Testing of a Hybrid FES-Robot Assisted Hand Motor Training Program in Sub-Acute Stroke Survivors

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***Abstract*—While hands-on therapy is the most commonly used technique for upper limb rehabilitation after stroke, it requires a therapist and residual activity and is best suited for active-assisted exercises. Robotic therapy on the other hand, can provide intention driven training in a motivating environment. We compared a robotic and standard therapy group, allowing intention driven finger flexion/extention respectively active-assisted exercises and a standard therapy only group. A total of 25 patients, 2 to 6 months post–stroke, with moderate motor deficit (Fugl-Meyer Assessment or FMA between 15 and 50), were randomly assigned in one of the groups. Patients practiced 30 minutes of hands-on therapy each day for 2 weeks with a supplementary 30 minutes of robotic therapy each day for patients in the experimental group. Subjects were evaluated using the FMA, Box and Blocks test (BBT) and Stroke Impact Scale (SIS) before and after the treatment. Patients in the experimental group showed higher average gain in all tests than those in the control group but only the SIS average gain was on the limit of statistical significance. This study shows the potential efficacy of robotic therapy for hand rehabilitation in subacute stroke patients.**

***Index Terms*—electrical stimulation, mechatronic hand, neuromuscular stimulation, rehabilitation robotics, robot control.**

I. Introduction

According to World Health Organization, around 15 million people suffer a stroke annually worldwide, from which 5 million die and another 5 million remain with permanent disabilities. More than one quarter of stroke survivors become dependent in Activities of Daily Living (ADL) [1].

Owing to population aging, a large number of people will require rehabilitation treatment after stroke. Clinical studies have not reported clear evidence about the optimal moment for rehabilitation treatment even if it seems logical that the best moment is the sub-acute phase (the first 6 months' post stroke), when there is a spontaneous neuroplasticity [2]. While almost 70% of stroke survivors regain walking ability, traditional rehabilitation treatment leaves between 30% and 60% of them without functional use of the paretic arm, even if the therapy is started in the sub-acute phase [1]. The factors that contribute to hand impairment are: finger flexor muscles hypertonia, muscle weakness that is not uniform between flexor and extensor muscles, tendency of regaining finger flexion and not extension and altered muscle activation patterns with co-contraction of antagonistic muscles during finger extension [3].

A wide body of literature has promoted the idea that "repetitively trying to achieve a goal" is important for motor learning [4]. In fact, repetitive goal-directed effort is so useful that even mental rehearsal of movement can improve arm motor impairment following stroke [5]. Alternative methods include: repetitive intensive mobilization [6], functional electrical stimulation (FES) [7], and transcranial magnetic stimulation (TMS) [8]. Nowadays, the most promising methods for upper limb rehabilitation are active-assisted exercises and Constraint Induced Motor Therapy (CIMT) but both require less impaired patients [9]. Robotic devices can complete conventional therapy, due to their applicability to a wider range of stroke patients, notably moderately and severely impaired ones.

Last but not least, training with a physical therapist during a stay in a rehabilitation clinic is so costly that the average length of stay in rehabilitation units in the United States decreased from 31 to 14 days [10]. Having this in mind, it is crucial that the patient continues intensive therapy at home after hospital discharge.

In order to meet these challenges, researchers began designing robotic devices for rehabilitation in the early 1990s. Robotic therapy represents a technique where a robot participates alongside with the patient, supervised or not by a therapist, in a process that is meant to facilitate and correct the rehabilitation phenomenon by enhancing neuroplasticity. The benefits that can be brought by robotic therapy are: providing intense repetitive training, giving quantitative feedback, collecting real time data of motor performance, providing assistance or resistance similar to a hand-on technique, training in an engaging environment [11] and promoting cortical plasticity [12]. An implicit idea is to offer patients the possibility to practice the repetitive aspects of rehabilitation therapy on their own, without the presence of a rehabilitation therapist.

The number of robotic devices and companies selling them is growing constantly. However, there are only a few scientifically proven research directions in this field and the use of robotic devices worldwide is still rare. In a study that

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compared the effects of robotic versus conventional rehabilitation therapy conducted on 143 subjects, the FMA showed greater improvements in the robotic therapy group, but the absolute difference between groups was of weak significance [13]. Another study showed significant improvement in motor scores for robot training patients but without persistence of the differences at the 6 months follow-up [14].

