also been effectively improved using VR, generally combined with robotic-like devices [2, 15, 16]. Fourth, controlled trials suggest that VR may be beneficial to improve upper limb function and performance in activities of daily living, to a greater extent than same dosage of conventional therapy [3]. Finally, mixed-reality systems involving virtual and tangible objects may be useful in improving both functionality and the kinematics of reaching [17, 18]. Mixed-reality systems are particularly interesting because they combine interesting features of VR with tangible objects that subjects must manipulate. For instance, proprioceptive feedback has been suggested to exploit multimodal aspects of the observation of goal-oriented

movements and the feedback on one's actions [12]. However, clinical research so far with these systems has mainly focused on shoulder and elbow training without specific involvement of hand and finger dexterity.

Basing on the existing evidence, we have developed a mixed reality system that satisfies the motor learning and neural plasticity principles to promote the rehabilitation of task-directed movements of the paretic upper limb involving hands and fingers. The system fits the motor condition of each subject allowing the training of a wide spectrum of movements, from gross proximal movements to finger dexterity, while being portable and inexpensive, in contrast to robotic systems. The objective of this paper is twofold: first, to determine the clinical effectiveness of an experimental intervention with the system to improve the motor function of arm, hand, and fingers in individuals with chronic stroke; and second, to determine the acceptance of this intervention as defined by users' ratings of usability and motivation.

## Methods

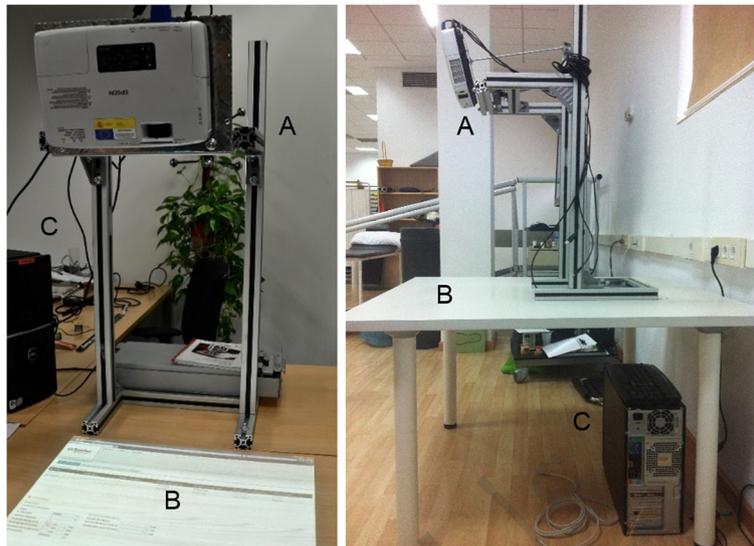
### Subjects

All the outpatients who had suffered a stroke and presented a residual hemiparesis derived from the lesion, and were attending a long-term rehabilitation program in the Brain Injury Service of NISA Hospitals were potential candidates to participate in the study. Inclusion criteria were 1) age  $\geq 35$  and  $< 65$  years old; 2) chronicity  $> 6$  months; 3) no increase or slightly increase in muscle tone as defined by Modified Ashworth Scale [19]  $< 3$ ; 4) ability to move the joints (proximal and distal) as defined by Medical Research Council Scale for Muscle [20]  $\geq 2$ ; 5) fairly good motor condition as defined by Motricity Index [21]  $\geq 55$ ; 6) absence of severe cognitive impairment as defined by Mini-Mental State Examination [22]  $> 23$ ; and 7) able to follow instructions as defined by Mississippi Aphasia Screening Test [23]  $\geq 45$ . The exclusion criteria were 1) individuals with ataxia or any other cerebellar symptom; 2) orthopedic alterations or pain syndrome of the upper limb; 3) peripheral nerve damage affecting the upper extremities; 4) individuals whose visual or hearing impairment does not allow possibility of interaction with the system; and 5) individuals with severe hemispatial neglect. Ethical approval for the study was granted by the Institutional Review Board of NISA Hospitals. All the eligible candidates who agreed to take part in the study were required to provide informed consent.

### Materials

#### Hardware setting

The mixed reality rehabilitation system consisted of a projective tabletop system that allowed multitouch interaction with the hands or via manipulation of tangible objects (Fig. 1). Essentially, the system consisted of a Kinect™ depth



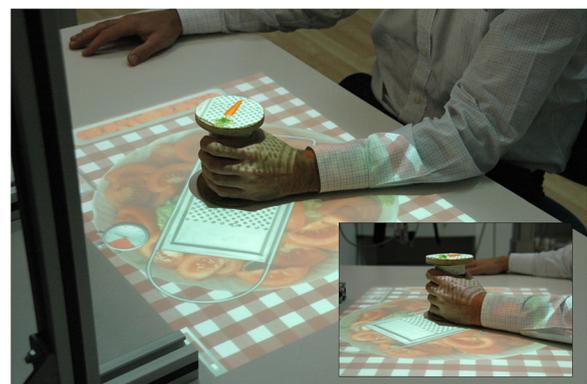
**Fig. 1** Prototype of the virtual reality-based system. The hardware used in this experiment consisted of: **a**) a Kinect™ (Microsoft®, Redmond, WA, USA), which estimated the depth information of the scene, and a LCD projector EB-1720 (EPSON, Suwa, NGN, Japan), which projected the VR; **b**) a conventional table; and **c**) a computer Vostro 420 (Dell Inc., Round Rock, TX, USA) equipped with a QuadCore @ 2.83 GHz and 4 GB of RAM, which generated the VE, tracked the movements of the user on the area of interest, and modified the VE according to them

sensor (Microsoft®, Redmond, WA, USA) and a projector EB-1720 (Epson®, Suwa, Japan) separated 8 cm and attached to the upper plane of a rigid frame at 70 cm of height. The system was 95 x 70 x 40 cm and was fully portable. The sensor and the projector pointed down so that when the frame was placed on a table a field of view overlapped on its surface, thus defining an area of interaction of 55 x 40 cm<sup>2</sup> [24]. The system projects a virtual environment on that area, which reacts according to the users' movements, mimicking the interaction with the real world. In each exercise, the required movements of the upper limb segments, fingers, and tangible objects were detected from the depth information of the scene, tracked, and the interaction with the virtual objects was calculated to update the virtual environment (Fig. 2) (See Additional file 1 for more information).

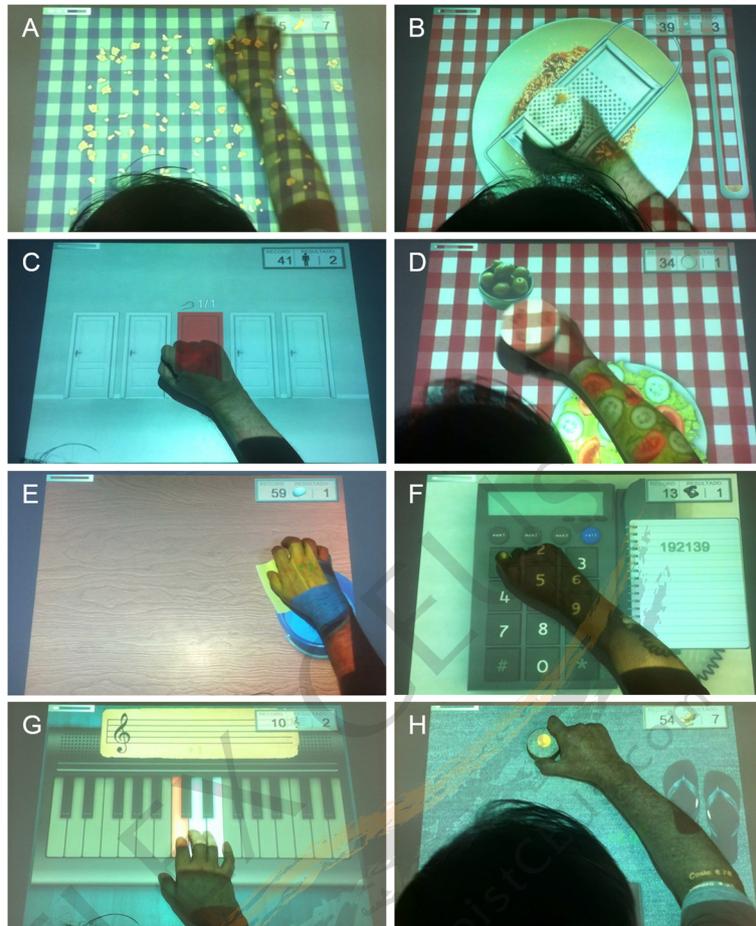
### Exercises

The exercises consisted of a wide range of planar unimanual tasks that involved arm and hand movements, focused on the flexion and extension of the elbow, the wrist, and the metacarpophalangeal joint, and represented tasks that were likely to belong to the participant's motor repertory (previous to the onset), aiming to maximize the relationship with activities of daily living (Fig. 3). The interaction with some exercises required tangible objects of different sizes to be grasped and moved. Handles with different thickness were available. Within each exercise, participants had to perform a task (to grate an item, to dial a number, etc.) as many times as possible. The task, in turn, was achieved if a number

of repetitions were performed accurately enough within a time interval. The system controlled compensation during the exercises, requiring those segments not involved in the movement to be fixed in certain position. For instance, in the grating exercise, the forearm had to remain still and on the table while flexing and extending the wrist. Otherwise, repetitions were not valid (See Additional file 1 for more information). The difficulty of the exercises was determined by adjusting the required speed, number of repetitions, and accuracy of the movements. Before the intervention, therapists defined different levels of difficulty for each exercise by varying these



