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ORIGINAL ARTICLE

Using robot fully assisted functional movements in upper-limb rehabilitation of chronic stroke patients: preliminary results

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ABSTRACT

BACKGROUND: Robotic rehabilitation is promising to promote function in stroke patients. The assist as needed training paradigm has shown to stimulate neuroplasticity but often cannot be used because stroke patients are too impaired to actively control the robot against gravity.
AIM: To verify whether a rehabilitation intervention based on robot fully assisted reaching against gravity (RCH) and hand-to-mouth (HTM) can promote upper-limb function in chronic stroke.
DESIGN: Cohort study.
SETTING: Chronic stroke outpatients referring to the robotic rehabilitation lab of a rehabilitation centre.
POPULATION: Ten chronic stroke patients with mild to moderate upper-limb hemiparesis.
METHODS: Patients underwent 12 sessions (3 per week) of robotic treatment using an end-effector robot Every session consisted of 20 minutes each of RCH and HtM; movements were fully assisted, but patients were asked to try to actively participate. The Fugl-Meyer Assessment (FMA) was the primary outcome measure; Medical Research Council and Modified Ashworth Scale were the secondary outcome measures.
RESULTS: All patients, but one, show functional improvements (FMA section A-D, mean increment 7.2±3.9 points, $P<0.008$).
CONCLUSIONS: This preliminary study shows that a robotic intervention based on functional movements, fully assisted, can be effective in promoting function in chronic stroke patients. These results are promising considering the short time of the intervention (1 month) and the time from the stroke event, which was large (27±20 months). A larger study, comprehensive of objective instrumental measures, is necessary to confirm the results.
CLINICAL REHABILITATION IMPACT: This intervention could be extended even to subacute stroke and other neurological disorders.

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Key words: Rehabilitation - Robotics - Stroke - Upper extremity.

Stroke is a leading cause of serious long-term disability in developed countries,[1] and has an enormous emotional and socioeconomic impact on patients, families and, health services. Upper-limb impairments and functional problems are, in fact, very common after a stroke. Impairments commonly include difficulty moving and co-ordinating the arms, hands and fingers, often resulting in difficulty carrying out activities of daily living (ADLs) such as eating, dressing and washing. More than half of people with upper-limb impairment after stroke will still have difficulties in performing ADLs many months to years after their stroke.[2, 3] Robotic rehabilitation systems have the potential to deliver large doses of motor training in a cost-effective manner and, although the debate on the

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efficacy of robotic therapy is still open, they are emerging as valid solutions to help stroke survivors in the rehabilitation of the upper limb.[4, 5] The study of Lum *et al.*[6] demonstrated in 2002 that a robotic treatment was superior to conventional therapy in the reduction of the impairment in the short term. Furthermore, at 6-month follow-up, the robot group had larger improvements in the Functional Independence Scale. Recent reviews show that the effect of a robotic training is comparable to a conventional therapy training of the same length and intensity.[7] A recent Cochrane systematic review [8] included 34 trials (involving 1160 participants) showed that electromechanical and robot-assisted arm training improved ADLs scores (SMD 0.37, 95% confidence interval [CI] 0.11 to 0.64, P=0.005, I^2=62%), arm function (SMD 0.35, 95% CI 0.18 to 0.51, P<0.0001, I^2=36%), and arm muscle strength (SMD 0.36, 95% CI 0.01 to 0.70, P=0.04, I^2=72%), but the quality of the evidence was low to very low. Unfortunately, the mechanisms leading to impairment reduction following the robotic training are still unclear.[9] It is known that neuroplasticity plays an important role in the motor recovery process of stroke patients [10] and, furthermore, that the patient should be engaged during the treatment in order to foster a process similar to motor learning.[11] To promote engagement and maximize neuroplasticity, two main methods have been studied in robotic rehabilitation: 1) the assist-as-needed training paradigm; and 2) the Detection of Patient Intent (DPI) [12] method, also called guided force training.[13] The first one, which consists in providing the minimal assistance needed to the subject to complete the task required, has shown promising results in enhancing the participation to the treatment, especially in medium-high functional patients.[14-16] The DPI method is based on triggering the movement of the robot using the patient's exerted force or induced velocity.[17-19] In some cases, the DPI method may even exploit biomedical signals like EMG or EEG to initiate the given task.[20, 21]

Besides the modality of interaction between patient and robot, another important feature that can determine the success of the therapy is the type of movement proposed. It is known that treatments based on purposeful movements show better results in the recovery of the upper-limb function than those based on movements without a goal.[22] Therefore, a proper rehabilitation program should include high repetition task-oriented movements.[23]

Unfortunately, the assist-as-need principle and the DPI method are often of little applicability in training against gravity, especially in the case of low functioning patients with high strength and coordination impairments. In these cases, when the patient is not able to control actively the robot, full assistance, based on a rigidly imposed trajectory (path and motion law), is the only remaining option in robotic rehabilitation.