Robotics based rehabilitation began by using robots to passively mobilize the patients' limbs during the first stages of rehabilitation but the effectiveness of such passive movements was shown to be limited [15]. Another paradigm is the "cooperative arm therapy". Usually, this means providing the minimum level of assistance necessary to perform a specific task while providing a visual, auditory or haptic feed-back [16]. Several research groups developed robotic therapy devices for the arm, but the first robotic devices clinically tested were MIT-Manus, MIME, and the ARM Guide [11]. All of them focused on providing active assisted exercises for elbow flexion/extension and for limited shoulder movements using actuators. The most popular are the electrical actuators which are easy to control and available in low cost. Alternatives are: pneumatic actuators, which are lightweight and fast but have complex control algorithms and hydraulic motors which have the best power to weight ratio but need an expensive installation [17].

Another direction of research is the design of lightweight hybrid FES - exoskeleton systems. FES therapy combines preprogrammed coordinated electrical muscular stimulation and manual assisted passive motion by a therapist to establish physiologically correct movement. In a randomized controlled study, it has been shown that FES therapy had positive effects on upper-limb functions, especially in sub-acute stroke patients. Patients that underwent FES therapy plus conventional therapy for 12 weeks improved significantly more than patients who only had conventional therapy (a difference of 24 points on the FMA – with 10 points showing clinically relevant change) [18]. Later studies proposed to replace the therapist with an exoskeleton that would work in a parallel synchronized way to assist/complete the FES-based induced motion, FES generated contraction partially providing the necessary force during arm and forearm movement [19].

Our group developed a glove-like hand exoskeleton combined with a FES system that actively assists flexion and extension movements in each finger. In present, according to Maciejasz et al. review [20], this is a relatively rare feature for such a device. From a total of 131 upper limb rehabilitation devices enumerated, 28 assist finger(s) movement, and only 7 assist each individual finger in extension and flexion movements. A number of 5 devices cited are glove type from which only 2 are able to move each finger. Our bimanual proposed therapy method adds to most known robotic training programs firstly, the fact that it is a hybrid system that combines FES with a distal exoskeleton structure, thus replacing the therapist that would normally assist the FES induced motion [18,21] and secondly, by copying the healthy hand movement, the system generates a desired movement that is expected to enhance motivation for training and induce cortical reorganization at patient level. In this respect, the system is similar with the more sophisticated neuroprosthesis developed by Ambrosini et al. where electrical muscle stimulation was controlled using EMG signals extracted from partially paralyzed muscles [22]. Also, bimanual exercises additionally enhance activation of primary motor cortex compared to unilateral paretic hand movement, as it has been shown in a functional MRI study [23].

II. Materials and Methods

This paper presents the results of an experimental study with a hybrid FES - mechatronic glove system for dexterity rehabilitation in sub-acute stroke patients along a program consisting of 12 sessions of motor training exercises. The device and the control algorithm were built by Hartopanu S. et al. [24]. This study comes as a logical and necessary continuation of his work in that it assesses the therapeutical utility of the device on stroke patients. The exoskeleton part consists of a left side medium size leather glove with metal "tendons" attached to it on the dorsal side of the hand for active finger flexion-extension movements (Figure 1, left). The FES part consists of a two channel electrical stimulator, one for the interosseous muscles and the other for the extensor digitorum muscle. Input information comes from a second leather glove with bending sensors attached, for the right hand (Figure 1, right), whose movements the left one intends to copy.

Figure 1. The exoskeleton glove with metal tendons (left) and the glove with sensors for copying the healthy hand movements (right)

One limitation of the device is that it is dedicated to left hemiparesis patients (the gloves are not interchangeable) because of a high probability that right hemiparesis patients also have speech impairments that would make communication difficult. Secondly, it doesn`t assist the fingers through the whole range of motion (ROM) because of limited adjustability to patient's hand size and excessive elasticity of the leather glove after multiple uses. Anyway, a glove set aiming to be used in patients with right hemiparesis will be a further outcome of the IHRG project, as well as a better FES control algorithm so that the device will assist the fingers for their entire range of motion, especially on the thumb.

