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The MIME robotic system for upper-limb neuro-rehabilitation: results from a clinical trial in subacute stroke

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Abstract— **Results from a randomized, controlled clinical trial of the MIME robotic device for shoulder and elbow neuro-rehabilitation in subacute stroke patients are presented. MIME incorporates a PUMA 560 robot that applies forces to the paretic limb during unilateral and bilateral 3-dimensional movements. The training dose was 15 1-hour sessions within a 4-week period. Analysis of clinical data found the MIME training at least as effective as an equivalent dose of hands-on therapy by a therapist. The MIME training provided added-value by increasing the rate of recovery on some motor impairment scales. Combined unilateral and bilateral training yielded similar functional outcomes compared to equivalent doses of unilateral-only robot training, but with reduced hypertonia and abnormal synergies. Robot group gains exceeded that expected from spontaneous recovery.**

Introduction

Efforts toward developing robotic treatments are motivated by the need to improve clinical outcomes, the public health burden associated with stroke-related disability [1], and the emphasis on cost reduction in health care [2]. Most stroke survivors receive one-on-one physical and occupational therapy for the resulting sensorimotor impairments. In the upper-limb, attempts at neuro-rehabilitation are often abandoned early on in favor of compensatory strategies. This is motivated by decreasing reimbursable patient-therapist contact time, and the fact that most activities of daily living involving the upper-limbs can be performed by the remaining intact limb with proper training and adaptive aids. However, performing ADLs one-handed is often cumbersome, increasing the time required and difficulty of the task compared to two-handed performance. These factors suggest that a role exists for robotic devices that can provide effective training for neuro-rehabilitation, while not increasing the burden on the clinical staff or increasing the costs of health care. Integration of robotic therapy into current practice could increase the efficiency and effectiveness of therapists by alleviating the labor-intensive aspects of neuro-rehabilitation.

Previous studies have illustrated the potential of robotic therapy systems. A series of clinical trials using the MIT-MANUS robot have shown that it provides an effective treatment. Acute stroke subjects who trained in MIT-MANUS had greater gains in motor function than controls that only received a placebo treatment [3,4]. Clinical trials with chronic stroke subjects have demonstrated that MIT-MANUS training produces significant clinical gains in this population as well [5-7]. Training in the ARM-Guide robot by chronic stroke subjects resulted in functional gains and improvements in reaching kinematics [8]. However, a control group that received a matched amount of unassisted reaching movements had statistically identical gains. This emphasizes that highly repetitive active movements have therapeutic value, and the added-value of robotic assistance remains to be demonstrated. In addition to MIT-MANUS and ARM-Guide, several less-tested approaches are under development (see reviews [9-11]).

In previous work we developed the MIME robotic system and showed that in chronic stroke subjects, training in MIME had advantages to conventional treatment in terms of clinical and biomechanical measures [12-14]. The robot-trained subjects had a larger rate of improvement on a motor impairment scale compared to controls that received an equal dose of conventional treatment. The robot group also had greater gains in active range-of-motion, and greater strength gains at the shoulder and elbow. Further examination of the data collected during the robotic training provided evidence of improved muscle activation patterns during robot-assisted reaching [15].

The goals of this study were to confirm the previous results in chronic subjects and to identify the essential therapeutic features of the MIME robot therapy. In particular, the bilateral mode is unique to MIME and the study was designed to evaluate the potential unique benefits of this mode. Our working hypothesis was that when given in combination, the bilateral mode enhances the effects of the more conventional unilateral modes.

Methods

Subjects were seated and torso movement was limited by straps and a contoured seat (Jay Medical). The affected limb was strapped to a forearm splint that restricted wrist and hand movement. A robot manipulator (Puma 560 series, Staubli Corp.) attached to the splint applied forces to the limb that would normally be provided by a therapist (Fig. 1). The robot's 6 degrees-of-freedom allowed the forearm to be positioned within a large range of positions and orientations

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in 3-dimensional space. The forces and torques between the robot and the affected limb were measured by a 6-axis sensor.