In this preliminary study, an upper-limb rehabilitation program based on robot fully assisted (rigidly imposed) goal-oriented movements is presented. The objective of the work was to verify the efficacy of the intervention in the short term in reducing motor impairment in chronic stroke patients.

Materials and methods

Study population

This is a single-centre observational study. Ten patients were enrolled among those who had previously referred to Villa Beretta Rehabilitation Centre Costa Masnaga (Lecco) during the period December 2013 – June 2015. The inclusion criteria were: 1) hemiplegia after first stroke; 2) time from the stroke event >6 months; 3) absence of severe attentive deficits; 4) ability to perform active arm movements (shoulder flexion MRC>1 and AROM>60°, elbow flexion-extension MRC>1 and AROM>90°) and able to hold the robot handle; 5) Modified Ashworth Scale Score ≤3 (see section Outcome). Exclusion criteria were: 1) other concurrent upper-limb rehabilitation interventions; 2) presence of global aphasia and/or cognitive impairments that could interfere with understanding the instructions during evaluation and treatment (Mini-Mental State Examination Test >24/30); 3) concomitant progressive central nervous system disorders, peripheral nervous system disorders or myopathies.

Written informed consent was obtained from each subject before inclusion in the study. Ethical approval of the treatment and evaluation protocol was granted by the local ethics committee at A. Manzoni, Lecco.

Equipment

1. An end-effector robot (Pa10-7, Mitsubishi, Japan) customized for rehabilitation purposes (Figure 1), which allows for the execution of functional movements performed at physiological velocity.[24]

2. A wireless 8 channel surface EMG acquisition system (FreeEMG 300, BTS, Italy), which was used to define the movements velocities for each patient and to

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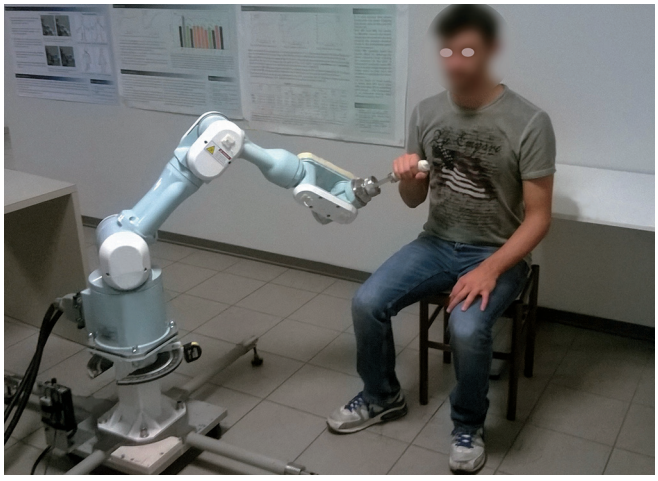

Figure 1.—The robotic platform (Mitsubishi Pa10-7, Mitsubishi, Japan) used to perform rehabilitation at the Robotic Rehabilitation and Translational Reserch Lab installed at Villa Beretta Rehabilitation Center.

monitor the neuromuscular activation pattern during the intervention sessions.

3. Two digital video camera (Vixta, BTS, Italy) film patients' movements.

Study design

Patients selected from the Villa Beretta database were phone called and asked to participate to the study after having verified that inclusion criteria were met. Before treatment, patients were further evaluated by their referent physician. All patients were submitted to the same intervention, only movement ranges and velocities were customize based on the patients' residual abilities and the EMG activation pattern (see the intervention section). One physical therapist, the same for all patients, performed all outcome assessments (pretreatment as well as post-treatment) with the supervision of the patient's referent physician, which could double check the clinical tests results even consulting the videos of the patients. To minimize biases during post-treatment evaluation, he could not have access and view the pretreatment results.

Intervention

The rehabilitation protocol consisted in a 1-month intervention, 12 sessions, 3 per week. Every session consisted of 40 minutes of robot-assisted training, 20 minutes of reaching movement (RM) and 20 minutes of the hand-to-mouth movement (HtMM).

The two functional movements were selected for the robotic training because of their importance in ADLs. In fact, these are key movements from a functional point of view because they allow, respectively 1) to reach for objects placed in front of the subject up to the shoulder height, and 2) to take objects towards the body and face. The RM and HtMM are two compound movements that involve both motion towards and away from the body and, just as importantly, are movements continuously repeated during common life. Finally, in the case of HtMM, it also recalls eating, and ancestral need, which involves brain emotional processes making the exercise for the patient highly engaging and stimulating.