The system uses a software which allows users to set the electrical stimulation intensity and the possibility to follow the patient's performance: number of movements, amplitude of movement, and intensity of stimulation. Figure 2 presents

a schematic diagram of the hardware system detailing the connections between the glove exoskeleton, sensors and electrical stimulation.

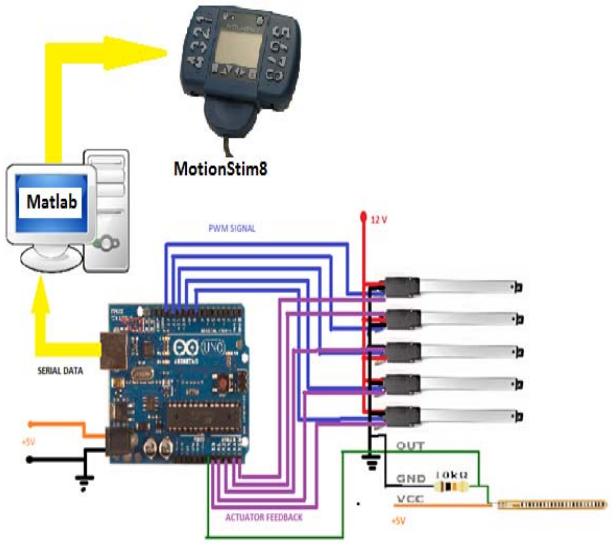

Figure 2. The hardware structure of the proposed IHRG system

The system principle is that the FES works together with the glove-like exoskeleton, being activated when the fingers reach an intermediate degree of extension. The movement in the "tendon" glove is generated by the electrical signal received from the healthy hand, therefore resulting in a bimanual motor training in which the paretic hand copies the healthy hand movements. The exoskeleton was built according to several principles: the forces generated by the "tendons" are harmless for the corresponding anatomical segment, the movement of the system is along the natural trajectory of the human finger, the fingers can move freely with the attached exoskeleton.

The robotic glove is made of leather and it suits several hand sizes. Clamps on the glove fix the metal wires (tendons) in two points: top and root of each finger. The bending sensors placed in the interior of the gloves (each finger for the sensory glove, only middle finger for the robotic glove) have electric resistance proportional with the bending angles: straight corresponds to 10 kΩ, the 90-degree angle corresponds to approximately 40 kΩ. The analogical signals from the bending sensors, which are proportional with the level of finger flexion/extension, are received by an Arduino Uno microcontroller which controls the Firgelli L12 linear servomotors in actuating each finger of the robotic glove. At the same time, these signals are sent also to a computer which controls the FES.

The Figure 3 shows the patient controlled exercise of copying the healthy hand movements when voluntarily trying to move also the impaired hand. On the top picture the green line shows the hand opening stage while the open hand is translated in a low level in green signal. On the bottom picture the healthy hand fingers movement is recorded and the signal is used to control the exoskeleton on the impaired hand. The magenta correspond to the thumb which doesn't show a high signal level because it is superposed over other fingers while hand closes. When the patient performs a cognitive action to move both hands the exoskeleton reacts and precisely copies the healthy hand movement.

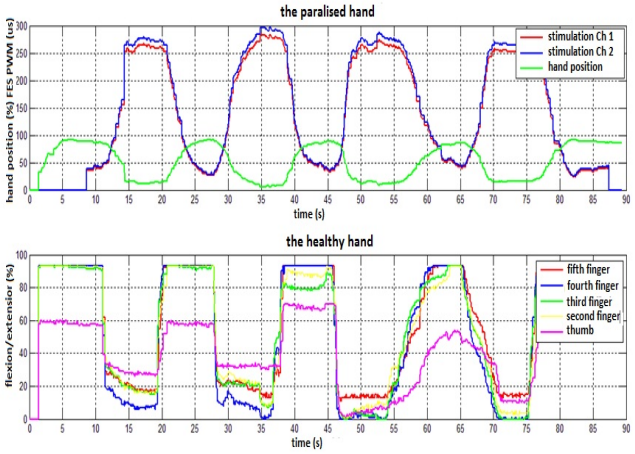

Figure 3. The controlled exercise of copying the healthy hand movements (Ox – time scale) during a clinical trial on a patient. Top: The electrical stimulation (red-Ch1; blue-Ch2) applied over forearm and hand; Bottom: The recorded movements at the fingers level (Oy: percent of the maximal displacement); PWM= pulse width modulation; (based on Hartopanu et al [20] work)