**Fig. 2** Participant training with the system. A participant interacts with the system using a tangible object. Participant must grate a carrot, represented on the top surface of the item, on a salad. The task is achieved through repeated flexion-extension of the wrist, while maintaining the forearm on the table and the elbow still



**Fig. 3** Description of the exercises. The exercises covered a wide range of hand and arm movements, mostly focusing on the flexion and extension of the elbow and the wrist. **a** *Exercise*: to sweep the crumbs from the table. *Movement*: flexion-extension of the wrist without involving the fingers. **b** *Exercise*: to grate. *Movement*: Grasping and flexion-extension of the wrist. **c** *Exercise*: to knock on doors. *Movement*: flexion-extension of the wrist against gravity. **d** *Exercise*: to cook. *Movement*: grasping involving flexion-extension of the elbow and rotation of the shoulders. **e** *Exercise*: to squeeze a sponge. *Movement*: flexion-extension of the metacarpophalangeal-interphalangeal joint. **f** *Exercise*: to dial a number. *Movement*: tapping. **g** *Exercise*: to play piano. *Movement*: flexion-extension of the thumb, index, and middle finger. **h** *Exercise*: to buy items. *Movement*: pincer grasping with the thumb and index involving flexion-extension of the elbow and rotation of the shoulders

parameters. After each exercise, the success rate was estimated as the percentage of tasks successfully achieved. When the success rate was higher than 80 %, the system automatically increased the level of difficulty. When the success rate was lower than 20 %, the system decreased the level. Exercises provided audiovisual feedback of the virtual environment and showed information about the remaining time, the repetitions successfully completed, and the previous records achieved by the participant. During the exercises, positive audiovisual reinforcement was provided when a task was achieved. In case of the task was not achieved, a negative feedback was provided. After each exercise, the system provided the success rate achieved.

### Procedure

A reversal (A-B-A) design was chosen to characterize the effects of the experimental intervention and to quantify

the maintenance of gains. Phase A consisted of 30 training sessions of conventional physical therapy, and phase B consisted of 30 sessions of an experimental intervention with the mixed reality system. This design allowed to determine the effects of physical therapy, the effects of the experimental intervention, and the maintenance of gains after it when returning to physical therapy. The duration of both interventions was paired. In both phases, sessions were 45-min long and were administered three to five days a week. All the training sessions were supervised by a physical therapist, who in case of compensation, provided a tactile cue to correct the performance. No concomitant therapies were administered.

The conventional physical therapy intervention included active upper extremity tasks equivalent to those trained by the mixed reality system, which involved shoulder, elbow, wrist, and fingers and grasping of different items (in the

absence of a virtual feedback). For example, the exercise that simulated knocking on doors in the mixed reality system (Fig. 3c) was matched with repetition of knocking movements (flexion-extension of the wrist with the forearm still) on square-shaped pieces of paper placed on a table. Two two-minute breaks were allowed after 15 and 30 min of the beginning of the session. The difficulty of the training was determined by a physical therapist in a previous exploratory session. During the intervention, exercises gradually increased in resistance (weights) and in repetitions. The experimental intervention included eight exercises in randomized order (Fig. 3). Duration of the exercises was set to five minutes each. Two-minute breaks were allowed after the third and sixth exercise. The difficulty of the experimental intervention was also initially determined in a previous exploratory session, and was automatically adjusted by the mixed reality system during the intervention or by the physical therapist who supervised the sessions to correct one-time alterations related to pain, motor performance, or inattention. The thickness of the handles of the tangible objects was also determined in the exploratory session to fit the grasp opening of each subject.

All the participants were assessed by a physical therapist, who was blind to the design of the study, 1) at the beginning of the initial phase A ( $A_i$ ); 2) at the end of the initial phase A, which was the beginning of phase B ( $B_i$ ); at the end of phase B, which was the beginning of the second phase A ( $B_f$ ), at the end of the second phase A ( $A_f$ ). In accordance with the International Classification of Functioning, Disability and Health [25], the assessment protocol evaluated 1) the body structures, with the Modified Ashworth Scale [26]; 2) the body functions, with a strength test with a dynamometer [27], the Motricity Index, and the upper extremity subscale of the Fugl-Meyer Assessment Scale [28]; 3) the body activities, with the Manual Function Test [29], the Wolf Motor Function Test [30], the Box and Blocks Test [31], and the Nine Hole Peg Test [32]; and 4) the participation, with the subscales of Quality of Movement and Amount of Use of the Motor Activity Log [33]. In addition, acceptance of the experimental system was assessed in  $B_f$  with the System Usability Scale [34] and with four subscales of the Intrinsic Motivation Inventory [35]. The System Usability Scale is a simple ten-item scale that serves as a global assessment of subjective usability. It employs a Likert scale with scores ranging from 0 to 100. The Intrinsic Motivation Inventory is a multidimensional questionnaire structured into various subscales. Each subscale includes different questions rated on a seven-point Likert scale. In this study, this questionnaire was used to assess participant interest/enjoyment, perceived competence, pressure/tension, and value/usefulness measures. Scores approaching seven in each subscale represent positive

values in terms of motivation, with the exception of the pressure/tension subscale, for which high scores represent high levels of tension.

### Statistical analysis

For each scale and test, scores in all the assessments were compared using repeated measures analyses of variance (ANOVA). ANOVA findings that violated the sphericity assumption were accommodated by Greenhouse and Geisser's conservative degrees of freedom adjustment. Post-hoc simple contrasts (Bonferroni) were conducted for each significant time main effect to determine the source of the significant difference. Data were confirmed to have a normal distribution using the Shapiro–Wilks normality test. The  $\alpha$  level was set at 0.05 for all analyses (two-sided). All analyses were computed with SPSS for Mac, version 15 (SPSS Inc., Chicago, USA).

## Results

### Subjects

A cohort of 108 individuals with stroke were examined for eligibility. A sample of 32 participants (29.6 %) satisfied the inclusion criteria in the study and accepted to participate. All of them were enrolled. Two subjects were discharged and dropped out the study, consequently, their data were not included for analysis. The final sample (17 men and 13 women) was aged  $58.3 \pm 10.1$  years old and had a chronicity of  $357.5 \pm 270.1$  days. Lesions were ischemic ( $n = 17$ ) or hemorrhagic ( $n = 13$ ), with a preponderance of right-sided occurrence ( $n = 17$ ). Ischemic lesions presented total anterior circulation infarcts ( $n = 4$ ), partial anterior circulation infarcts ( $n = 9$ ), and lacunar circulation infarcts ( $n = 4$ ).

### Clinical effectiveness

Repeated measures ANOVA at every assessment of the clinical trial revealed a significant time effect in most of the scales that assessed the body activities (the Wolf Motor Function Test, the Box and Blocks Test, and the Nine Hole Peg Test) and in the participation, and a strong trend towards significance in the Fugl-Meyer Assessment Scale (Table 1). With respect to these scales throughout the therapy, post-hoc analysis showed significant improvement after the experimental intervention (from  $B_i$  to  $B_f$ ). However, this improvement was detected neither after the following conventional intervention (from  $B_f$  to  $A_f$ ) nor the previous (from  $A_i$  to  $B_i$ ), but in the Amount of Use subscale of the Motor Activity Log (Fig. 4). No significant differences were detected in either the body structures or functions.

### Acceptance

With regards to the usability, scores in the System Usability Scale ( $79.13 \pm 7.54$  from a total score of 100) showed good