We used four modes of robot-assisted movement. In passive mode, the subject relaxed as the robot moved the limb toward a target with a predetermined trajectory. In active-assisted mode, the subject triggered initiation of the movement with volitional force toward the target and "worked with the robot" as it moved the limb. In active-constrained mode, the robot provided a viscous resistance in the direction of the desired movement and spring-like restoring forces perpendicular to the movement direction as the subject attempted to reach toward the target with maximal effort. In bilateral mode, the subject attempted bilateral mirror-image movements while the robot assisted the affected limb by continuously moving the affected forearm to the contralateral forearm's mirror-image position and orientation. During bilateral mode, the two forearms were kept in mirror-symmetry by a position digitizer (Microscribe 3DL, Immersion Corp.), which measured the movement of the contralateral forearm and provided coordinates for the robot motion controller.

Subjects were included in the study if they had a diagnosis of a single cerebrovascular accident (CVA), and were 1-5 months post-CVA. Subjects were allowed to continue with any outpatient therapies they were enrolled in at the time of intake into the study. Subjects were excluded from the study if they exhibited any upper extremity joint pain or range-of-motion limitations that would limit their ability to complete the protocols. Subjects with any unstable cardiovascular, orthopedic, or neurological conditions were also excluded. Cognitive impairments were screened with the Folstein Mini-Mental exam, and subjects were excluded if they were unable to cooperate with the study tasks.

Subjects were stratified by Fugl-Meyer score and the cerebral hemisphere in which the stroke occurred, then randomly assigned to 4 treatment groups. Over a 4-week period, all groups received 15 one-hour treatment sessions held in the same treatment area and supervised by a single occupational therapist. Thus all subjects received equal intensity and duration of treatment. In the three robot groups, subjects received 50 min of robot-assisted movement each session, while control group subjects received 50 min of conventional treatment. All subjects received 5 min of tone normalization and limb positioning at the beginning and end of each session. All protocols were approved by the local institutional review committee and informed consent was obtained from all subjects.

The robotic treatment was similar to that used in the previous chronic study. A core set of 12 targeted reaching movements was used that was identical to the patterns used in the chronic study. Subjects practiced some or all of these movements in each session. The four treatment groups were as follows: 1) The robot-unilateral group performed exercises that progressed from the easiest exercise modes (passive) to the most challenging (active-constrained). No bilateral exercise was performed. 2) The robot-bilateral group practiced the same 12 reaching movements, but only in bilateral mode. Rhythmic circular movements were also performed. 3) The robot-combined group spent approximately half of the treatment time in the unilateral modes and half of the time in the bilateral mode. This group received essentially the same robotic treatment as the previous chronic study. 4) The control group received an equivalent intensity and duration of conventional therapy targeting proximal upper limb function based on NeuroDevelopmental Therapy [16].

An occupational therapist blinded to group assignment tested all subjects with a battery of clinical evaluations immediately before the start of treatment, immediately post-treatment, and 6 months after the end of treatment. Motor and sensory impairment was assessed with the upper limb portion of the Fugl-Meyer Assessment (FM) [17] and the Motor Status Score (MSS) [18]. The MSS is similar to the motor FM, but provides a more complete description by adopting a 6-point scale for each item. The Functional Independence Measure (FIM) [19] was used to measure improvements in basic ADLs. The Ashworth Test [20] was used to test for hypertonia in several upper limb joints. The Motor Power exam was used to assess strength in several joints of the proximal upper-limb (5-point scale).

The motor FM was divided into proximal (shoulder and elbow - 42 points) and distal (hand and wrist - 24 points) portions for statistical analysis. The proximal MSS (shoulder and elbow parts) was separated into the movement scale (46) that assesses the degree of completion of several movements, and a synergy scale (20) that assesses the ability to suppress abnormal synergies during the attempted movements. The Ashworth scores for individual joints were grouped into a proximal score (max=15: shoulder internal rotators, elbow extensors, elbow flexors), and a distal score (max=30: pronators, supinators, wrist flexors, wrist extensors, digit flexors, digit extensors). For the FIM, only the self care and transfers sections were considered (max=63).