The FES is generated by a programmable MotionStim 8 neurostimulator (KRAUTH+TIMMERMANN GmbH, Germany). One channel provides FES for wrist extension and the other for finger extension. The placement positions of the four 3/5 cm electrodes for the extension of the wrist and fingers are shown in Figure 4.

The FES was delivered in 50 Hz biphasic pulses, with a pulse width varying between 150 and 300 μs and intensity between 15 and 30 mA. The parameters were set individually in the limits of tolerability, until full functional wrist extension was obtained.

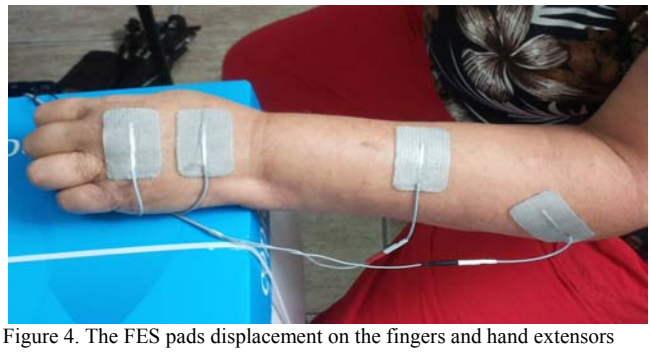

Figure 4. The FES pads displacement on the fingers and hand extensors

III. Study Design

We conducted a clinical randomized study in which we used 2 groups of patients: a control group which underwent standard conventional therapy and an experimental group that underwent conventional therapy and robotic therapy. The robotic therapy was administered in 12 sessions, each lasting 30 minutes with a total of 6 hours for each patient. Conventional therapy totalized 10 sessions, each one lasting 30 minutes. The inclusion criteria were: patients with left hemiparesis, patients with a single ischemic or hemorrhagic stroke on CT (computed tomography) or MRI (magnetic resonance imaging), patients between one month and six months' post stroke (sub-acute), patients with a FMA between 15 and 50, patients that signed the informed consent approved by the Rehabilitation Hospital Ethics Committee. The exclusion criteria were: patients with severe comorbidities, patients with other neurological, muscular or

orthopedic disorders, patients with apraxic, perceptual or cognitive deficit (Mini Mental State Examination below 25). The subjects were recruited from the Neurology Clinic within Rehabilitation Hospital from Iasi between September 2015 and February 2016. They were randomly assigned in one of the two groups after performing 3 motor evaluation tests: the upper limb section of the FMA, the BBT and the 5 item hand section of the SIS.

The patients in the experimental group were seated in a chair in front of a work desk as shown in Figure 5. First, the FES pads were placed on the skin and the right level of applied electrical stimulation was set-up, then the right hand glove was installed and finally the robotic glove was adjusted on the left (paretic) hand. Then patients were instructed to flex/extend their right fingers so that the robotic glove would replicate the movements. One complete cycle lasted approximately 15-20 seconds taking into account that the servomotors accomplish a complete opening in about 7 seconds.

Subjects continued to perform flexion/extension movements for 30 minutes under guidance. The average number of repetitions was 90 per session. A real time computer's display of the right hand fingers and the left hand middle finger was available for patients to watch.

The control group patients followed standard therapy for 10 sessions, 5 days per week, 2 weeks. In each session 30 minutes were dedicated for the rehabilitation of the upper limb - passive and active mobilization, with the aim of improving the patient's motor control of the paretic arm.

Figure 5. The hybrid FES-exoskeleton system for left hand rehabilitation: fingers flexion (up), fingers extension (down)

At the end of the second week program, patients were evaluated again.

