REACHING AND GRASPING TRAINING BASED ON ROBOTIC HYBRID ASSISTANCE FOR NEUROLOGICAL PATIENTS

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ABSTRACT

This research tunes and validates advanced robot-based technologies to facilitate recovery of arm and hand function in stroke survivors. RETRAINER system is robotic hybrid assistance allowing the end-users to use their own arm and hand as much and as soon as possible after the stroke, to achieve the best outcomes in rehabilitation. Residual functionality is trained and improved. RETRAINER uses two sub-systems: S1 to train the arm movements and S2 to train the hand movements. S1 provides the end-user with an exoskeleton that does not completely take over the end-user's tasks and substitute the functionality of the body, but supports the end-user only whenever he/she really needs support. Arm movements is supported by the combined action of the passive exoskeleton described above for weight relief and Neuromuscular Electrical stimulation (NMES) delivered to subject-specific arm muscles in a controlled manner. S2 is a hand orthosis equipped with a novel wearable NMES system with multiple electrode arrays, which is a modular tool usable as a platform for grasp rehabilitation potentially improving the clinical applicability of NMES. Both the systems benefit from the use of smart interactive objects. A set of prototypes of the RETRAINER systems are being produced to allow a wide clinical testing of the effectiveness of robotic hybrid assistance in upper limb rehabilitation. High cooperation of technical and clinical experts since the early phases of design and development to the setup and running of the clinical trial is an added value of the implemented scientific approach.

KEY WORDS

Robotics assistance - Neuromuscular electrical stimulation – Upper-limb rehabilitation - Embedded control system – Stroke - Reaching and grasping

1. Introduction

The standard stroke's definition by WHO [1] is "rapidly developing clinical signs of focal (at times global) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin". Stroke is the main cause of permanent and complex long-term disability in adults [2]. In 2013, stroke was the third-leading cause of years-of-potential-life lost worldwide, causing around 6.4 million of deaths [3]. The age is one of the most principal risk factor for stroke, and now the ageing of the world population implies a growing number of stroke cases [4], and a total of 195,000 new cases per year are expected in 2020 [5].

Upper limb hemiparesis is widely reported in the literature as one of the primary impairments following stroke. While many patients recover ambulatory function after dense hemiplegia, restoration of arm motor skills is often incomplete. Rehabilitation's outcomes often conclude in incomplete motor recovery and over 60% of patients cannot use their paretic hand in functional activities [6]. Stroke's ranking as a major cause of DALY (Daily Adjusted Life Years) loss will increase by 2030 [7].

Nevertheless, the recovery of voluntary arm movements is one of the most important goals during stroke rehabilitation in order to avoid long- term disability in activities of daily living (ADL), social and occupational activities, and depression. The aim of rehabilitation is to reduce impairment and minimize disability and a number of interventions to achieve these aims and improve arm function after stroke have been suggested.

RETRAINER project is an Innovation Action funded by the European Commission under the Horizon2020 work programme. The aim is to tune and validate advanced, robot-based technologies to facilitate recovery of arm and hand function in stroke survivors. RETRAINER will allow the end-users to use their own arm and hand as much and as soon as possible after the trauma so to achieve the best outcomes in rehabilitation.

This paper aims at sharing the innovative approach in the design and development including clinicians and patients since the early stages better addressing crucial usability and acceptability issues of the robotic technology. Furthermore, the comprehensive design of the multicenter clinical trial aims at supporting the developers with valuable quantitative feedback on clinical outcomes when the system is still at a prototypal stage.

2. RETRAINER architecture

2.1 General description

The driving principle behind RETRAINER is that more the patient uses his/her body, more the functions are recovered. Thus, RETRAINER will allow the users to use their own arm and hand as much as possible and as soon as possible after the trauma so to achieve the best outcomes in rehabilitation. The main goal of the project is to introduce new technologies able to recover and support the person's ability to perform Activities of Daily Living (ADL).

A continuous iterative process between the technology development and the testing feedbacks drives the whole project. RETRAINER makes available two systems: S1 which aims at training the arm movements and S2 which aims at training the hand movements. Both systems, S1 and S2, benefit from the use of interactive objects to enhance rehabilitation results. Interactive objects are daily life objects able to supply the robotic system with some information on themselves (e.g. physical characteristics, expected sequence of use) to drive their usage in the rehabilitation exercises.