**Table 1** Clinical data

Measure	Start of phase A (A <sub>i</sub> )	Start of phase B (B <sub>i</sub> )	End of phase B (B <sub>f</sub> )	End of phase A (A <sub>f</sub> )	Significance
Modified Ashworth Scale					
Proximal	0.5 ± 0.5	0.5 ± 0.5	0.4 ± 0.5	0.3 ± 0.5	NS ( <i>p</i> = 0.090)
Distal	0.3 ± 0.5	0.3 ± 0.5	0.3 ± 0.4	0.3 ± 0.4	NS ( <i>p</i> = 0.400)
Dynamometer (kg)	32.2 ± 14.3	32.0 ± 12.8	33.2 ± 12.7	31.7 ± 12.1	NS ( <i>p</i> = 0.240)
Motricity Index	73.2 ± 11.9	72.1 ± 12.5	73.3 ± 12.9	73.6 ± 12.12	NS ( <i>p</i> = 0.100)
Fugl-Meyer Assessment Scale. Upper extremity subscale	50.2 ± 5.0	50.2 ± 5.0	51.1 ± 4.8	50.9 ± 4.9	NS ( <i>p</i> = 0.061)
Manual Function Test	19.3 ± 3.6	18.9 ± 3.6	19.2 ± 3.5	19.3 ± 3.6	NS ( <i>p</i> = 0.090)
Wolf Motor Function Test (s)	53.9 ± 15.7	52.2 ± 16.6	48.1 ± 15.7	49.5 ± 16.1	Bf < Bi** ( <i>p</i> = 0.001) Bf < Ai** ( <i>p</i> < 0.001) Af < Bi* ( <i>p</i> = 0.010) Af > Ai** ( <i>p</i> < 0.001)
Box and Blocks Test (blocks)	22.4 ± 5.2	22.3 ± 4.4	24.8 ± 5.4	25.3 ± 5.3	Bf > Bi** ( <i>p</i> = 0.001) Bf > Ai** ( <i>p</i> < 0.001) Af > Bi** ( <i>p</i> < 0.001) Af > Ai** ( <i>p</i> < 0.001)
Nine Hole Peg Test (s)	63.1 ± 4.3	60.4 ± 3.2	50.9 ± 2.2	52.5 ± 2.3	Bf < Bi** ( <i>p</i> < 0.001) Bf < Ai** ( <i>p</i> < 0.001) Af < Bi** ( <i>p</i> < 0.001) Af > Ai** ( <i>p</i> < 0.001)
Motor Activity Log – Quality of Movement	68.5 ± 30.2	70.4 ± 26.3	88.5 ± 38.9	84.2 ± 32.1	Bf > Bi** ( <i>p</i> < 0.001) Bf > Ai** ( <i>p</i> < 0.001) Af > Bi** ( <i>p</i> < 0.001) Af < Ai** ( <i>p</i> < 0.001)
Motor Activity Log – Amount of use	56.3 ± 38.2	61.6 ± 34.9	79.4 ± 39.7	75.9 ± 40.7	Bi > Ai* ( <i>p</i> = 0.015) Bf > Bi** ( <i>p</i> < 0.001) Bf > Ai** ( <i>p</i> < 0.001) Af > Bi** ( <i>p</i> < 0.001) Af < Ai** ( <i>p</i> < 0.001)

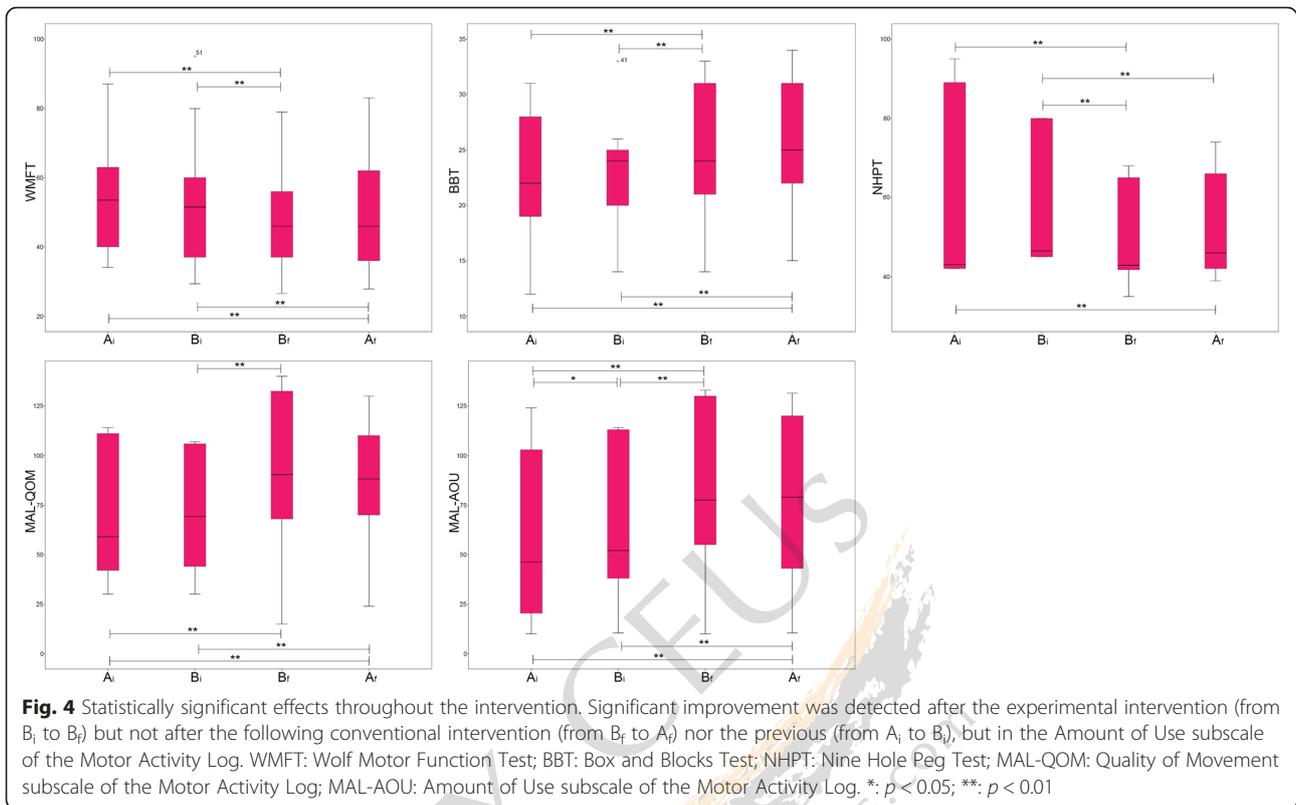
Results are expressed in terms of mean and standard deviation. In case of significance was detected in each scale, only significant temporal relationships are shown. NS: no significant; \* *p* < 0.05; \*\* *p* < 0.01

acceptance of the experimental system. According to the Intrinsic Motivation Inventory, participants reported high levels of interest and enjoyment ( $5.73 \pm 0.79$  of 7), found themselves competent ( $5.21 \pm 0.98$ ) but not pressured ( $1.98 \pm 0.58$ ), and considered the intervention useful ( $6.17 \pm 0.69$ ).

## Discussion

This study evaluates the effectiveness and acceptance of a low-cost mixed reality instrument that provides intensive task-oriented exercises for arm, hand, and finger function rehabilitation in a population of chronic stroke survivors with hemiparesis. Positive effects of the experimental intervention were detected in both activity and participation, and also influenced the progression of the participants.

The significant improvement in timed tests related to activity after the experimental intervention must be highlighted, since task performance is considered an indicative of functional improvement in individuals with chronic stroke [36], and since movement speed and quality of movement are interrelated [37]. Our results supports previous findings using mixed reality systems in the Wolf Motor Function Test [17]. Interestingly, changes detected by the Wolf Motor Function Test have been reported to be of clinical importance [37]. The strong tendency towards statistical significance detected in the Fugl-Meyer Assessment Scale are also in line with previous reports [17, 18]. The different nature of this scale and the Wolf Motor Function Test and the chronicity of our sample could have prevented greater effects.



This scale has been shown to be more sensitive in the acute phase [38] and for chronicity of less than six months [39]. However, it may separate motor recovery from functional recovery and, therefore, may not be responsive to functional improvements in chronic populations [40]. The Fugl-Meyer Assessment Scale focuses on multijoint upper extremity function and examines synergy patterns that may no longer form the basis of our intervention [41]. Moreover, it is a 3-point scale and do not differentiate changes in the less affected extremity. In contrast, the Wolf Motor Function Test assesses the performance time involving single joint or interjoint movements, which were frequently engaged in our intervention. The significant improvement in the gross manual dexterity, assessed by the Box and Block Test, could have been facilitated by an improvement in control of the elbow and wrist synergies and the grasping mechanism promoted by the interaction with tangible objects, which supports previous findings [18]. In addition, the specific training of the flexion and extension of the wrist in different positions and the metacarpophalangeal and interphalangeal joint promoted by our system, could also explain the improvement detected in the Nine Hole Peg Test. It is important to highlight that previous research on stroke survivors involving some robotic systems has shown no improvement after intervention in the Box and Block Test [12, 42] unless the wrist joint [43] or

finger dexterity [44] are specifically trained. However, these two last robotic systems failed to provide improvement reflected in the Nine Hole Peg Test, even in acute phase [45]. This should highlight the benefits of our system, since it can promote hand dexterity, as measured by the Box and Block Test and the Nine Hole Peg Test, while being cheaper and more portable than robotic systems.

Although clinical scales do not allow the ultimate distinction between true recovery and behavioural compensation [46, 47], the results suggest effective motor learning and motor skill retention derived from the experimental treatment. We hypothesize that the improvement in the clinical condition of the participants could be explained by the nature of the exercises, which satisfied the motor learning and neural plasticity principles. First, exercises were intensive and repetitive, characteristics that have been reported to influence improvement [5]. Second, they represented meaningful tasks specially designed to address functional activities, which has been reported of major importance for motor rehabilitation [5, 6] and is known to positively affect arm-hand function recovery and motor control in stroke patients [46]. Third, augmented extrinsic feedback, a major aspect of motor learning [6, 8, 46], was provided during the training in the visual, auditory, and tactile channels. Interestingly, auditory augmentation of visual feedback can be beneficial during the execution of

upper limb movements [48]. Fourth, the training drove subject's attention to the effect of the action, which has been reported to enhance learning [49]. Finally, the difficulty of the training was particularized to each participant in each session, which is essential for motor learning and neural reorganization [6, 46, 49]. Previous research has found that functional improvement, which has been associated with cortical reorganization by different neuroimaging studies [10, 50], can occur at any time [12, 51, 52]. However, the chronicity of the sample, which ensured that the functional improvement was externally driven by the intervention [1, 5], could have limited greater improvement. It is important to highlight though that clinical improvement provided by the experimental intervention was retained after the second A-phase, it is, after returning to physical therapy. The practice under varied conditions promoted by the experimental system could have supported this retention, which has been reported as a better indicator of motor learning than the performance during or just after the practice [6].