The frame series of the RM and HtMM are shown in Figures 2, 3, respectively. Both movements started from the same rest position (hand on the thigh and shoulder slightly extended) and ended with shoulder flexed at 90° and elbow fully extended in the case of the RM or with

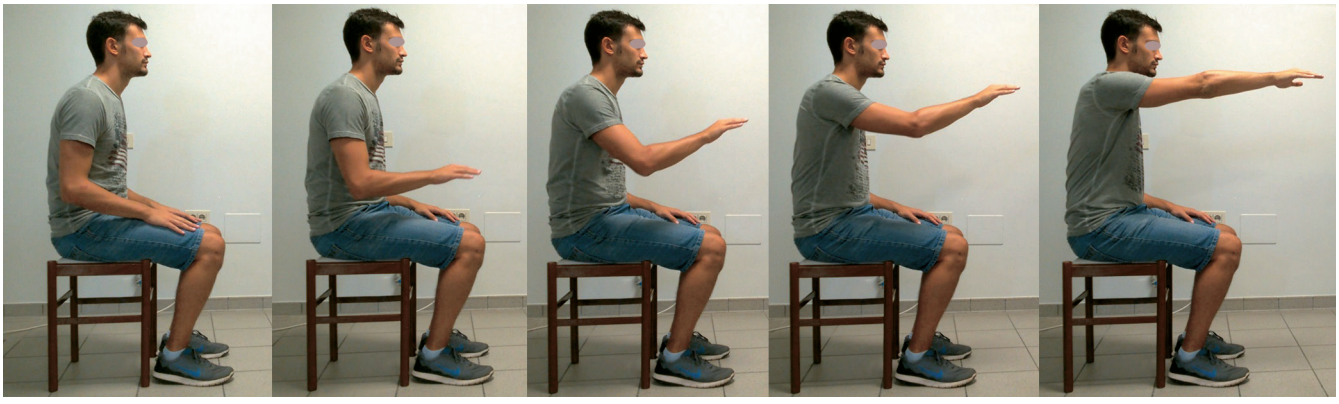

Figure 2.—Frames sequence of the RM performed by a healthy subject.

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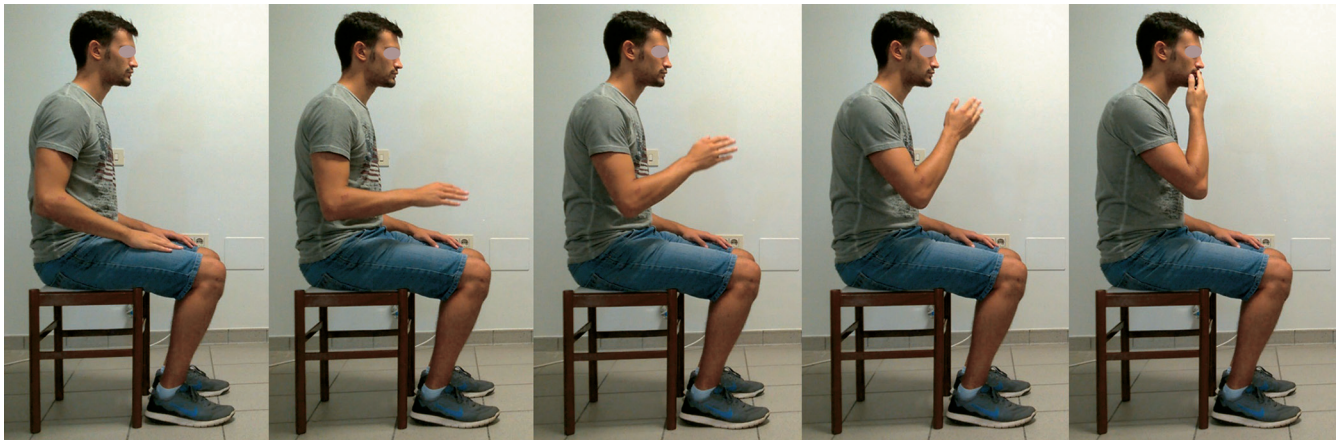

Figure 3.—Frames sequence of the HtMM performed by a healthy subject.

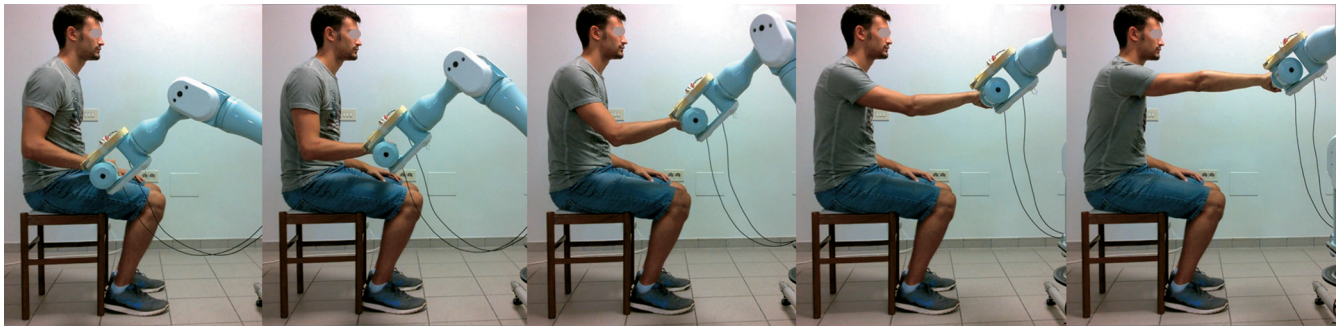

Figure 4.—Frames sequence of the robot assisted RM performed by a healthy subject.