The RETRAINER project aims to build on the results of the previous FP7 European project MUNDUS[8]. However, some important differences exist among the two approaches. First of all, the architecture of the system. In MUNDUS, each module was managed by its own intelligence installed on a devoted machine. In RETRAINER, the Embedded Control System has been developed to better integrate most of the existing real time modules and simplify the system. RETRAINER also differs in the targeted use. MUNDUS was a system aimed at assisting disabled people in everyday life, while RETRAINER is a rehabilitation system. This difference asked for a complete redesign of the Graphical User Interface (GUI) of the system to implement functions needed to run rehabilitation exercises and to record outcomes of the performance. Last, but not least, the obsolescence of the technology. MUNDUS project run on the time span 2010- 2013 while RETRAINER started on January 2015, requiring a full revision of the selected components and sensors for all modules.

2.2 S1 module

The S1 module (Figure 1) is the RETRAINER sub-system aimed at improving the functionality of the paretic arm. It consists of a lightweight and non-cumbersome passive arm exoskeleton which provides weight relief at the shoulder and elbow joints so as to reduce the muscular effort required to move the arm. If needed, NMES can be used to provide additional support to the arm muscles. Interactive objects, an embedded control architecture for real-time control, and a GUI complete the apparatus.

The exoskeleton is characterized by 3 degrees of freedom (DOFs): shoulder elevation, shoulder rotation in the transversal plane and elbow flexion/extension, while the humeral rotation and the prono-supination are instead fixed at customized positions. Each DOF is equipped with an electromagnetic brake so that the user can keep anti-gravity postures without any muscle contractions. The gravity compensation module at the shoulder joint consists of a carbon fiber-tube with two springs inside; the level of the compensation can be adjusted electronically by the operator at the beginning of each training session. The weight relief of the forearm is instead realized by means of an elastic band and can be adjusted by the operator manually at the beginning of the training session.
The exoskeleton can be mounted on the user's wheelchair or on a normal chair by means of an universal clamping mechanism which assures easy and stable mounting.

To improve the recovery of upper limb functions after stroke the S1 module also exploits NMES. Recent neurophysiological studies [9] [10] [11] advocated the use of NMES co-incidentally with the voluntary drive to enhance its beneficial effects on the motor re-learning process. Thus, within RETRAINER, the residual volitional EMG signal of the affected muscle is detected and used to trigger the onset of a predetermined stimulation sequence applied to the same muscle. After each repetition, a feedback on the voluntary activity concurrent to NMES is visually displayed to the user in order to promote the active involvement of the subject. Up to two muscles can be stimulated simultaneously and the target muscles are selected by the therapist according to the specific need of each user.

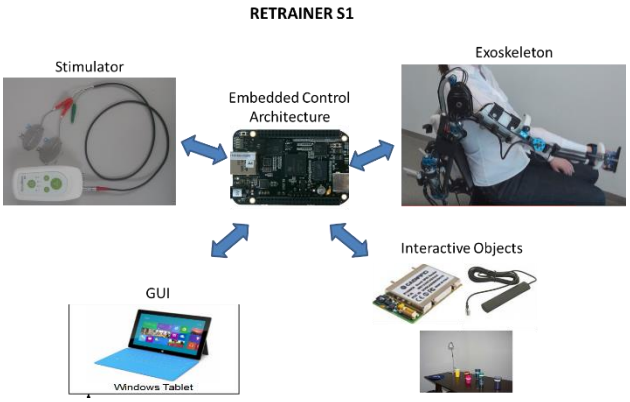

Figure 1. RETRAINER S1

2.3 S2 module

The S2 module is the RETRAINER sub-system aimed at improving the functionality of the paretic hand. It consists of a lightweight, sensorized, forearm-hand orthosis, designed for object interactivity. Hand actuation is obtained with NMES stimulation of hand extrinsic muscles.

The S2 module shares the technological and conceptual rehabilitative framework of S1, and it's structured to operate in standalone mode or in cooperation with the other sub-system.

The core components comprising the module are the hand orthosis with the sensorized clasp system and a GUI system for calibration, exercise guidance, visual and auditory feedback. A real-time embedded system

completes the module by providing real-time NMES control of a multi electrode-array system.

Differently from S1, triggering for each task comes from the interactive objects described below, used for object and landmark detection, and from force and kinematic feedback from the orthosis are used to trigger and acknowledge the execution of tasks, to be executed in a coordinate fashion within preprogramed exercises.

The hand orthosis is available in two variants. The first variant provides a simple structure to host sensors aimed at tracking hand-wrist movements; the second variant extends the functionality by locking the hand-wrist relative movements and by constraining the thumb in opposition, tracks the movement of fingers, and allows detecting grasp. Additionally, the RF antenna is placed on the dorsal side of the orthosis by means of Velcro straps. The clinician, depending on the severity of the motor damage, the progression of the treatment, and the chosen exercise, can select the module matched with the rehabilitative needs of the patient. The orthosis is, at the moment, available in five different sizes. To best match one's anthropometric characteristics, the orthosis can be thermoshaped to adapt the wrist extension angle, hand curvature, and the level of the thumb opposition.