We collected the data from 13 patients in the experimental group and 12 patients in the control group. In both groups ischemic stroke prevailed, with only one hemorrhagic stroke in each group. All patients were in the sub-acute phase, between 2 and 5.25 months' post stroke. In total, there were 11 men and 14 women (5 men and 8 women in the experimental group and respectively 6 men and 6 women in the control group). The patients ages ranged from 39 to 78. Statistically, the two groups were comparable from the time since stroke, age and autonomy in daily activities (Barthel index) point of view.

IV. Outcome Measures

The FMA was designed to assess the motor function, balance, sensations and joint functions in hemiplegic/hemiparetic stroke survivors. In this study, FMA refers to the upper limb motor function, with a total score of 66. In addition, the shoulder and elbow (proximal) subset score of the FMA (maximum score = 36) and the wrist and hand subset score of the FMA (maximum score = 24) were also analyzed separately in order to specifically evaluate changes in proximal and distal joints functionality.

The BBT was adopted as an outcome measure because of its reliability and its ability to assess not only proximal control of the arm, but also its dexterity. It consists of 100 wooden cubes of 2,5 cm in length and a wooden box divided in two by a partition. The cubes were placed in the compartment of the box where the left hand was. A 15 second trial period preceded the testing then the subject began grasping and transporting as many cubes as he could from one compartment to the other over the partition, one at a time, in a one-minute period. The score represents the number of cubes transported in one minute.

SIS is a specific questionnaire for stroke patients and is divided in multiple sections: force, hand function, activities of daily living, range of motion, communication, emotions, memory and though and social participation. We used only the hand function section rated between 5 and 25 (normal), being the most relevant for our study.

V. Statistical Analysis

The collected data were analyzed using the SPSS 20.00 (SPSS, Inc; Chicago, Illinois). The descriptive characteristics were calculated for the distributions of the motor and functional indicators that included mean and standard deviation or median and q1 and q3 quartiles, depending on the specific of the tests used for the comparison analysis. The characteristics of the experimental and the control group at the start of the therapy were compared by using: a) the Student's T test for independent samples (for continuous quantitative variables such as age or time period since stroke); b) the χ^2 test for nominal variables like gender or the type of the stroke; c) the nonparametric U Mann-Whitney test for continuous quantitative variables with non-normal distribution, measured within small samples. The comparisons for motor and functional outcome measures before and after therapy were made for each group using Wilcoxon test for repeated measures. This nonparametrical test was used due to the non-normal distributions of the indicators and the small size of the

samples. U Mann-Whitney test was used for establishing the significant differences between the two groups regarding the mean values of the gain for motor and functional indicators, namely the upper limb motor impairment (FMA proximal, distal and total) and the functional disability of the hand (BBT and SIS). For all the comparisons, the p value was set to ≤ 0.05.

VI. Results

The Table I. summarizes the demographic characteristics and the values for the motor and functional indicators obtained at the start of the therapy for all 25 patients. The experimental and control group were equivalent, with insignificant differences for age (t = - 0.49; p = 0.622), gender (χ^2 = 0.33; p = 0.561), type of stroke (U Mann-Whitney = 0.003; p = 0.953), time period since stroke (t = - 0.21; p = 0.836), degree of disability (U Mann-Whitney = - 1.77; p = 0.076), upper limb motor impairment (U Mann-Whitney = - 1.14; p = 0.250 – for the proximal FMA, U Mann-Whitney = - 1.13; p = 0.258 – for distal FMA, U Mann-Whitney = - 1.73; p = 0.083 – for total FMA, U Mann-Whitney = - 0.35; p = 0.721 – for BBT score), and for autonomy in daily activities (U Mann-Whitney = - 0.09; p = 0.928 – for the Barthel index).

Considering the possible areas of variation of FMA scores, patients from both groups showed low levels for both proximal and distal sections, with lower scores for the distal one.