The limited results obtained in the body structure and in the body function domains may be related to task-specific effects of motor learning [5, 46]. In line with the tendency of the last decade to shift the efforts of hand-arm rehabilitation from the function level towards the activity and participation level [46], the mixed reality system was designed to train specific tasks that imply the use of the affected arm, hand, and fingers, without explicit focus on strength or joint movement. This orientation, together with the discrete nature of the Manual Function Test (with scores ranging from 1 to 4), and, again, with the chronicity of the sample, could have prevented significant improvement in these components.

The positive reports on perception of improvement and on the use of the paretic arm after the experimental intervention evidenced by the Motor Activity Log, and the high scores about usefulness and enjoyment evidenced by the Intrinsic Motivation Inventory, could depict a relationship between acceptance of the intervention and its repercussion to daily life. This fact could be explained by the ability of the system to motivate patients, which would support previous studies [12, 15, 51, 52]. Importantly, motivation is believed critical for learning [7, 49], and is considered one of the basic principles that should be satisfied by any rehabilitation approach [6, 9]. Finding the rehabilitation enjoyable is thought to increase the level of engagement, participation, and compliance [15], thus increasing the effectiveness of a rehabilitation program.

These results must be interpreted taking into account the limitations of the study. First, the characteristics of the sample are inherently linked to the specialized neurorehabilitation service where the study took place, which could restrict the generalization of the results. Second, no kinematic analysis was performed. Consequently, although

compensatory strategies were restricted during the intervention, they were not controlled during the assessment, which could have influenced the performance in the scales and tests. Third, although the physical therapist who assessed the participants' condition did not know the protocol, the therapists who administered and controlled the intervention were not blind. Fourth, the requirements of the system could restrict interaction of some individuals. Participants were required to have enough motor control to actively move the hemiparetic arm, hand, and fingers along the table and enough cognitive and communication skills to understand and follow instructions. Finally, the sample of the study ( $n = 30$ ) actually can be considered as a small sample, which can also limit the extrapolation of the results.

However, the improvement detected in our sample supports the clinical effectiveness of mixed reality interventions that satisfy the motor learning and neural reorganization principles to improve upper extremity motor ability and finger dexterity in chronic stroke survivors. The effectiveness of the system together with its low cost, its portability, and its acceptance could promote its integration in the clinical practice as an alternative to more expensive systems, such as robotic instruments.

## Conclusions

The mixed reality intervention was shown to be effective and motivating for rehabilitation of the upper extremity motor ability and manual dexterity in chronic individuals with stroke. The low cost of the system, its portability, and its acceptance could promote its integration in the clinical practice as an alternative to more expensive systems.

## Additional file

**Additional file 1:** Operation of the tracking system. (PDF 175 kb)

## Abbreviations

VR: virtual reality; ANOVA: analyses of variance.

## Competing interests

The authors declare that they have no competing interests.

# Arm rehabilitation in post stroke subjects: A randomized controlled trial on the efficacy of myoelectrically driven FES applied in a task-oriented approach

## Abstract

### **Purpose**

Motor recovery of persons after stroke may be enhanced by a novel approach where residual muscle activity is facilitated by patient-controlled electrical muscle activation. Myoelectric activity from hemiparetic muscles is then used for continuous control of functional electrical stimulation (MeCFES) of same or synergic muscles to promote restoration of movements during task-oriented therapy (TOT). Use of MeCFES during TOT may help to obtain a larger functional and neurological recovery than otherwise possible.

### **Study design**

Multicenter randomized controlled trial.

### **Methods**

Eighty two acute and chronic stroke victims were recruited through the collaborating facilities and after signing an informed consent were randomized to receive either the experimental (MeCFES assisted TOT (M-TOT) or conventional rehabilitation care including TOT (C-TOT). Both groups received 45 minutes of rehabilitation over 25 sessions. Outcomes were Action Research Arm Test (ARAT), Upper Extremity Fugl-Meyer Assessment (FMA-UE) scores and Disability of the Arm Shoulder and Hand questionnaire.

### **Results**

Sixty eight subjects completed the protocol (Mean age 66.2, range 36.5–88.7, onset months 12.7, range 0.8–19.1) of which 45 were seen at follow up 5 weeks later. There were significant improvements in both groups on ARAT (median improvement: MeCFES TOT group 3.0; C-TOT group 2.0) and FMA-UE (median improvement: M-TOT 4.5; C-TOT 3.5). Considering subacute subjects (time since stroke < 6 months), there was a trend for a larger

proportion of improved patients in the M-TOT group following rehabilitation (57.9%) than in the C-TOT group (33.2%) (difference in proportion improved 24.7%; 95% CI -4.0; 48.6), though the study did not meet the planned sample size.

## Conclusion

This is the first large multicentre RCT to compare MeCFES assisted TOT with conventional care TOT for the upper extremity. No adverse events or negative outcomes were encountered, thus we conclude that MeCFES can be a safe adjunct to rehabilitation that could promote recovery of upper limb function in persons after stroke, particularly when applied in the subacute phase.

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## Introduction

Stroke is the leading cause of disability in adults in the world and can result in highly complex clinical situations. The insult often involves the sensory-motor system leading to hemiparesis and impairment of the upper limb in over 50% of survivors [1,2]. Although some structural recovery is possible, especially in the first months after stroke, only a small percentage of persons recover pre-morbid movement patterns and functionality [3].

Limitations in reaching and grasping have an important role in determining the level of independence of the person in their daily activities and the subsequent impact on their quality of life. Tailored goal oriented rehabilitation is therefore an essential factor in reducing impairment and augmenting functionality of a hemiplegic arm. A plurality of interventions may help the subject to restore participation and adapt to the new clinical status including task oriented therapy (TOT) that has been shown to be effective for motor recovery [4,5], as well as constraint induced movement therapy (CIMT) [6], biofeedback and robot assisted therapy [7-9]. Moreover, electrostimulation has been applied to improve muscle recruitment and aid motor recovery. Since resources and time in rehabilitation are limited it is important to identify and employ effective interventions [10].

The inability to use the arm in an efficient way may lead to non use of the arm and hand that can lead to changes also at the neural level [11]. It is therefore essential that arm use is facilitated in meaningful activities. Approaches that assist the person during purposeful voluntarily activated movement could be important for inducing neuroplasticity and increasing function. Neuromuscular electrical stimulation (NMES) has been employed in rehabilitation of stroke patients either to generate muscle contraction or be a support during movements; however, with inconsistent results [11-20]. A prerequisite for neuroplasticity through training is the volitional intent and attention of the person and it therefore follows that the user should participate consciously in the rehabilitative intervention [21,22].

Through the use of EMG it is technically possible to register the myoelectric activity from voluntary contraction of a muscle while its motor nerve is being stimulated by electrical impulses [23]. MeCFES is a method where the FES is directly controlled by volitional EMG activity. In contrast to EMG triggered FES, the controlling muscle is continuously controlling the stimulation intensity. Thus the resulting movement and intrinsic multisensory activation is synchronized with the active attention and intention of the subject and the muscle contraction can be gradually modulated by the subject himself facilitating motor learning and recovery of function. This has been demonstrated to be possible in spinal cord injured subjects [24,25] and a pilot study has shown that when the controlling and stimulated muscles are

homologous or they are synergistic it may lead to a marked increase in motor function of the hemiparetic forearm of selected stroke patients [26]. Motor learning principles required for CNS-activity-dependent plasticity, in fact, include task-oriented movements, muscle activation driving practice of movement, focused attention, repetition of desired movements, and training specificity [21,22,27]. The use of MeCFES during active challenging goal oriented movements should help the patient and the therapist overcome the effect of learned non use by turning attempts to move the arm into successful movements.

We hypothesize that applying MeCFES in a task oriented paradigm to assist normal arm movements during rehabilitation of the upper limb in persons with stroke will improve the movement quality and success and thus induce recovery at the body functions level (impairment) and the activity level (disability) of the International Classification of Function, Disability and Health (ICF) [28] superior to that induced by usual care task-oriented rehabilitation.

## Materials and methods

### Study design

An observer-blinded block-randomized controlled multicenter trial with post-acute stroke patients was carried out. The trial involved four rehabilitation centers of the Don Carlo Gnocchi Foundation located in Milano (two centers, Santa Maria Nascente (SMN), the trial leading center, and Palazzolo), Roma and Rovato. Participants that met the inclusion criteria were allocated to one of two groups; an experimental group (M-TOT) or the control group (C-TOT). In the experimental group the MeCFES was applied to support impaired movements while the participant was working on task-oriented activities under guidance of the therapist. In the control group, participants were treated with standard rehabilitation care that included task-oriented activity. The study was approved by the local ethics committees in April 2010 ("Ethical Committee of IRCCS Don Carlo Gnocchi Foundation"), the first participant was enrolled in April 2011 and the last in August 2015. The study was retrospectively registered in the clinical trials list as ClinicalTrials.gov (NCT03019744). Registration was done retrospectively since at the moment of study beginning year 2011 registrations of clinical trials, although recommended by World Health Organization, were not general practice in our institute. However, we confirm that all ongoing and related trials for this intervention are registered.