The clasps, made of rubber-like material, constrain finger movements and can be positioned at the convenience of the clinician on the proximal phalanges, or on the intermediate phalanges, or on both. As NMES-induced movements show a dominant finger, the clasp allows to maintain the fingers joint-wise aligned along with the movement. The clasps, available in eleven different sizes, are also used to measure the relative motion of the fingers from the wrist and to detect the grasp intensity. The clasps include thin force sensors (Tekscan Inc., FSR A401) and an IMU module (Inversense Inc., MPU 9250) used to estimate the relative flexion angle between the monitored phalanx and the hand.

The electrode arrays are an extension of the classical electrodes for NMES. Typically surface electrodes require to be precisely positioned over the motor point to obtain a meaningful and selective muscle activation. Imprecise positioning or skin-muscle displacement caused by motion (e.g. pronation-supination) lower the efficacy of stimulation, and cause the use of stimulation patterns more intense than needed. Electrode arrays limit those issues in a two-fold way. First, they cover a larger area than regular electrodes by using multiple smaller, more selective electrodes. Second, by allowing a post-wearing calibration which replaces the standard trial-and-error, position-stimulate-remove-repeat approach, the muscle response can be topographically mapped for different conditions, and the stimulation can be dynamically adapted in terms of location, pattern, and intensity. Three electrode arrays can be placed on the user's forearm, two of them to elicit extrinsic extensors of the hand, and one to elicit extrinsic flexors. If needed, NMES can be used to provide support to the forearm muscles.

Selected materials respond to lightweightness requirements with an overall weight not exceeding 250 g, to appear as transparent for the end-user as possible.

2.4 Interactive Objects

The use of radio frequency identification technology to improve and enhance the effectiveness of the upper extremity rehabilitation is a recent method under testing. Some studies collected and quantified training data for a better understanding of the recovery status of the patient [12] [13].

As previously introduced, the interactive objects support the proper working of both S1 and S2 allowing the driving of the rehabilitation exercise by the system itself. Indeed, the objects, able to communicate by radio frequency their proximity to the hand of the subject, allow the setup of interactive exercises where the user is prompted to perform each task according to its relative position (e.g. the following sequence of elementary tasks "start from the rest position"- "move to lateral target"- "grasp the bottle"- "move it to the internal target"-"go back to the rest position" may be easily monitored by looking at the information supplied by targets and objects when reached by the subject and the individual commands may be played only when needed), The use of passive tags to identify targets and objects allow to label any personal object allowing the tailoring of the exercise to the single patient. A devoted processing of Received Signal Strength Indication (RSSI) and environmental constraints allow the recognition of the selected objects among several ones.

In the perspective of the RETRAINER clinical trial, a predefined set of objects has been designed and manufactured by 3D printing prompting the patient with objects of different diameters and weights to allow a wide set of exercises (Figure 2) (see section 3.2). The proposed solution can help medical personnel to record and manage the rehabilitation course of the patient in a more effective manner [14] and it can improve patient's commitment in exercise performance [15].

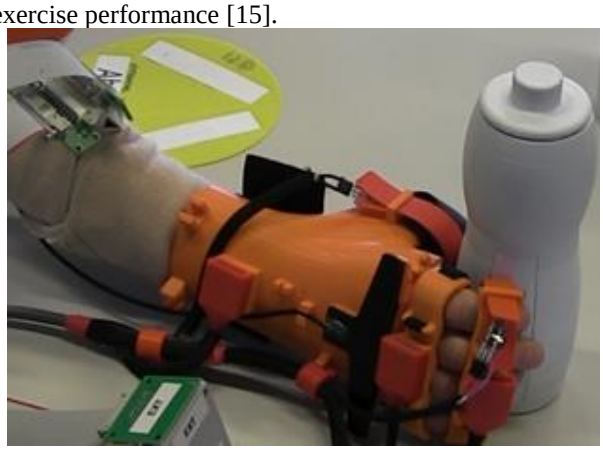

Figure 2. Hand orthosis interacting with a smart object

Both S1 and S2 subsystems share the same communication architecture depicted in Figure 3, the same Graphical Use Interface and the smart objects concept to setup and run the rehabilitation program.