The Table II. shows the characteristic values for motor and functional indicators, which were measured at the beginning of the therapy and also immediately after therapy for both groups. In order to compare the motor gain brought from therapy for each group, indicator values obtained before and after therapy were compared. For both groups, improvements after therapy were statistically significant (p < 0.01). Thus, at the end of therapy, motor impairment of the upper limb was reduced in both groups, result confirmed by significantly higher FMA scores. The average value of gain was slightly higher for the experimental group for the distal section score, but the difference was not statistically significant (U Mann-Whitney = - 0.41; p = 0.677; Table III). On the other hand, patients from the control group showed higher gains regarding the proximal section but these differences were once again statistically insignificant (U Mann-Whitney = - 1.38; p = 0.167).

TABLE I. Clinical and Demographic Characteristics of Patients in the Two Groups (Baseline)

Characteristics	Experimental group (N = 13)	Control group (N = 12)	Statistical test t- (Student/χ^2 / U Mann-Whitney)	P
Age *	62.76 ± 9.23	64.75 ± 10.60	- 0.49	0.622
Sex †	5/8	6/6	0.33	0.561
Side of the lesion (R/L) †	12/0	12/0	-	-
Type of stroke (I/H) †	12/1	11/1	0.003	0.953
Time since stroke (months) *	3.69 ± 1.03	3.76 ± 0.73	- 0.21	0.836
SIS ‡	8 (7-9)	9 (8-9)	- 1.77	0.076
Fugl-Meyer sh-e ‡	12 (10-16)	14 (12-16)	- 1.14	0.250
Fugl-Meyer w-h ‡	5 (4-7.50)	6.50 (5.25-7.75)	- 1.13	0.258
Fugl-Meyer total ‡	17 (16-21.50)	21 (19-22)	- 1.73	0.083
BBT ‡	11 (9-12.50)	11 (9.25-13)	- 0.35	0.721

* mean ± SD (standard deviation)
† number of cases
‡ mean (Q1 and Q3 quartiles)
R/L = right/left
I/H = ischaemic/hemorrhagic
sh-e = shoulder and elbow
w-h = wrist and hand

TABLE III. Average Gain (mean ± SD) at the End of Therapy for the Two Groups and Comparison between Groups

	Gain before-post therapy			
Outcome measures	Experimental group	Control group	U Mann Whitney test	P
SIS	4.30 ± 0.85	3.50 ± 0.98	- 1.88	0.059
Fugl-Meyer sh-e	1.38 ± 0.65	1.25 ± 0.45	- 0.41	0.677
Fugl-Meyer w-h	1.84 ± 0.68	2.25 ± 0.75	- 1.38	0.167
Fugl-Meyer total	3.23 ± 0.91	3.50 ± 0.79	- 0.89	0.371
BBT	5.76 ± 1.09	5.41 ± 0.99	- 0.77	0.441

TABLE II. Outcome Measures Values (mean and Q1,Q3 quartiles) before and after Therapy and Comparison between the Two Groups

	Experimental group (N = 13)				Control group (N = 12)			
Outcome measures	Before therapy	After therapy	Wilcoxon test	P	Before therapy	After therapy	Wilcoxon test	P
SIS	8 (7-9)	12 (11-13)	- 3.22	0.001	9 (8-9)	12 (11.25-13)	- 3.01	0.003
Fugl-Meyer sh-e	12 (10-16)	13 (11-17)	- 3.30	0.001	14 (12-16)	15 (13-17.75)	- 3.21	0.001
Fugl-Meyer w-h	5 (4-7.50)	7 (6.50-9)	- 3.24	0.001	6.50 (5.25-7.75)	8 (7.25-10.75)	- 3.11	0.002
Fugl-Meyer total	17 (16-21.50)	20 (18-25)	- 3.22	0.001	21 (19-22)	24.50 (22.25-25.75)	- 3.10	0.002
BBT	11 (9-12.50)	17 (14-18)	- 3.21	0.001	11 (9.25-13)	16.50 (15-18)	- 3.09	0.002

Moreover, at the end of the recovery therapy, patients from both groups showed improvements regarding the functionality of the affected upper limb, as reflected in the SIS score which evaluates the ability to perform some common tasks and in the BBT score which evaluates the whole upper limb functionality and in some degree the hand dexterity.