### Participants

Adult persons with a first ischemic or haemorrhagic stroke were recruited from collaborating rehabilitation centers within the four-year project. To be included the subjects had to be at least a month post stroke at first evaluation (T0), be able to cognitively, physically and logistically participate in the study, have a minimum voluntary muscle activation of shoulder flexors (at least 1 on the Manual Muscle test (Medical Research Council scale) [29]), have a passive range of motion of the shoulder and elbow of more than 90° and no severe spasticity ( $\leq 3$  Ashworth scale) [30] of upper limb muscles. Exclusion criteria were presence of implanted electronic devices, epilepsy, respiratory insufficiency, pregnancy, peripheral neuropathies, cutaneous ulcers at the stimulation zone and other use of FES on the upper limb.

After signing an informed consent participants were randomized according to four random allocation sequences, generated before the beginning of the study according to time since stroke (subacute  $\leq 6$  months post stroke or chronic,  $>6$  months post stroke) and functional level (high, FMA-UE score  $>22$  or low FMA-UE  $\leq 22$ ). A random order block of 2 (experimental) + 2 (control) assignments was used for each of the four categories. The allocation sequences were concealed from clinicians enrolling patients.

## Evaluation

Outcome measures of the study were the improved 15 item Action Research Arm Test (ARAT) [31], and the Upper Extremity section of the Fugl Meyer scale (FMA-UE) [32], representing respectively the activity level of the ICF and the neurological state at the body function level of the ICF. The Quick version of the Disability of the Arm Shoulder and Hand questionnaire (DASH, score of maximum limitation 100) [33] was used to measure the impact of treatment on participation. The 15 item ARAT is a shorter version of the original ARAT that was suggested after a Rasch analysis of the ARAT carried out by Van der Lee [31] that showed that 4 of the original 19 items were redundant. The improved ARAT assesses the ability to grasp and move objects (maximum total score 45) such as the original version while the FMA is a stroke-specific, performance-based impairment index designed to assess motor functioning (FMA-UE, maximum total score 66). For both ARAT and FMA-UE a higher score indicates better arm function while a higher score on the DASH indicates a greater limitation. A change on the ARAT equal or more than five points is considered an improvement in function. Participants also filled out a VAS for perceived pain (maximum pain score = 10).

Assessments were made by a trained physical therapist, blind to group assignment, at 4 similarly spaced time intervals over 6 weeks, T0, T1, T2 and T3, and T4 at Follow up 5 weeks later. The whole evaluation protocol was administered at baseline (T0), at post-treatment (T3 at week 6) and at 5-week follow-up (T4), while only ARAT was administered at intermediate time points, respectively after 8 (T1) and 16 (T2) rehabilitation sessions.

Eight different physiotherapists served as assessors, two per site. All assessors took part in a training session prior to the commencement of the study. The same assessor performed the serial assessments for each individual participant. Participants were not blinded to the intervention, however they remained naive as to the supposed efficacy of the 2 intervention conditions.

## Intervention

Each subject was assessed and treated in the same rehabilitation center where he/she was enrolled. Treatment and evaluation protocols were agreed upon and therapists in all four centers were specifically trained to use the MeCFES approach in order to reduce variation in treatment protocol application. A number of possible preset protocols had been prepared in collaboration with therapists at the leading site to form an Investigators Brochure with detailed descriptions. The treating therapists underwent a training course and were instructed to read a user manual describing how to apply the MeCFES and giving indications of appropriate TOT exercises with which the MeCFES could be used. Each center thus had a MeCFES device at its disposal and physical therapists were trained to use it.

The intervention protocol for both groups consisted of 25 sessions, lasting 45 minutes each, that were applied 5 days per week over 5–6 weeks. In addition to the 25 daily sessions of the study protocol, all participants received usual care physical therapy as planned for their individual problems.

**MeCFES added to Task-oriented arm rehabilitation (M-TOT).** The physical therapist used the MeCFES to assist volitional movements of the patients during task-oriented therapy. Based upon the clinical needs of the patient, activity of one or more arm muscles was identified in order to control stimulation of that same muscle or synergic muscles.

One of the commonly used modalities was for example to let wrist extension and anterior deltoid control in synergy with the opening of the hand for reaching. Only when the patient actively used both muscles the stimulation would induce hand opening. A variant of this was to let activity of the long flexors of the fingers inhibit stimulation controlled by wrist extensors,

in order to promote unlearning of undesirable co-contraction of antagonist muscles. Therapists were furthermore encouraged to use the last half of the session to let the patient repeat the TOT exercises without the MeCFES in order to promote a carry-over or learning effect. The TOT exercises included movements of reaching, grasping, manipulating and moving appropriate objects.

**Task-oriented arm rehabilitation (C-TOT).** Usual care arm therapy typically consisted of task-oriented exercises, similar to those in the experimental group, aimed to improve arm functionality.

## Material

The MeCFES device, described in detail elsewhere [23,24], is composed of four independent EMG amplifiers and four outputs for muscle-nerve stimulation. Digital signal processing algorithms reduce stimulation artifacts and transform each input into an estimate of the volitional myoelectric activity of the controlling muscle. These estimates are combined by addition or subtraction to control each of the four FES output generators. The relation between myoelectric effort and stimulation is controlled by a piecewise linear function where offset, gain and a maximum can be adjusted by the therapist using a portable computer. The computer is connected wireless to the MeCFES while the therapist is adjusting these settings. For each stimulation channel, the therapist may also adjust the maximum stimulation intensity as to protect the subject against excessive stimulation. Through a graphical interface the therapist can combine the inputs with outputs and the sign of the gain determines if the input acts as an excitatory or inhibitory component of the correspondent stimulation channel.

## Sample size estimation

A minimal clinically important difference (MCID) of 5 points or more on the improved ARAT between baseline (T0) and post treatment (T3) was considered to divide the sample into improved and not improved [34]. Based on a statistical power of 80% with a two-sided level of significance of 5% and assuming that 75% of patients in the experimental group and 50% in the control group would exceed the MCID (25% in favor of the experimental group), a sample size of 110 subjects was required. A sample size of 120 subjects (sixty per group) was planned to account for an expected dropout of 10%.

## Data collection and statistical analysis

Outcome measures were retrieved on site by the assessing therapist and sent as excel file or fax to the principal investigator and inserted into the trial registry database.

Descriptive statistics for the two treatment arms are reported as means and ranges, medians with interquartile ranges, or counts and percentages. A primary endpoint was defined as an improvement on the ARAT score of 5 points (MCID) or more, from the pre-treatment (T0) to the post-treatment visit (T3): patients were accordingly categorized as improved or not improved. Results are reported as differences in proportions with 95% confidence intervals. The same results are reported for subgroups defined according to stroke chronicity (chronic or subacute).

Secondary endpoints were the changes of ARAT, FMA-UE and DASH scores over the treatment period (T0-T3), and during the follow-up period (T3-T4). These endpoints were evaluated, separately, using different multivariable repeated measures mixed models (with an unstructured variance-covariance matrix). Three different models, with ARAT, FMA-UE, and DASH scores as dependent variables, with treatment group as independent variable, and with stroke chronicity and rehabilitation center as covariates, were used both to evaluate changes

during the treatment period (from T0 to T3), and then separately to evaluate changes over the entire follow-up (from T0 to T4). Medians of the differences from baseline scores were reported for each outcome measure at each available visit. Results of the repeated measures models are reported as treatment effect, visit effect and treatment\*visit interaction effect. The significance level was set at 5% and all tests were two-tailed. Analyses were performed using SAS 9.2 (SAS Institute Inc., Cary, NC, USA).

## Results

Within the duration of the project (April 2011 and August 2015), 82 patients (mean age years: 66.6, range: 36.5–88.7, mean onset months: 12.6, range: 0.8–190.1) from the four rehabilitation centers were recruited and randomized (M-TOT group, 38; C-TOT group, 44). The last evaluation was performed in October 2015. Fourteen patients left the study before the post-treatment visit (T3): 5 were randomized but dropped out before their baseline assessment (T0) (1 died, 1 had an epileptic seizure, 1 refused the treatment, 2 for unknown reasons); Nine of the 77 patients that had a baseline evaluation (T0) did not finish at least 90% of the rehabilitation sessions and so were considered drop outs resulting in a drop-out rate of almost 12% after baseline evaluation (5 dismissed from center prior to the study end, 1 as being non-compliant with the treatment, 3 for unknown reasons). None of the dropouts was due to dissatisfaction with type of treatment received. Dismissal from the center prior to study end happened for practical reasons, such as the patients being moved to rehabilitation centers nearer to their home. The patient that was non-compliant with the treatment missed many rehabilitation sessions due to sickness and so was unable to finish the protocol in time.

Sixty eight patients (experimental group, 32; control group, 36) completed the assigned treatment and 45 could be seen at the 5-week follow-up visit (T4) (see CONSORT flow-chart in Fig 1). The low rate of patients turning up for a follow up is of concern, but in all cases it was because it was inconvenient for the persons, they lived too far away from the center or did not have anyone that could assist them in getting to the center.

No adverse events or negative outcomes were encountered during the treatment period. The median VAS for pain was 0 at baseline and remained unchanged which implies that both treatments were safe and did not lead to an increase in shoulder pain.