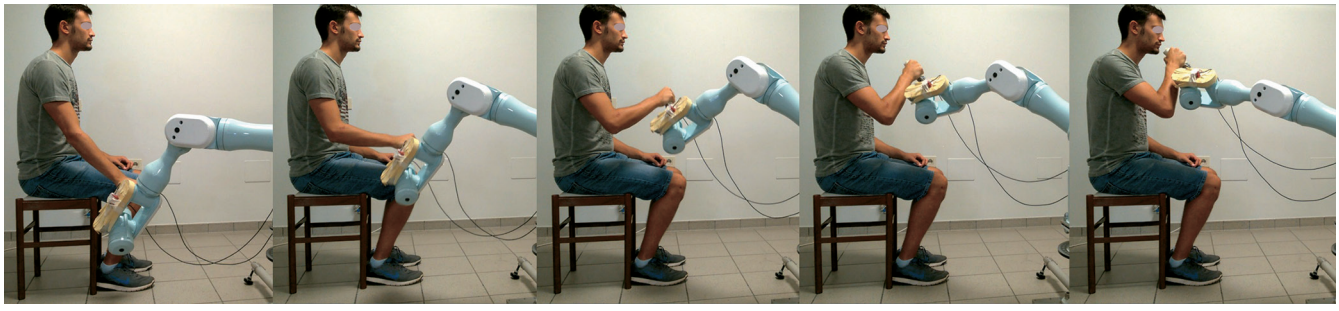

Figure 5.—Frames sequence of the robot assisted HtMM performed by a healthy subject.

the hand touching the mouth (elbow fully flexed and shoulder flexed around 30°) in the case of the HtMM.

The hand paths of both the RM and HtMM were taken from a healthy subjects' database of movement acquired using the 3D-motion capture system and the procedure described in Caimmi *et al.*[25] The trajectories were scaled on each patient's anthropometric measures and velocities on his functional residual abilities for creating customized exercises. In the case of the HtMM, in order to avoid collisions with the robot, the assisted movement started a little more sidewise than the freely executed movement. The frame series of the robot assisted RM and HtMM are shown in Figures 4, 5, respectively. Velocities, characterized by bell-shaped profiles, were rigidly imposed; that is, the robot handle followed the predefined path and motion law independently of the forces applied by the patient.