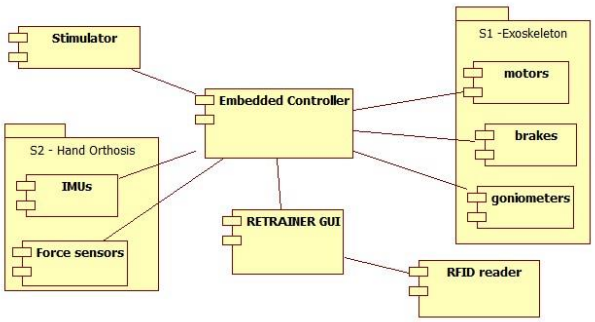

Figure 3. RETRAINER system architecture

2.5 System setup

The GUI guides the operator during the donning, the calibration, and the doffing of both S1 and S2 systems. Besides that, the GUI includes a patient database, visualization of the patients' performance during the sessions and digital assessment test (see table 2,3,4). For both systems the procedure during a training session is divided in three parts: trainings preparation, training walkthrough and training execution.

Concerning S1, during preparation, the operator has to mount the exoskeleton on his/her wheelchair (or normal chair if the user does not need a wheelchair for ambulation), to measure the lengths of the arm and forearm, set the exo lengths accordingly, and identify the weaker arm muscles which need NMES support. On these muscles, electrodes are placed and proper placement is checked. Afterwards, the operator helps the user to don the exoskeleton and sets the gravity compensation level. Based on the choice of the exercises for the training session, the required interactive objects are selected and calibrated.

The following step is then to calibrate the current amplitude and the threshold of the volitional EMG signal used to trigger NMES for each selected muscle. Once the calibration is finished, all the configuration parameters are stored. On the following days, the procedure is simplified since the therapist can load the parameters of the previous day, check and eventually update them.

Analogously, concerning S2, during the training preparation, the appropriate hand-wrist orthosis can be selected in a library of 5 different sizes. The template which best matches the patient anthropometry, if needed, can be customized by modifying the standard wrist extension angle, and the profile of the thumb opposition locking. Customization for the rigid parts is performed by heating, either by immersing the template in hot water for more spread changes or with a standard heat-gun for more localized adaptations. Constraining of fingers two to five, at the level of the proximal phalanges, is provided with clasp templates of 11 different sizes.

Custom orthoses are then temporarily removed, and electrode arrays are positioned on the extrinsic hand muscles. Selective elicitation of the necessary muscle is supervised by the caregiver, who moves one or more virtual stimulation points on a visual representation of the electrode arrays on the touch-responsive GUI. A stimulation map is created for each unique exercise task. Based on the choice of the exercises for the training session, the required interactive objects are selected and calibrated. Once the calibration is finished, all the configuration parameters are stored and made available for the following days of training. Starting from Day One, with the orthosis already customized, the process is simplified. The therapist can position the electrode arrays on the expected skin area, load the previously set stimulation parameters, check them, and if needed update them. The process is completed by donning the custom orthosis.

A training walkthrough has to be performed whenever a patient performs a training exercise for the first time. The purpose of the training walkthrough is twofold. On the one hand most of the thresholds needed for the training execution are patient specific and need to be specified. On the other hand, the patient doesn't know the exercises yet. Therefore the GUI guides the patient and the supporting therapist through the specified exercises. All sensor data of this walkthrough are recorded and the necessary thresholds for the execution are extracted. The walkthrough is performed without stimulation and with the help of a therapist giving the patient confidence and a feeling of safety in a potentially uncomfortable situation.

3. Clinical trial design

RETRAINER will be clinically validated by a multicenter randomized controlled trial (RCT) which has been designed according to the CONSORT Statement recommendations [16]. Potential end users will be selected among stroke patients. A subject will be considered eligible if his/her brain hemispheric lesion is unilateral, if s/he has no history or evidence of previous neurological and/or psychiatric disorders, if s/he is vigilant, collaborative and without global cognitive impairment. This last feature will assure the possibility for the potential participant subject to accept and sign by him/herself the informed consent.

Two parallel clinical trials will be carried out in order to evaluate separately the effectiveness of the two RETRAINER systems (S1 and S2) with respect to conventional therapy. It is calculated that a sample size of 68 patients per center would be capable of detecting a between-group difference of 5.67 points in the primary endpoint Action Research Arm Test), this is the value indicated like Minimally Clinically Important Difference in Chronic Stroke population with a standard deviation of 12.5, a type I error of 5%, and a power of 80% [17] [18]. In total 136 subjects will be recruited, treated and evaluated according to protocol. The whole sample will be equally shared for the two clinical trials.