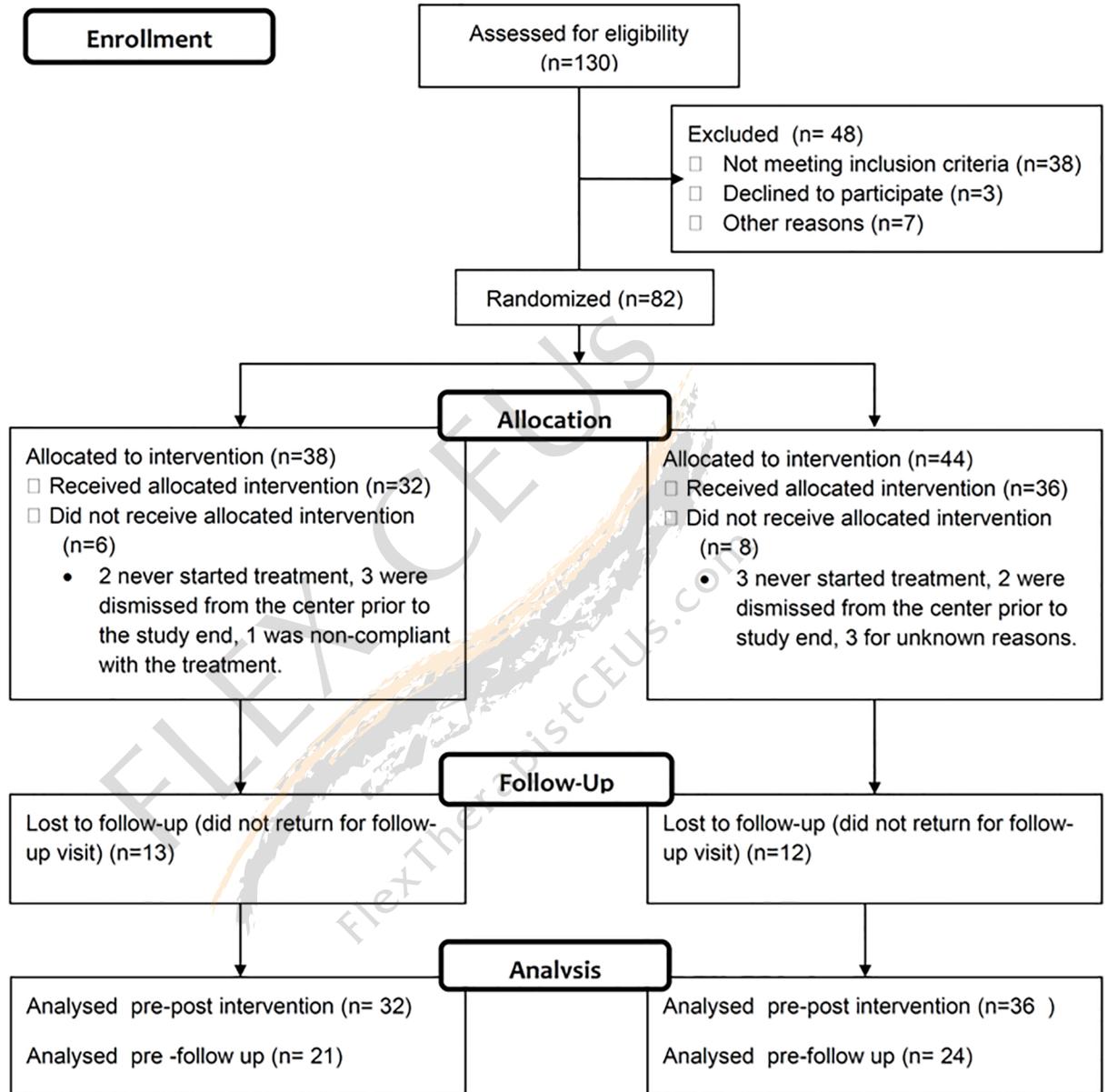
The demographic and clinical features of the 68 patients with post-treatment evaluation are illustrated in Table 1. The mean age at the baseline visit was 65.9 years for the M-TOT group and 67.9 years for the C-TOT group, with a mean time since stroke of 20.1 and 10.1 months, respectively. Females predominated in both groups, and ischemic stroke was the most common type. Subacute patients were more represented in the C-TOT group (75%) than in the M-TOT group (59%).

All analyses of treatment effect subsequently reported were performed in the 68 subjects with post-treatment evaluation (See Table 2 for results of all outcome variables expressed as medians, means and range). Median baseline score of ARAT was 6 and 6.5 out of a total score of 45 in the M-TOT and C-TOT group respectively while following treatment the median scores were 21 and 12.5 respectively. Median FMA-UE score at baseline was 28 and 32 out of a total score of 66 respectively for the M-TOT and C-TOT group and following treatment it was 39 and 36, respectively.

Fig 2 depicts the change over time of the median ARAT and FMA-UE scores for both groups and subgroups, chronic and subacute, at baseline and post intervention.

The results of the primary endpoint analysis are shown in Table 3. In the M-TOT group, 14 patients out of 32 (43.8%) showed an improvement of 5 points or more on the ARAT score at the post-treatment assessment. The number of improved patients in the C-TOT group was 12

## CONSORT Flow Diagram



**Fig 1. CONSORT flow-chart.**

<https://doi.org/10.1371/journal.pone.0188642.g001>

out of 36 (33.3%). No significant differences were observed between the two treatment arms (difference in proportions: 10.5; 95% CI: -12.2; 31.8). Subgroup analyses showed that “usual care” TOT had a similar effect in chronic (33.3% improved) and subacute patients (33.2% improved), while M-TOT appeared to be more effective in subacute (57.9% improved) than in chronic patients (23.1% improved); nevertheless, neither in chronic (difference in proportions: -10.2; 95% CI: -44.9; 24.3) nor in subacute (difference in proportions: 24.7; 95% CI: -4.0; 48.6)

**Table 1. Demographic and clinical features of experimental and control groups.**

Variable	M-TOT (N = 32)			C-TOT (N = 36)		
	N	Median	Range	N	Median	Range
Age (years)	32	68.3	36.5–84.8	36	67.7	38.0–88.7
Disease duration (months)	32	4.5	0.9–190.1	36	3	0.9–97.4
	N	%		N	%	
<b>Sex</b>						
F	19	59.4		20	55.6	
M	13	40.6		16	44.4	
<b>Stroke type</b>						
Hemorrhagic	5	15.6		7	19.4	
Ischemic	26	81.3		29	80.6	
Ischemic and hemorrhagic	1	3.1		0	0.0	
<b>Stroke site</b>						
Cortical	5	15.6		8	23.5	
Cortical and subcortical	11	34.4		15	44.1	
Subcortical	11	34.4		9	26.5	
Brainstem	5	15.6		2	5.9	
Not specified				2		
<b>Chronicity</b>						
Chronic	13	40.6		9	25.0	
Subacute	19	59.4		27	75.0	
<b>Rehabilitation center</b>						
Milano (Palazzolo)	2	6.2		7	19.4	
Roma	11	34.4		11	30.6	
Rovato	6	18.8		7	19.4	
Milano (SMN)	13	40.6		11	30.6	

N: number; M-TOT: Myoelectric control of functional electrical stimulation-task oriented training; C-TOT: control-task oriented training.

<https://doi.org/10.1371/journal.pone.0188642.t001>

subgroups, was a significant difference found between the two treatment arms. When adjusting for stroke chronicity and centers results remained substantially unchanged (data not shown).

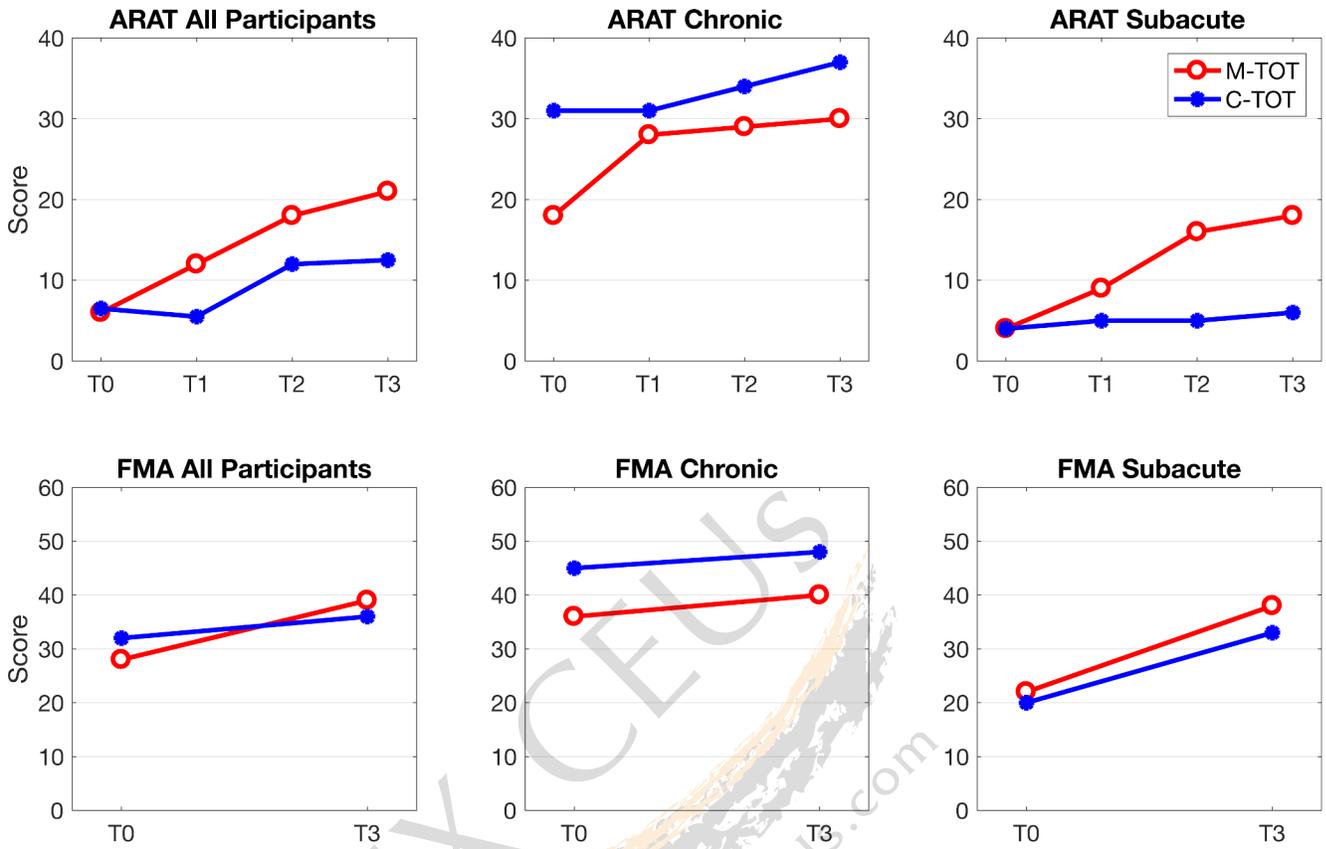
Medians of the changes from baseline of ARAT, FMA-UE and DASH scores at each available treatment evaluation are shown in Table 4 along with the results of the repeated measures