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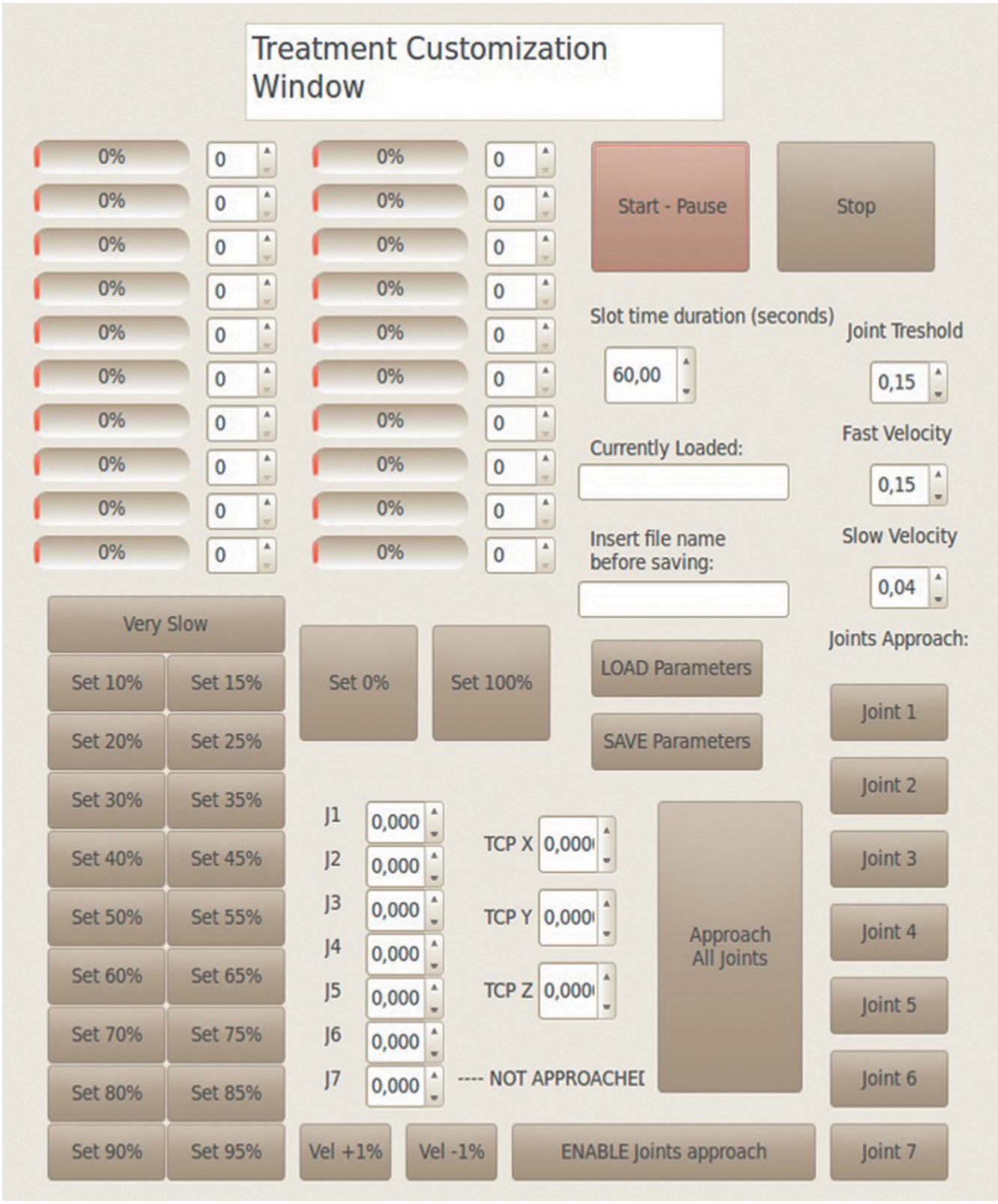

Figure 6.—Graphical interface.

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In rehabilitation, this kind of intervention is commonly defined as continuous passive mobilization (CPM) because the patient does not have to actively participate. In order to avoid this, the patient was explicitly asked to participate by trying to follow (slightly anticipate) the moving handle. The operator, a specialized physiotherapist, could monitor on video the forces of interaction between the patient and the robot and EMG pattern activation pattern and, if necessary, could encourage the patient to try to participate more. In order not to make the exercise too fatiguing (it is worth recalling that both movements were against gravity), the patient was asked to change the level of engagement every 5 movements by alternately relaxing during movement and actively participating. Furthermore, in the case of the HtMM, the patient had to actively orientate the robot handle, which was provided by a turning point, toward the mouth (Figure 3).

To better stimulate proprioception and, to maintain patient's engagement and attention, every minute the velocity profile was scaled with peak velocities comprised between 0.30 and 0.80 m/s. Slow movements were alternated to physiological ones, customizing the movement parameters (velocity and range of movement) on the patient's capability and the EMG activation pattern. In Figure 6, the graphical interface used to administer the treatment is reported. Each progress bar represents 1 minute of exercise; velocity is expressed as percentage of the velocity needed to perform the movement in 2 seconds (1 second each for the forward and backward phases). The EMG was monitored during the creation of the exercises to set up the movement parameters, the maximum velocities above all. They were set up in such a way that no stretch-reflex activity was present at any of the investigated muscles (the upper trapezius, the deltoid anterior, the deltoid medium, the deltoid posterior, the *triceps brachii* lateral head, the biceps long head, and the *brachioradialis*).

Outcome measure

The following tests were carried out at baseline (T0) and at the end of treatment (T1).

1. The Fugl-Meyer Assessment (FMA) [26] assessment (sections A-D) was used to assess the upper-limb global functional impairment. The A-D sections test the functionality of: shoulder and elbow (A), wrist (B), hand (C) and coordination of the upper limb (D).

2. The Medical Research Council scale for muscle strength (MRC) [27] was used for evaluating the muscles (joint) strength of three targeted movements: shoulder abduction, elbow extension and fingers extension. MRC is a 15-point scale (5 points for each item).

3. The Modified Ashworth Scale (MAS) [28] was used to assess spasticity. Each tested movement is given a 0 to 5 score (0 no spasticity, 1 slight increase in muscle tone at end movement, 2 slight increase in muscle tone up to half of the ROM, 3 more marked increase in muscle tone through most of the ROM, 4 considerable increase in muscle tone, 5 affected part rigid in flexion or extension; see footnote [1]). The tested movement were: wrist extension, elbow extension and shoulder abduction, for a total of 15 (negative) points.

The FMA was chosen as the primary outcome measure.