3.1 Recruitment process

In general, the recruitment criteria and the related process are conceived to ensure the safety of research participants and the fulfillment of the objectives of the study. According to international guidelines such process will

ensure the respect for following ethical principles: equitable selection of participants, respect for privacy, lack of pressure, unbiased presentation of the objectives and characteristics of the research and avoiding misconceptions about the study. Since the usability of the two systems will be tested on stroke subjects, the process of identifying, contacting, and recruiting participants will entail the review of the subjects' medical records, as may be seen in Figure 4.

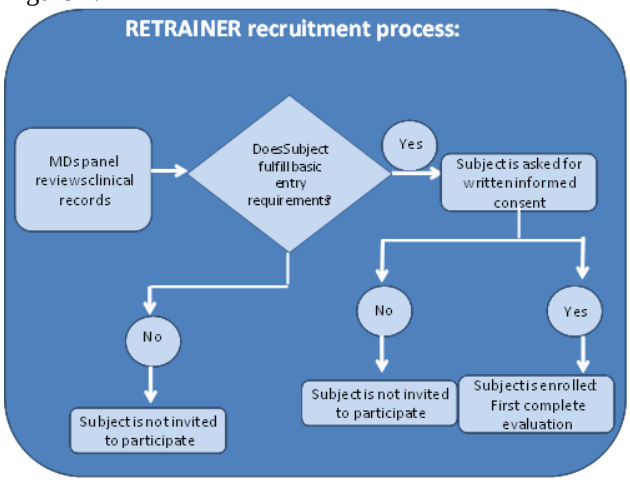

Figure 4. RETRAINER recruitment process

The whole selection and recruitment process will be related to eligibility criteria described as inclusion/exclusion criteria, which are:

1. Adults male and/or female, 18-80 years old.
2. Patients who have suffered stroke with major unilateral functional impairment using Motricity Index (MI) and Medical Research Council (MRC). In this sense, morphological criteria of the stroke will not be considered.
3. MI score must be under 80% of best expected performance.
4. The impairment may be on any side of the body. No major contralateral (MI score more than 80% of normality) lesion of impairment must be present.
5. Sample will include paretic stroke subjects. Subjects completely paralyzed will be excluded. The muscular activity for arm and shoulder must be at least 1 (MRC) with a visible contraction.
6. Subjects will be in what is defined as a sub-acute or early chronic condition. This means that time passed from acute event will be between two weeks and nine months. Month nine allows to expose patients to both systems when and if clinically eligible.
7. No limitation for using the device due to impairment of Passive Range of Motion PROM and/or Pain due to Spasticity evaluated using Modified Ashworth Scale
8. No history of previous major neurological or psychiatric disorders
9. Mini Mental State Examination (MMSE) >20
10. Muscle response (MRC >= 2 for stimulated muscles power)and comfort with FES (VAS <= 3) with the possibility to perform the required actions

Since the sample size is considered small according to randomization criteria (n < 100), and we need to ensure similar size groups to be compared, the "Block Randomization" method will be used [19].

A block size of four has been established (multiple of the number of groups). Afterwards, all possible balanced combinations of assignment within the block have been determined (n = 6) (Figure 5).

Since a careful follow-up of recruitment process will be performed during RETRAINER Project trials, three main measures will be used to establish the accuracy of such process: the number of persons who were screened for eligibility, the number who were eligible, and the number who were definitively enrolled.

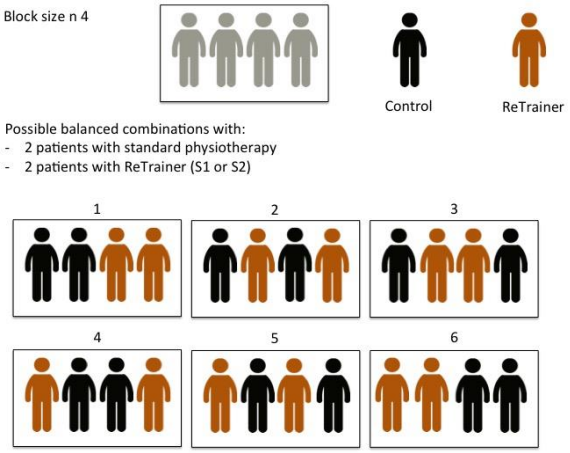

Figure 5. Block Randomization Method

3.2 Exercises design

In terms of treatment to be applied, FES treatments literature suggests that effective treatments have prolonged duration and frequent sessions (Thrasher 2008: 10-12 weeks, 5 sessions per week. Popovic : 9 weeks, 3-5 sessions per week) [20]. In this study, we suggest to have not less than 30 minutes of effective NMES per session. Each session will last one hour considering the don on and off time, setup and calibration. The treatment will include three sessions a week for nine weeks for each research participant.