Interestingly, the patients in the experimental group showed an average motor gain slightly higher than patients in the control group, but this difference was not statically significant (U Mann-Whitney = - 0.77; p = 0.441). Notably, the patients from the experimental group showed higher scores for the SIS, the average gain being at the limit of statistical significance (U Mann-Whitney = - 0.35; p = 0.721).

VII. Conclusion

In conclusion, we conducted a clinical randomized study in which we compared from a motor outcome perspective two groups of patients: one mixed therapy group (conventional and robotic training) and one conventional therapy group. Our study shows that added robotic therapy with a FES - glove-like exoskeleton for finger flexion/extension training is a viable tool for improving upper limb functionality in moderately impaired sub-acute stroke patients. The improvements on the outcome measures for the two groups are cohesive with data from other studies. However, it should be noted that the period of treatment was smaller in our study (2 weeks vs at least 5 weeks in other studies). Higher treatment intensity and the patient's more active participation are the most likely explanations for the enhanced results in motor outcome measures. We consider that the main reason for which we didn`t obtain statistically significant motor improvement in the experimental group is the short period of therapy. Therefore, longer periods of therapy or multiple sessions per day are necessary in future studies.

The limitations of the study include the unblinded assessment of the outcome measures and the fact that it compares a mixed therapy group (conventional and robotic) with conventional therapy only group. Even so, the fact that some benefit can be obtained from added robotic therapy, that the patient could self administer, is a potentially important issue, knowing that during hospitalization, a complete conventional therapy session lasts for about one hour a day.

References

[1] V.L. Feigin, G.A. Mensah, B. Norrving, C.J. Murray, G.A. Roth, "Atlas of the Global Burden of Stroke (1990-2013): The GBD 2013 Study", Neuroepidemiology, vol. 45, no. 3, pp. 230-236, 2015. doi: 10.1159/000441106

[2] S.C. Cramer, "Repairing the human brain after stroke: I. Mechanisms of spontaneous recovery", Ann. Neurol., vol. 63, pp. 272–287, 2008. doi: 10.1002/ana.21393

[3] D.G. Kamper, W.Z. Rymer, "Impairment of voluntary control of finger motion following stroke: role of inappropriate muscle coactivation", Muscle Nerve, vol. 24, no. 5, pp. 673-681, 2001.

[4] D.J. Reinkensmeyer, S.J. Housman, "If I can't do it once, why do it a hundred times?: Connecting volition to movement success in a virtual environment motivates people to exercise the arm after stroke", in Proc. Virtual Rehabilitation Conference, 2007, pp. 44-48. doi: 10.1109/ICVR.2007.4362128

[5] V. Crocher, A. Sahbani, J. Robertson, "Constraining Upper Limb Synergies of Hemiparetic Patients Using a Robotic Exoskeleton in the Perspective of Neuro-Rehabilitation", IEEE Transactions on Neural Systems and Rehabilitation Engineering, vol. 20, pp. 247-257, 2012.

[6] C. Bütefisch, H. Hummelsheim, P. Denzler, H. Mauritz, "Repetitive training of isolated movements improves the outcome of motor rehabilitation of the centrally paretic hand", J Neurol Sci, vol. 130, no. 1, pp. 59–68, 1995.

[7] D.B. Popovic, T. Sinkaer, M.B. Popovic, "Electrical stimulation as a means for achieving recovery of function in stroke patients", NeuroRehabilitation, vol. 25, no. 1, pp. 45–58, 2009. doi: 10.3233/NRE-2009-0498

[8] S. Machado, J. Bittencourt, D. Minc, C.E. Portella, B. Velasques, M. Cunha, H. Budde, L.F. Basile, G. Chadi, M. Cagy, R. Piedade, P. Riberio, "Therapeutic applications of repetitive transcranial magnetic stimulation in clinical neurorehabilitation", Funct. Neurol., vol. 23, no. 3, pp. 113–122, 2008

[9] A. McIntyre, R. Vlana, S. Janzen, S. Mehta, S. Pereira, R. Teassel, "Systematic review and meta analysis of constraint induced movement therapy in the hemiparetic upper extremity more than six months post stroke", Top Stroke Rehabil, vol. 19, pp. 499-451, 2012. doi: 10.1310/tsr1906-499