**Table 2. Outcome assessments at baseline and post intervention.**

Test		M-TOT (N = 32)			C-TOT (N = 36)		
		Median	Range	Mean(SD)	Median	Range	Mean (SD)
ARAT	PRE	6.0	0–43	13.9 (16.1)	6.5	0–44	15.1 (16.4)
	POST	21.0	0–45	20.5 (17.1)	12.5	0–45	20.0 (18.7)
FMA-UE	PRE	28.0	4–64	29.4 (19.4)	32.0	2–63	30.4 (19.9)
	POST	39.0	8–66	37.0 (19.9)	36.0	8–66	34.9 (21.9)
DASH	PRE	62.5	8–68	60.8 (17.5)	54.5	14–75	51.0 (18.3)
	POST	56.5	18–71	55.9 (17.9)	52.5	6–66	44.2 (20.6)

IQR: interquartile range; SD: standard deviation; M-TOT: Myoelectric control of functional electrical stimulation-task oriented training; C-TOT: control-task oriented training. ARAT: action research arm test; FMA-UE: Fugl Meyer assessment for the upper limbs; DASH: disability of the arm, shoulder and hand questionnaire.

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**Fig 2. Change over time of median ARAT and FMA-UE scores for M-TOT and C-TOT groups, and their subgroups.** ARAT: Action research arm test; FMA-UE: Fugl Meyer assessment for the upper limbs. M-TOT: Myoelectric control of functional electrical stimulation-task oriented training; C-TOT: control-task oriented training. T0: baseline visit; T1: after 8 rehabilitation sessions; T2: after 16 rehabilitation sessions; T3: post-treatment visit (after 25 rehabilitation sessions, 6–7 weeks).

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analysis. There was a significant improvement from baseline to post-treatment scores for all outcome measures in both groups; however, no significant interactions between treatment and visit were detected (Table 3), meaning that the change from baseline was similar in the two treatment groups, although FMA-UE showed a trend for interaction ( $p = 0.07$ ) with bigger changes in the M-TOT group. The median change scores for ARAT from baseline to the end of treatment: were 3.0 in the MeCFES group, and 2.0 in the C-TOT group; for FMA-UE 4.5 in the M-TOT group, and 3.5 in the C-TOT group; and for DASH -4.5 in the M-TOT group, and -4.8 in the C-TOT group.

**Table 3. Number of improved patients ( $\Delta\text{ARAT}_{\text{pre-post}} \geq 5$ ) at post-treatment visit in the M-TOT and the C-TOT group, with differences and confidence intervals.**

	M-TOT (N = 32)	C-TOT (N = 36)	p-value	Difference in proportions	95% CI
	N Improved (%)	N improved (%)		%	
All patients	14 (43.8)	12 (33.3)	0.45	10.5	-12.2; 31.8
Chronic stroke	3 (23.1)	3 (33.3)	0.65	-10.2	-44.9; 24.3
Subacute stroke	11 (57.9)	9 (33.2)	0.09	24.7	-4.0; 48.6

CI: confidence interval; M-TOT: Myoelectric control of functional electrical stimulation-task oriented training; C-TOT: control-task oriented training; N improved: number improved. ARAT: action research arm test.

<https://doi.org/10.1371/journal.pone.0188642.t003>

**Table 4. Median differences of ARAT, FMA-UE and DASH scores from baseline (T0) to post-treatment visit (T3).**

Test	Time	M-TOT (N = 32)			C-TOT (N = 36)			p-value (treatment)	p-value (visit)	p-value (treatment*visit)
		N	Median	IQR	N	Median	IQR			
ARAT	T1	31	0.0	0.0;5.0	34	0.0	0.0;2.0			
	T2	32	2.0	0.0;11.0	33	1.0	0.0;7.0			
	T3	32	3.0	0.0;12.5	36	2.0	0.0;9.5	0.77	<0.0001	0.27
FMA-UE	T3	32	4.5	1.5;14.0	36	3.5	0.5;6.5	0.58	<0.0001	0.07
DASH	T3	32	-4.5	-11.4;1.5	34	-4.8	-14.0;0	0.07	<0.0001	0.32

M-TOT: Myoelectric control of functional electrical stimulation-task oriented training; C-TOT: control-task oriented training; IQR: interquartile range. ARAT: action research arm test; FMA-UE: Fugl Meyer assessment for the upper limbs; DASH: disability of the arm, shoulder and hand questionnaire.T0: baseline visit; T1: after 8 rehabilitation sessions; T2: after 16 rehabilitation sessions; T3: post-treatment visit (after 25 rehabilitation sessions, 6–7 weeks). p-values for treatment effect (differences between treatment arms), visit effect (differences between visits) and treatment\*visit interaction (differences in the change over time between treatment arms) were obtained from a multivariable repeated measures mixed model, adjusting by stroke chronicity and rehabilitation center.

<https://doi.org/10.1371/journal.pone.0188642.t004>

### Follow up measures

The same outcome measures were analyzed in the 45 patients with the 6-week follow-up assessment (Table 5). Repeated measures models, with an additional time point for the follow-up assessment, showed comparable results. In addition, contrasts between T0 and T3, and between T3 and T4 revealed that there was a significant improvement of ARAT, FMA-UE and DASH scores from pre- to post-treatment assessment, and with no subsequent variations until the 6-week follow-up assessment, although there was a trend for continued improvement ( $p = 0.07$ ) on the FMA-UE from the post-treatment assessment to the follow up.

### Discussion

This multicenter, randomized controlled trial investigated the effect of adjunct of myoelectrically controlled functional electrostimulation (MeCFES) to task oriented training (TOT) of the

**Table 5. Median differences of ARAT, FMA-UE and DASH scores from baseline (T0) to Post (T3) and to the 6-week follow-up visit (T4).**

Test	Time	M-TOT (N = 21)			C-TOT (N = 24)			p-value (treatment)	p-value (visit)	p-value (treatment*visit)	p-value (visit contrasts)
		N	Median	IQR	N	Median	IQR				
ARAT	T1	20	1.0	0.0;6.5	23	0.0	0.0;2.0	0.78	0.0006	0.13	
	T2	21	2.0	0.0;10.0	21	0.0	0.0;4.0				
	T3	21	4.0	0.0;14.0	24	1.5	0.0;5.0				T0-T3: <0.0001
	T4	21	4.0	0.0;14.0	24	3.0	0.0;4.0				T3-T4: 0.62
FMA-UE	T3	21	5.0	2.0;14.0	24	3.5	0.5;6.5	0.37	<0.0001	0.13	T0-T3: <0.0001
	T4	21	7.0	2.0;15.0	24	4.0	0.0;7.0				T3-T4: 0.07
DASH	T3	21	-6.8	-13.6;-2.3	22	-4.5	-13.6;0	0.10	<0.0001	0.81	T0-T3: <0.0001
	T4	21	-10.5	-18.2;-2.3	19	-16.5	-23.0;0				T3-T4: 0.31

M-TOT: Myoelectric control of functional electrical stimulation-task oriented training; C-TOT: control-task oriented training; IQR: interquartile range. ARAT: action research arm test; FMA-UE: Fugl Meyer assessment for the upper limbs; DASH: disability of the arm, shoulder and hand questionnaire.T1: after 8 rehabilitation sessions; T2: after 16 rehabilitation sessions; T3: post-treatment visit (after 25 rehabilitation sessions, 6–7 weeks); T4: 6-week follow-up visit. p-values for treatment effect (differences between treatment arms), visit effect (differences between visits), treatment\*visit interaction (differences in the change over time between treatment arms) and visit contrasts (change between selected visit times) were obtained from a multivariable repeated measures mixed model, adjusting by stroke chronicity and rehabilitation center.