The protocol will include conventional rehabilitation methods for the control groups and specific exercises supported by the one of the two RETRAINER systems for the experimental groups.

The "conventional" rehabilitation pathway for upper limb will include the following methods:

- Upper limb passive motion Arm Cycle ergometer with or without FES
- Neuro Muscular Electrical Stimulation
- Upper limb exercises using augmented or virtual reality environment
- Occupational therapy exercises
- Constraint induced movement therapy (CIMT), modified concept

- Upper limb active movement (reaching, grasping, elevation, spatial orientation)
- Repetitive task training
- Mirror therapy
- Writing training
- Chemodenervation Therapy

For the RETRAINER groups a set of exercises has been defined. Among them, a personalized set of exercises is selected by the clinician, according to patient's functional conditions, choosing among several available exercises.

During the exercise execution the patient is guided through the specified exercises. This is done using audio messages, pictures of the task to be performed and written instructions from the GUI. The therapist and the patient get a visual feedback for each sensor used. To keep the training process flexible, stimulation data and exercise thresholds can be changed during exercise execution. This is especially important since muscle fatigue will occur during electro stimulation.

The two categories of exercises are summarized in the following table 1:

S1: exercises are focused on the orientation of the upper limb movement with or without an object in the hand	
Movement category	***Selected tasks***
Spatial exploration with upper limb	• Anterior reaching with or without wrist prono-supination • Lateral elevation of the arm • Hand to mouth gesture with free prono-supination of the wrist if the subject is able to control it or with the wrist fixed in an intermediate position if the patient is unable to control it
Moving objects	• On horizontal plain (on the table) • On vertical plane (if autonomous grasping is present)
S2: exercises are focused on grasping with or without orientation and flexo extension of the wrist	
Grasping and release	• All fingers move together • No independent fingers movement • No thumb movement
Flexion-extension of the wrist	Possibility of fixing it according to patient's condition: with free prono-supination if the subject is able to control it, fixed in an intermediate position if the patient is unable to control it.

Table 1. Two categories of exercises

The whole study will take 15 months. The duration of the study for each single subject will take 15 weeks starting with the recruitments phase to the follow-up.

3.3 Evaluation metrics

Additionally, to the main outcome measure, other specific outcomes will be measured to best evaluate the effects of the trials. Patients are assessed at baseline, soon after the end of the intervention and in a 4-week follow-up visit, as shown in Figure 6.

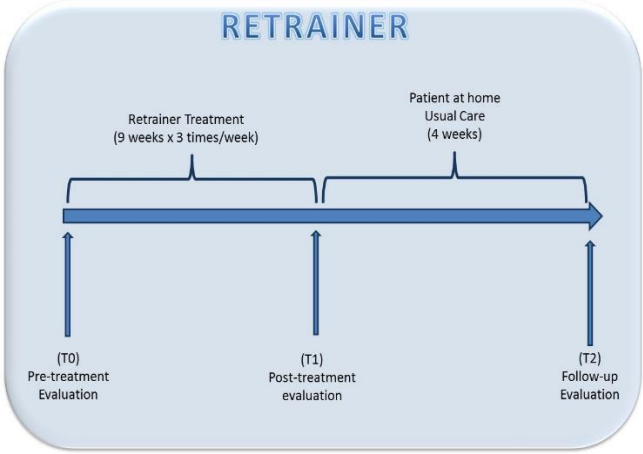

Figure 6. RETRAINER Evaluation and treatment schema

The following tables, 2, 3 and 4 summarizes the outcome measures proposed.

Outcome	Assessment	T0	T1	T2
Cognitive Evaluation	Mini-Mental State Examination (MMSE)	✓		
Effectiveness	Medical Research Council (MRC)	✓	✓	✓
Effectiveness	Motricity index	✓	✓	✓
Effectiveness	Motor Activity Log (MAL)	✓	✓	✓
Effectiveness	Action Research Arm Test (ARAT)	✓	✓	✓
Effectiveness	Box & Blocks Test (BB)	✓	✓	✓
Usability Acceptance	System Usability Scale (SUS)		✓	
Usability Acceptance	Technology Acceptance Model (TAM)		✓	
Quality of Life	Stroke Specific Quality Of Life scale (SS-QOL)	✓	✓	✓