[10] S.M. Schmidt, L. Guo, S.J. Scheer, "Changes in the status of hospitalized stroke patients since inception of the prospective payment system in 1983", Arch Phys Med. Rehabil, vol. 83, pp. 894-898, 2002. doi:10.1053/apmr.2002.33219

[11] L. Pignolo, "Robotics in Neuro-Rehabilitation", Journal of Rehabilitation Medicine, vol. 41, pp. 955-960, 2009. doi: 10.2340/16501977-0434

[12] A. Risedal, B. Mattsson, P. Dahlqvist, "Environmental influences on functional outcome after a cortical infarct in the rat", Brain Res Bull, vol. 58, pp. 315–321, 2002

[13] V. Klamroth-Marganska, J. Blanco, K. Campen et al. "Three-dimensional, task-specific robot therapy of the arm after stroke: a multicentre, parallel-group randomized trial", Lancet Neurol., vol. 13, pp. 159-166, 2014

[14] E. Susanto, R. Tong, C. Ockenfeld, N. Ho, "Efficacy of robot-assisted fingers training in chronic stroke survivors: a pilot randomized-controlled trial", J. of Neuroeng. and Rehab., vol. 12, no. 42, 2015, doi: 10.1186/s12984-015-0033-5

[15] D. Lynch, M. Ferraro, J Krol, "Continuous passive motion improves shoulder joint integrity following stroke", Clin. Rehabil, vol. 19, pp. 594–599, 2005. doi: 10.1191/0269215505cr901oa

[16] J.L. Patton, F.A. Mussa-Ivaldi, "Robot assisted adaptative training: custom force fields for teaching movement patterns", IEEE Rev. Biomed. Eng., vol. 51, pp. 636–646, 2002.

[17] A. Otten, C. Voort, A. Stienen, "LIMPACT: A Hydraulically Powered Self-Aligning Upper Limb Exoskeleton", in ASME Transactions on mechatronics, vol. 20, pp. 2285-2298, 2015.

[18] N. Kawashima, M. Popovic, V. Zivanovic, "Effect of Intensive Functional Electrical Stimulation Therapy on Upper-Limb Motor Recovery after Stroke: Case Study of a Patient with Chronic Stroke", Physiotherapy Canada, vol 65, pp. 20–28, 2013. doi 10.3138/ptc.2011-36

[19] F. Serea, M.S. Poboroniuc, S. Hartopanu, R. Olaru, "Preliminary Tests on a Hybrid Upper Arm Exoskeleton for Upper Arm Rehabilitation for Disabled Patients", in Proc. 8th Int. Conf. and Exposition on Electrical and Power Engineering, IEEE, Iasi, Romania, Catalog Number CFP-1447S-USB, pp. 153-157, 2014. doi: 10.1109/ICEPE.2014.6969887

[20] P. Maciejasz, J. Eschweiler, K. Gerlach-Hahn, "A survey on robotic devices for upper limb rehabilitation", J. of Neuroeng. and Rehab., vol. 11, no. 3, 2014. doi: 10.1186/1743-0003-11-3

[21] T.A. Thrasher, V. Zivanovic, W. McIlroy et al. "Rehabilitation of reaching and grasping function in severe hemiplegic patients using functional electrical stimulation therapy", Neurorehabil Neural Repair. vol. 22, pp. 706-714, 2008

[22] E. Ambrosini, S. Ferrante, T. Schauer, "A myocontrolled neuroprosthesis integrated with a passive exoskeleton to support upper limb activities", Journal of Electromyography and Kinesiology, vol. 24, pp. 307–317, 2014.

[23] W.R. Staines, W.E. McIlroy, S.J. Graham, „Bilateral movement enhances ipsilesional cortical activity in acute stroke: a pilot funtional MRI study", J. of Neurology, vol. 56, pp. 401-404, 2001

[24] S. Hartopanu, F. Serea, D. Irimia, M. Poboroniuc, G. Livint, "New issues on FES and robotic glove device to improve the hand rehabilitation in stroke patients", the 6th Int. Conf. on Modern Power Systems, Cluj-Napoca, 2015, in Acta Electrotehnica, vol.56, No.3, pp.123-127, ISSN 1841-3323, 2015.