Results

Thirty subjects completed the treatments and the post-treatment evaluations. Six-month follow-up data was

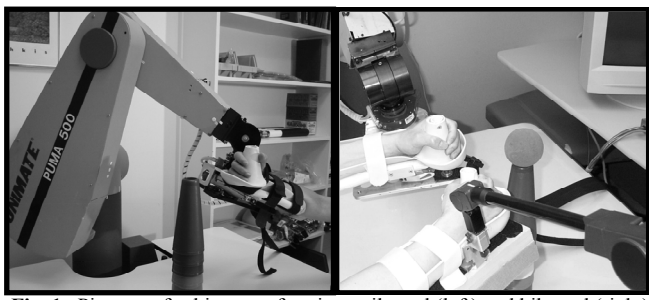

Fig. 1. Pictures of subjects performing unilateral (left) and bilateral (right) movements in the MIME system.

available from 23 subjects. One subject dropped out of the study for reasons unrelated to the study. Table 1 summarizes the baseline characteristics of the subjects. Compared to the robot-unilateral group, the robot-combined group had significantly higher tone in proximal joints (proximal Ashworth scale, $P<0.05$), and more abnormal synergies (MSS synergy, $P<0.05$) at baseline. There were no significant baseline differences between groups in terms of age, weeks post-CVA, gender, side of lesion, or any of the other clinical evaluations.

Table 2 summarizes the gains in clinical outcomes. First, we considered the comparison between the robot-combined and robot-unilateral groups. Significant gains were present in both groups in the proximal FM, distal FM, MSS movement, motor power and FIM ($P<0.05$). The robot-combined group had significantly larger gains in the MSS synergy score than the robot-unilateral group ($P<0.05$), and the robot-combined group tended to have better Ashworth score changes compared to the robot-unilateral group ($P<0.1$, a negative change is an improvement on the Ashworth). There were no other differences between groups in the any of the other measures. At the follow-up, the only difference between groups was a greater improvement in the distal FM in the robot-unilateral group compared to the robot-bilateral group ($P<0.05$).

When compared to the control group at post-treatment, the robot-combined group had greater gains in the proximal FM and MSS synergy ($P<0.05$). The control group did significantly better than the robot-unilateral group in terms of the proximal Ashworth ($P<0.05$). The robot-bilateral group did poorer on the Motor Power ($P<0.05$) compared to all other groups, and did poorer on the FIM compared to the robot-unilateral and control groups ($P<0.05$).

Discussion

These results are consistent with the previous study on chronic stroke subjects. In both this and the previous study, proximal FM scores indicated that at post-treatment, robot-combined training resulted in significantly greater gains than the control group. However, in both studies, gains in robot and control groups were equivalent at a 6-month follow-up. A similar pattern was observed in the MSS synergy score. Thus, the robot-combined treatment is equivalent to conventional treatment in terms of long-term clinical outcomes, but may accelerate the rate of recovery on some clinical scales. It is unlikely that the gains observed were due entirely to spontaneous recovery. We observed mean gains on the total upper-limb FM (max=66) at post-treatment of 7.6 and 7.9 in the robot-combined and robot-unilateral groups. Gains at the 6-month follow-up were 9.0 and 16.2 respectively. A recent review estimated that FM gains due to spontaneous recovery between 90 to 1000 days post-CVA are approximately 5 points [11].