Statistical analysis

The statistical analysis was performed using the WinSTAT® for Microsoft® ver.2012.1.0.94.

Considering the small size of the sample, the authors wanted to be prudent and preferred to use a nonparametric method to test for the significance of pre- and post-treatment differences. In fact, small samples simply do not contain enough information to let you make reliable inferences about the shape of the distribution in the entire population and, consequently, normality tests have little power to detect whether or not a sample comes from a Gaussian population. In these cases the use of nonparametric methods seems more appropriate because, if a nonparametric test is used when the parametric assumptions are actually met, you are just likely to get a P value that is too large. This is because nonparametric tests have less power than the parametric ones (around 95%) in the analysis of normally distributed data.[29]

For the reasons above the Wilcoxon's Signed Rank Test was used to compare pre- and post-treatment data. Alpha was set at 5%. No mathematical transform was applied to data before analysis.

Results

The group of patients included 10 subjects, 6 men and 4 women, 6 suffering from right hemiparesis and

[1] For the sake of simplicity in the calculation, the authors substituted the original score calculation of Bohannon (0,1,1+,2,3, and 4) with a 5 points score (0,1,2,3,4 and 5).

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TABLE I.—*Patients' data.*

Patients	Age (years)	Sex	Affected side	Months from stroke
Pt 1	65	F	Left	6
Pt 2	62	M	Right	76
Pt 3	24	F	Right	32
Pt 4	65	M	Left	11
Pt 5	76	F	Right	27
Pt 6	68	F	Right	51
Pt 7	55	M	Left	32
Pt 8	65	M	Right	6
Pt 9	73	M	Left	8
Pt 10	49	M	Right	19
	60±15	6 men	4 left	27±20

TABLE II.—*Fugl Meyer Assessment results.*

FMA	T0	T1	Δ	P
Section A (max 36) (shoulder and elbow)	22.0±5.4	25.5±5.2	3.5±2.2	<0.02
Section B (max 10) (wrist)	4.1±3.3	5.0±3.1	0.9±1.0	<0.05
Section C (max 14) (hand)	5.6±3.9	8.5±4.1	2.9±3.0	<0.02
Section D (max 6) (coordination/velocity)	3.4±1.3	4.3±1.1	0.9±0.5	<0.02
Total score (max 66)	36.1±12.0	43.3±11.6	7.2±3.9	<0.008

Sub-sections Fugl Meyer Assessment scores at T0 (before intervention), at T1 (after intervention).
Δ: score difference (T1-T0); P: level of statistical significance at the Wicoxon Test.

4 from left hemiparesis. The patients' average age was 60±15 years and the average time from the stroke event was 27±20 months. Data are shown in Table I.

All patients were fully compliant with the treatment and were able to complete all the 12 robotic rehabilitation sessions.

The pre- and post-treatment FMA total score (primary outcome) and sub-scores along with level of statistical significance p are reported in Table II. Secondary outcome measures and total FMA score are shown in Table III. Furthermore, patients' specific items results regarding MRC and MAS are reported in Tables IV, V, respectively.

The improvement in the Fugl-Meyer Assessment was statistically significant (FMA section A-D, mean increment 7.2±3.9 points, P<0.008) and seven patients even overtook the minimal detectable change (MCD), which for this scale is set at 5.2 points.[30] Statistically significant improvements were found for all 4 subscores, hand and wrist included. Responsiveness to the intervention according to Cohen's definition was large for coordination/velocity, moderate for shoulder and elbow, hand and total FMA score, small for wrist scores. No correlation was found between the FMA improvements and patients' age (R^2=8E-05, P=0.49) (Figure 7, right panel). At a first glance, no correlation between FMA and time from stroke seemed to exist (R^2=0.031, P=0.31). Actually, two patients, number 2 and 8, showed a weird behavior (Figure 7, left panel). Specifically, patient 2 showed 12 FMA points improvement at 72 months from the stroke, which is a huge improvement while patient 8 showed totally no improvement (FMA=0) although he was 6 months from the stroke only. Therefore, the linear regression curve was recalculated and a statistically significant correlation was found (R^2=0.795, P<0.002). Interestingly, note that patient 8, showed no FMA improvement but, by contrast, showed increased strength (1 MRC point at shoulder and 1 at elbow) and decreased spasticity (1 MAS point at the elbow).

TABLE III.—*Clinical results.*

	FMA		MRC		MAS	
	T0	T1	T0	T1	T0	T1
Pt 1	29	39	9	9	3	0
Pt 2	50	62	12	15	0	0
Pt 3	41	48	9	12	5	5
Pt 4	22	32	5	6	4	2
Pt 5	18	25	4	5	2	2
Pt 6	45	47	12	12	4	4
Pt 7	24	28	5	5	3	2
Pt 8	56	56	11	13	3	2
Pt 9	40	52	10	12	3	3
Pt 10	36	44	8	9	2	2
Mean	36.1	43.3	8.5	9.8	2.9	2.2
Std	±12.0	±11.6	±3.0	±3.6	±1.3	±1.5

Patient's clinical evaluation before intervention (T0) and after intervention (T1).
FMA: Fugl-Meyer Assessment; MRC: Medical Research Council; MAS: Modified Ashwoth Scale.