Table 2. Clinical and quality of life outcome measurements

Outcome	Assessment	T0	T1	T2
Effectiveness	Modified Ashworth Scale (MAS), target muscles: Pectoralis Major, Deltoids, Biceps and Triceps	✓	✓	✓

Table 3. RETRAINER S1 muscular assessment

Outcome	Assessment	T0	T1	T2
Effectiveness	Modified Ashworth Scale (MAS), target muscles: Wrist flexor and extensor, fingers and thumb flexor and extensor	✓	✓	✓

Table 4. RETRAINER S2 muscular assessment

Instrumental Evaluation of RETRAINER S1 includes:

- Dynamic EMG target muscles: Pectoralis Major, Deltoids, Biceps and Triceps. The dynamic EMG will be performed pre and post the rehabilitation program. The signals will be recorded with and without exoskeleton to analyze the gravity compensation effect. The EMG data will be recorded using an external dynamic EMG system (BTS FreeEMG).
- Kinematic data from exoskeleton during trials. The data coming from the sensors inside the system will be used to have an evaluation of the functional range of motion during the therapy exercises. The data will be recorded using the angle sensors embedded in the exoskeleton.

Instrumental Evaluation of RETRAINER S2 includes:

- Dynamic EMG target muscles: Wrist flexor and extensor, fingers and thumb flexor and extensor. The dynamic EMG will be performed pre and post the rehabilitation program.
- Kinematic data from hand orthosis during training (FSR sensors and IMUs). The data coming from the sensors inside the system will be used to have an evaluation of the functional range of motion during the trials movements.

4. Conclusion

RETRAINER implements the current rehabilitative trend to combine several means of assistance included into a hybrid robotics system, to take benefits from the strength of each technology, overcoming the limited performance of each single approach. The use of the exoskeleton increases the possible range of motion, allowing the contraction of weak muscles to accomplish tasks otherwise too heavy and to post-pone the early onset of muscular fatigue, thanks to the posture freezing granted by brakes. On the other hand, the increased afferent feedback provided by NMES maximizes cortical plasticity, thus increasing motor learning [21].

Considering the easiness to use and the rehabilitation outcome expectations, the main need is a system supporting the patient in using his/her own arm and hand without substituting him/her. This way, the use of myocontrolled NMES has been chosen for the arm control together with the support of the exoskeleton and for the grasping tasks with the support of the hand orthosis. Interactive objects complete the system as a means to supply information on the autonomously performed actions (investigation of impact on the daily life) as well to drive specific rehabilitation exercises.

The final goal is to allow a continuative therapy at home, supporting normal daily activities facilitating the use of the two arms.

RETRAINER aims at demonstrating and validating a highly multidisciplinary approach in the design and development of the robotic system together with quantitative evidence of the rehabilitation outcomes by means of a multicenter clinical trial.

Usability and technological acceptance of robotics based rehabilitation systems and programs play a key role in a wide and effective diffusion of these systems in clinics and at home to foster innovative paradigms in rehabilitation design.

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References

[1] K. Aho, P. Harmsen, S. Hatano, J. Marquardsen, V. E. Smirnov, and T. Strasser, "Cerebrovascular disease in the community: results of a WHO collaborative study," *Bull. World Health Organ.*, *58 (1)*, 1980, 113–130.

[2] F. Coupar, a Pollock, V. W. F, J. Morris, P. Langhorne, F. Coupar, A. Pollock, F. Van Wijck, J. Morris, and P. Langhorne, "Simultaneous bilateral training for improving arm function after stroke (Review) Simultaneous bilateral training for improving arm function after stroke," *Heal. San Fr.*, *4*, 2010, 2–4.

[3] Y. Wang and D. Wang, "Hand in hand with the world to conquer stroke," pp. 1–3, 2016.

[4] A. Di Carlo, "Human and economic burden of stroke," *Age Ageing*, *38(1)*, 2009, 4–5.

[5] A. Di Carlo, M. Baldereschi, C. Gandolfo, L. Candelise, A. Ghetti, S. Maggi, E. Scafato, P. Carbonin, L. Amaducci, and D. Inzitari, "Stroke in an elderly population: Incidence and impact on survival and daily function: The Italian Longitudinal Study on Aging," *Cerebrovasc. Dis.*, *16(2)*, 2003, 141–150.

[6] A. Fusco, D. De Angelis, G. Morone, L. Maglione, T. Paolucci, M. Bragoni, and V. Venturiero, "The

ABC of tDCS: Effects of anodal, bilateral and cathodal montages of transcranial direct current stimulation in patients with stroke - A pilot study," *Stroke Res. Treat.*, *2013(2013)*, 2013, 1-6.