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affected arm in persons with stroke as compared to a control group that received the same amount of TOT without electrical stimulation. The MeCFES applied to forearm extensors during task oriented activity led to improved arm function at the neurological and activity level similar to that observed for usual care TOT of the arm, however, there were some indications that adding MeCFES was of more benefit to the persons in the subacute phase after stroke than a usual TOT. The planned sample size was not reached though and so definite conclusions as to a greater effectiveness of MeCFES-assisted TOT than usual TOT cannot be made. However, the results represent an important achievement that prompt further investigation.

These findings are in accordance with reviews of the literature done on the influence of NMES on arm motor recovery in persons after stroke. The general conclusion is that, while there are indications of benefit for arm function, strong evidence is still missing, especially when compared to other valid therapies such as TOT, used in the present study [11,12,14]. The positive response of both groups in the present study to task-oriented intervention is in line with findings of some authors that have included TOT [4,35,36] but in contrast with others [37]. These differences in findings may partly be due to differences in chronicity of stroke and differences in task-oriented activities proposed in the studies.

While both the M-TOT group and the C-TOT group improved their arm function, the proportion of clinically meaningfully improved subjects, denoted as an improvement of 5 points or more on the ARAT, was more than 10% higher in the M-TOT group (44% improved) than in the control group (33% improved). Further, while at baseline both groups with a median total ARAT score of 6 (M-TOT) and 6,5 (C-TOT) would be described as having no arm-hand capacity as classified by Nijland [38], at the post assessment the total score was 21 in the M-TOT group indicating that from being a group with no arm-hand capacity they had arrived at the borderline of being a limited arm-hand capacity group. The C-TOT group, with a final score of 13, would instead be classified as having poor arm-hand capacity. There was also a significant reduction in arm deficit in both groups as denoted by the FM-UE with a change in group median score from 28 points to 39 points in the M-TOT group while the C-TOT group had a change from 32 to 36 points. There was thus a trend for bigger change in favor of the M-TOT group indicating that adding MeCFES to a TOT protocol may have greater effect at the neuromotor level of arm function than does usual care TOT.

Several factors, besides the sample size necessary not being reached, may have influenced the inconclusive results of the present study. One of them is the amount of task specific practice with the stimulation on in every session. It may not have been enough to improve arm function in a significant manner beyond that of the TOT alone received by the control group [39]. In the present study the treatment time in each session was approximately 45 minutes, but this time included also the setup of the electrodes/stimulation parameters and TOT without stimulation (in the last half of the session), so the effective MeCFES treatment time was only about 20 minutes. Thus it is possible that with longer stimulation time effects would have been bigger similar to the treatment time effect seen in the study by Page and colleagues [39].

Another aspect that can have confounded the results is the functional heterogeneity of the participants. This study was carried out on persons with both subacute and chronic stroke, the persons also varied greatly in functional arm deficits and there was both a floor and ceiling effect on the ARAT. Improvement in arm function following rehabilitation in general appears to be tied strongly to the severity of arm disability [9,20]. In fact, it is known that the prognosis of arm recovery is quite poor for those with severe to complete upper limb paresis, while persons with mild to moderate upper limb paresis have a better chance of recovering with almost all of them achieving some dexterity with time and in response to rehabilitation [3,40–43]. In the present study a number of persons had severe upper limb paresis at the beginning of the study, resulting in a 0 on the ARAT. Since the persons with 0 on the baseline ARAT score were

similarly represented in both treatment groups (from 62–69%) it is unlikely that they contributed to differences between groups but it may have influenced the within group results. In the Excite study, a large multicenter study, Kwakkel and colleagues [20] saw no effect at all from NMES treatment of wrist and finger extension in a large group of subacute subjects that did not have at least 10% of voluntary wrist or finger extension against gravity. Cauraugh and colleagues [43] instead saw a positive impact of stimulation in their chronic subjects that improved, but unlike the study of Kwakkel and colleagues, an inclusion criterion was that they had at least 10° of voluntary movement at the wrist at the beginning of the study. It is thus likely that some voluntary extension is required for treatment effect of electrostimulation in both subacute and chronic stroke, with persons with mild to moderate hand impairment being more likely to improve whether they be subacute or chronic [8,42,44,45].

Subacute patients are, however, more likely to have an improvement in response to whichever treatment, due also to concomitant spontaneous recovery [9,41]. In the present study there appeared to be a further beneficial effect of adding electrical stimulation to the treatment protocol for the subacute participants, with approximately 60% (N = 11/19) improving 5 points or more on the ARAT against one-third (N = 9/27) of the subacute participants in the control group. The between group difference of number of persons improved was near significance ( $p = 0.098$ ) suggesting that the benefit of adding EMG controlled stimulation to a Task-oriented arm rehabilitation might have been proven for persons in the subacute phase after stroke if the planned sample size had been reached. The trend is underlined by a visual analysis of Fig 2 depicting both ARAT and FMA-UE for both groups and subgroups. This trend is in accordance with findings from several studies that have found a benefit trend from the application of EMG triggered neuromuscular electrical stimulation to wrist and finger extension in subacute persons after stroke [44,46,47].

Based on the present findings, in future studies a total of 63 subacute patients should be enrolled in each treatment arm in order to reach an 80% power and a 5% level of significance.

Forty five participants were available for a 5 week follow-up assessment, approximately 2/3 of each group. Both groups retained the benefit of the intervention at follow up and there was a nonsignificant ( $p = 0.07$ ) trend for further reduction of impairment in the MeCFES group that had gained a median of 7 points on the FM-UE at the 5 weeks follow up while the control group had gained a median of 4 points from baseline. This indicates that there may be a benefit beyond the stimulation period on the neuromotor function.

Self perceived participation and activity improved equally in both groups indicating a benefit from the intensity of the task-oriented approach in the study rather than a specific benefit of adding the MeCFES. Pain levels at the shoulder were low in both groups at baseline and remained so at the end of the study indicating that both approaches were beneficial for increasing activity and perceived health status without inducing an increase in pain.

## Limitations and generalisability

There are several limitations that must be considered for future studies. The predicted sample size was not reached within the project's time span which led to insufficient power to draw definitive conclusions as to the efficacy of the MeCFES when applied to arm muscles of persons after stroke during TOT exercises. Moreover, this is a multicenter study which made it difficult to standardize the use of the MeCFES during the rehabilitation sessions. Although efforts were made to standardize the intervention among centers by appropriate training, this may have been insufficient. The MeCFES requires understanding of the technological aspects of the device in order to successfully apply it and the optimal electrode configuration has to be found in every session. The actual use of the device may have differed between centers though

every attempt was made to standardize the technical assistance to the physical therapist using the device.

Attrition is the last limitation. Fourteen of the 82 patients enrolled in the study failed to provide some follow-up data, of those 9 patients had a baseline assessment. Our measures may have been affected by such missing data. However, the baseline characteristics of dropouts with only the first assessment did not differ from patients who completed the study (data not shown).

The results of this study are applicable to people with a minimal to severe deficit of the upper extremity in the subacute and chronic period after first stroke.

## **Conclusion**

This is the first large multicentre RCT to compare MeCFES assisted task oriented therapy with usual care that included a task-oriented component for the upper extremity. Both groups improved their arm function, indicating a general benefit from task-oriented arm rehabilitation, although more people improved with the addition of MeCFES. In particular, subjects who were in the subacute period after stroke appeared to benefit from adding the MeCFES to their training protocol. No adverse events or negative outcomes were encountered, thus it can be concluded that MeCFES may be a safe and promising adjunct to rehabilitation that can help promote recovery of upper limb function in persons after stroke.

## **Supporting information**

### **S1 Protocol.**

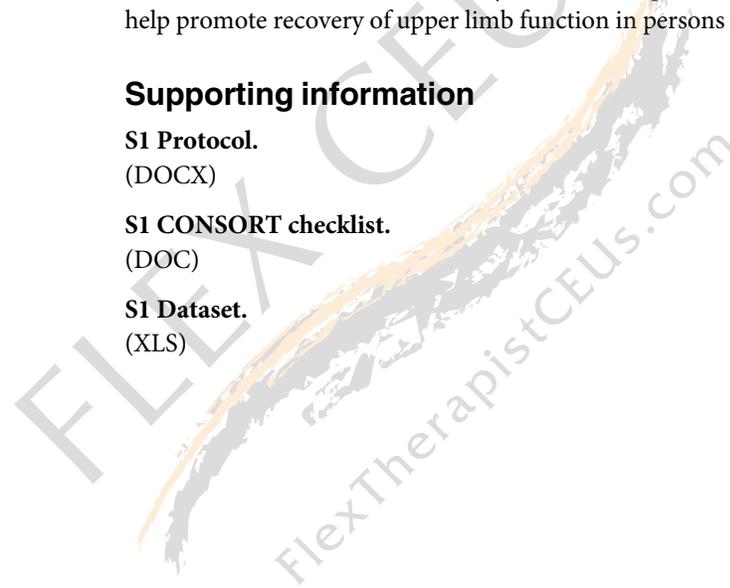
(DOCX)

### **S1 CONSORT checklist.**

(DOC)

### **S1 Dataset.**

(XLS)



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**\*Most recent references included**



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