As regards the MRC, although seven patients showed an improvement of 1 point at least (4 patients showed 1 point in shoulder abduction, 6 patients showed 1 point improvement in elbow extension and 3 patients showed 1 point improvement in finger extension; Table IV), the patients' group average improvement was not statistically significant.

Four patients showed a reduction of at least 1 MAS point (2 patients showed at least 1 point reduction at the shoulder adductors and 3 patients showed 1 point reduction at the elbow flexors). The group MAS reduction was not statistically significant.

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TABLE IV.—*Medical Research Council.*

	T0			T1			Δ		
	Shoulder (abd)	Elbow (ext)	Fingers (ext)	Shoulder (abd)	Elbow (ext)	Fingers (ext)	Shoulder (abd)	Elbow (ext)	Fingers (ext)
Pt 1	4	4	1	4	4	1	0	0	0
Pt 2	4	4	4	5	5	5	1	1	1
Pt 3	4	4	1	5	5	2	1	1	1
Pt 4	1	4	0	2	4	0	1	0	0
Pt 5	2	2	0	2	3	0	0	1	0
Pt 6	4	4	4	4	4	4	0	0	0
Pt 7	2	2	1	2	2	1	0	0	0
Pt 8	4	4	3	5	5	3	1	1	0
Pt 9	3	4	3	3	5	4	0	1	1
Pt 10	4	4	0	4	5	0	0	1	0
Mean	3.2	3.6	1.7	3.6	4.2	2.0	0.4	0.6	0.3
Std	±1.1	±0.8	±1.6	±1.3	±1.0	±1.9	±0.5	±0.5	±0.5

Medical Research Council items of each patient before intervention (T0), after intervention (T1) and difference.
Δ: MRC (T1)-MRC (T0); abd: abduction; ext: extension.

TABLE V.—*Modified Ashworth Scale.*

	T0			T1			Δ		
	Shoulder adductors	Shoulder adductors	Shoulder adductors	Shoulder adductors	Elbow flexors	Wrist flexors	Shoulder adductors	Elbow flexors	Wrist flexors
Pt 1	3	0	0	0	0	0	-3	0	0
Pt 2	0	0	0	0	0	0	0	0	0
Pt 3	2	2	1	2	2	1	0	0	0
Pt 4	2	2	0	1	1	0	-1	-1	0
Pt 5	0	0	2	0	0	2	0	0	0
Pt 6	1	3	0	1	3	0	0	0	0
Pt 7	1	2	0	1	1	0	0	-1	0
Pt 8	1	2	0	1	1	0	0	-1	0
Pt 9	1	2	0	1	2	0	0	0	0
Pt 10	0	1	1	0	1	1	0	0	0
Mean	1.1	1.4	0.4	0.7	1.1	0.4	-0.4	-0.3	0.0
Std	±1.0	±1.1	±0.7	±0.7	±1.0	±0.7	±1.0	±0.5	±0.0

Modified Ashworth Scale items of each patient before intervention (T0) and after intervention (T1) and difference.

Discussion

In the present study, patients were submitted to a short rehabilitation intervention based on robot fully assisted goal oriented functional movements (against gravity). First results demonstrate the short term efficacy of the intervention in stimulating motor recovery. In fact, the group's improvements, assessed through the Fugl-Meyer Scale, were statistically significant ($P<0.008$); all patients, but one, showed functional improvement. Seven patients, gaining more than 5 FMA points, even reached the MDC for this scale. Interestingly, patient 8, a high functioning one (FMA=56 at T0), increased his strength at elbow and shoulder and presented reduced spasticity at the elbow joint, but did not presented any functional improvement. A more detailed analysis should be done to explain the reason of this result. Maybe he should have been trained on tasks requiring more hand dexterity. In fact, an analysis of the FMA Scale (here not presented) showed that this patient's impairments regarded more the wrist and the hand fine movements. However, this hypothesis should be further investigated. The problem seems to be more complex as motor recovery at the hand occurred in 8 patients out of 10. In fact, although the improvement was moderate (2.9±3.0, *d'*=0.71) the group's average FMA improvement at the hand was statistically significant ($P<0.02$). This is not entirely surprising because the hand control is strongly affected by the proximal joints position as demonstrated by Dominici *et al.* Their findings suggest that there are differenc-