[7] C. D. Mathers and D. Loncar, "Projections of global mortality and burden of disease from 2002 to 2030," *PLoS Med.*, *3(11)*, 2006, 2011–2030.

[8] A. Pedrocchi, S. Ferrante, E. Ambrosini, M. Gandolla, C. Casellato, T. Schauer, C. Klauer, J. Pascual, C. Vidaurre, M. Gföhler, W. Reichenfelser, J. Karner, S. Micera, A. Crema, F. Molteni, M. Rossini, G. Palumbo, E. Guanziroli, A. Jedlitschka, M. Hack, M. Bulgheroni, E. D'Amico, P. Schenk, S. Zwicker, A. Duschau-Wicke, J. Miseikis, L. Graber, and G. Ferrigno, "MUNDUS project: MUltimodal Neuroprosthesis for daily Upper limb Support.," J. Neuroeng. Rehabil., *10*, 2013, 66.

[9] G. I. Barsi, D. B. Popovic, I. M. Tarkka, T. Sinkj??r, and M. J. Grey, "Cortical excitability changes following grasping exercise augmented with electrical stimulation," *Exp. Brain Res.*, *191(1)*, 2008, 57–66.

[10] G. M. Iftime-Nielsen SD, Christensen MS, Vingborg RJ, Sinkjaer T, Roepstorff A, "Interaction of electrical stimulation and voluntary hand movement in SII and the cerebellum during simulated therapeutic functional electrical stimulation in healthy adults." *Hum Brain Mapp*, *33(1)*, 2012, 40–9.

[11] M. Gandolla, S. Ferrante, F. Molteni, E. Guanziroli, T. Frattini, A. Martegani, G. Ferrigno, K. Friston, A. Pedrocchi, and N. S. Ward, "Re-thinking the role of motor cortex: Context-sensitive motor outputs?," *Neuroimage*, *91(100)*, 2014, 366–374.

[12] M. Bulgheroni, E. D'Amico, and L. Sartori, "RFID Technology for Objects Recognition and Their Position Estimation," *Converging Clinical and Engineering Research on Neurorehabilitation* (Berlin, Heidelberg, Springer Berlin Heidelberg, 2013).

[13] C.-C. Chen, Y.-L. Chen, and S.-C. Chen, "Application of RFID technology--upper extremity rehabilitation training.," *J. Phys. Ther. Sci.*, *28(2)*, 2016, 519–524.

[14] C. S. Wang, L. P. Hung, and N. Y. Yen, "Using RFID Positioning Technology to Construct an Automatic Rehabilitation Scheduling Mechanism," *J. Med. Syst.*, *40(1)*, 2016, 1–12.

[15] M. Bulgheroni, E. D'Amico, and F. Molteni, "18 th european congress of physical physical and rehabilitation medicine," *Eur J Phys Rehab Med*, *48(2)*, 2012, 48-49.

[16] G. Piaggio, D. R. Elbourne, S. J. Pocock, S. J. W. Evans, and D. G. Altman, "Reporting of Noninferiority and Equivalence Randomized TrialsExtension of the CONSORT 2010 StatementReporting Noninferiority and Equivalence," *JAMA J. Am. Med. Assoc.*, *308(24)*, 2012, 2594–2604.

[17] J. van der Lee, H. Beckerman, G. Lankhorst, and L. Bouter, "The responsiveness of the Action Research Arm test and the Fugl-Meyer Assessment scale in chronic stroke patients," *J Rehabil Med.*, *33(3)*, 2001, 110–3.

[18] J. H. van der Lee, V. de Groot, H. Beckerman, R. C. Wagenaar, G. J. Lankhorst, and L. M. Bouter, "The intra- and interrater reliability of the action research arm test: A practical test of upper extremity function in patients with stroke," *Arch. Phys. Med. Rehabil.*, *82(1)*, 2001, 14–19.

[19] M. Kang, B. G. Ragan, and J.-H. Park, "Issues in Outcomes Research: An Overview of Randomization Techniques for Clinical Trials," *J. Athl. Train.*, *43(2)*, 2008, 215–221.

[20] T. A. Thrasher, V. Zivanovic, W. McIlroy, and M. R. Popovic, "Rehabilitation of reaching and grasping function in severe hemiplegic patients using functional electrical stimulation therapy.," *Neurorehabil. Neural Repair*, *22(6)*, 2008, 706–714.

[21] L. M. Muratori, E. M. Lamberg, L. Quinn, and S. V Duff, "Extremity Rehabilitation," *26(2)*, 2014, 94–103.