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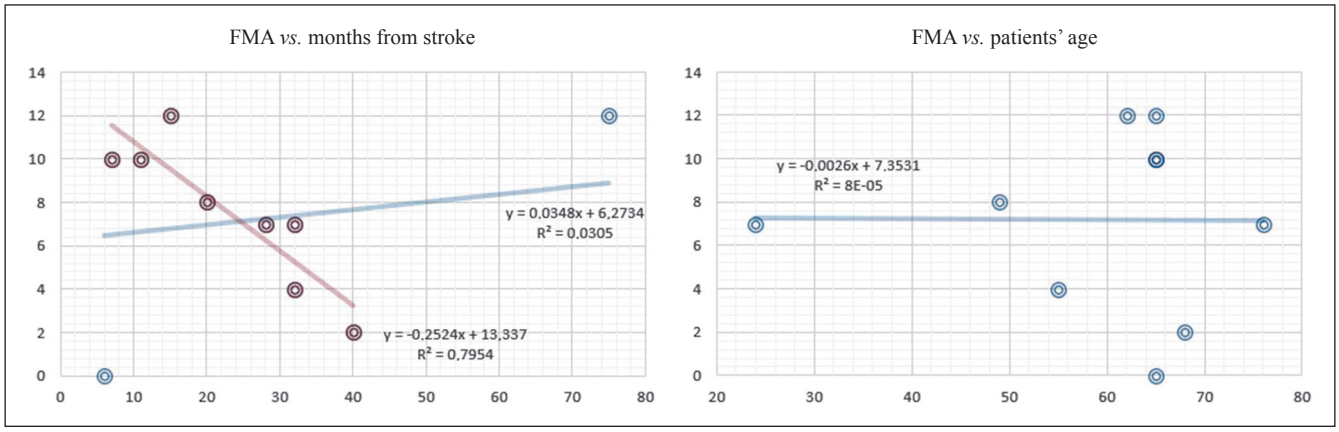

Figure 7.—FMA score plotted against number of months from stroke (left panel) and patient's age (right panel). The linear regression curve for "FMA" *vs.* "Months from stroke" was calculated twice: 1) considering all subjects, 2) excluding pt2 and pt8, who, in the authors' opinion, may be considered as outliers.

es in the corticospinal innervation to fingers muscles, possibly due to the different role of the muscles in hand function.[31] This could explain why patients recovered some hand function following the intervention; being the movements functional and goal oriented, even the hand motor area was stimulated as part of the task.

Finally, the improvement at shoulder and elbow was moderate (3.5±2.2, *d'*=0.66) and statistically significant (P<0.02). Even more importantly, the coordination/velocity items responsiveness to the intervention was large (*d'*=0.82) according to the Cohen's definition.

It is worth noting that the motor function improvement is not correlated to the patients' age. Furthermore, although a negative correlation seems to exist between motor function improvement and time from stroke, recovery is possible even some years from the stroke.

Limitations of the study

One limitation of this work is that no control group was tested for comparison. However, this is a preliminary study aiming at verifying the short term effect of the treatment on patients' impairments. Considering that patients were in the chronic phase of the disease (27±20 months from the stroke) and had already undergone a "standard" rehabilitation process at Villa Beretta Centre, the motor function gained is most likely due to the proposed intervention. Being the clinical evaluation not blinded, there is the risk that results may be affected by bias errors due to the subjectivity of the evaluation. To reduce this risk, the pretreatment data were kept by a third party and could not be consulted by physical therapist, thus trying to avoid possible involuntary comparison during the post-treatment evaluation. Furthermore, the clinical evaluations performed by the physical therapist were double checked by the patients' referent physicians.

Another limitation of this study is that no clinical assessment regarding the ICF activities and participation domains were performed. Therefore, results demonstrate impairment reduction but do not provide evidences about the effects of gained motor function on the patients' daily life. However, impairment reduction is surely a first step towards activity and participation improvement. Furthermore, activity and participation assessment are needed for a longer period of evaluation, which was not compatible with this preliminary study. Further assessments are ongoing.

Conclusions

In conclusion, results, in terms of impairment reduction, were extremely positive considering that the period of treatment was short (1 month), the number of sessions low (only 12) and, finally, the average time from the stroke event large (27±20 months). Interestingly, patients significantly improved even some years after stroke. This is promising considering that 6-month after stroke the recovery of body functions is poor.[4] Further studies are needed to confirm these results. Future assessments at 6- and 12-month follow-up will confirm whether the functional gains will be maintained or not. A new study is ongoing to verify whether the motor

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function gains after treatment do result in improved activity. To support the clinical results and to understand the mechanisms leading to improvement, instrumental measures regarding kinematics, EMG and patient-robot interaction forces will be used. Finally, further studies in combination with neuro-imaging techniques will be performed on patients for verifying and trying to demonstrate the presence of neuroplasticity effects.[24] The use of neuroimaging techniques could also help understanding for how long each patient should be treated.

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