There were no significant differences between the robot-combined and robot-unilateral treatment on any of the outcomes other than the MSS synergy scale, in spite of the fact that the robot-unilateral subjects spent more time training only the paretic limb. The robot-combined treatment showed an improvement in the MSS synergy score that was greater than in the robot-unilateral group, but this is confounded by the fact that the robot-combined group had a significantly poorer MSS synergy score at pre-treatment. There was also evidence that the bilateral exercise may help to control hypertonia. The robot-unilateral group had increased proximal tone after treatment, while all other groups had decreased tone. Differences between robot-unilateral and control was significant ($P<0.05$), while differences between robot-unilateral and robot-combined approached significance ($P<0.1$). But again, this is confounded by the fact that the robot-combined group had significantly increased tone at pre-treatment compared to the robot-unilateral group. Nevertheless, this suggests the bilateral treatment, when combined with the unilateral modes, might be effective at controlling abnormally increased tone or synergies that are exacerbated by the unilateral robot modes, which generally require more intensive effort. The results also suggest less benefit from bilateral therapy alone, as this group had the smallest gains in the FM proximal, FM distal, MSS movement, motor power and FIM.

Examination of gains in individual subjects suggests the robotic treatment is most effective for subjects in a middle range of motor impairment. Four subjects had gains of greater than 10 pts on the proximal FM (2 received robot-unilateral treatment and 2 received robot-combined treatment). These four subjects fell between 15 and 23 inclusive on the proximal FM, while all 30 subjects spanned the range from 7 to 37. Analysis of the data from the previous chronic study also supports this hypothesis. The top three performers in the robot group had pre-treatment proximal FM scores that were between 15 and 23. Thus it would appear that in the subacute-chronic phases of recovery, robotic training is most effective in subjects with moderate levels of motor impairment.

One of the most compelling rationales of investigation of robotic therapy is the potential to provide additional effective therapy to patients without increasing the costs of health care. If commercially-viable robotic devices can be developed that patients can use independently in the home or clinic, our data indicates that training with these robots can potentially be as effective as conventional one-on-one treatment from a therapist. However, the feasibility of achieving these positive treatment effects through independent use of a training robot has yet to be demonstrated.

The added-value of robotic training relative to conventional non-robotic forms of training remains to be conclusively demonstrated. Although this study and the previous chronic study indicate that robotic training increases the rate of impairment reduction compared to

conventional treatment, the groups were no different at the 6-month follow-up. Nevertheless, gains from both robotic training and conventional treatment were significant. It should be noted that most of the subjects had stopped all formal one-on-one therapy from physical or occupational therapists. Therefore the additional conventional treatment provided was effective and would not typically have been available to these subjects due to the current structure of the health care system. Robotic devices may be an alternative, equally-effective method for delivery of this additional therapy.

Table 1. Baseline characteristics.

	robot combined	robot unilateral	robot bilateral	control
N	10	9	5	6
Age	62.3±2.8	69.8±4.0	72.2±11.7	59.9±5.5
Weeks post CVA	13.0±2.1	10.0±1.9	6.2±1.0	10.6±2.7
Gender (m/f)	9/1	5/4	2/3	4/2
Side of Lesion (r/l)	5/5	5/4	3/2	4/2
Sensation (12)	10.4±1.2	10.2±0.9	8.2±2.4	11.2±0.8
Ashworth prox (15)	3.7±0.8 §	1.1±0.6	3.2±1.2	2.2±0.9
Ashworth distal (30)	3.6±0.9	1.9±0.8	2.2±1.4	1.2±0.5
FM proximal (42)	16.2±2.5	23.2±3.2	24.6±4.2	21.0±4.0
FM distal (24)	5.5±2.4	8.4±2.2	14.6±4.4	5.0±2.5
MSS movement (46)	15.1±3.3	23.3±3.8	24.4±5.2	21.5±4.5
MSS synergy (20)	4.4±1.4 §	10.3±1.8	8.4±3.4	9.0±2.0
Motor Power (70)	30.4±5.1	38.7±4.8	40.8±8.1	39.0±4.8
FIM (63)	48.1±3.2	45.0±4.0	51.0±3.3	52.8±3.4

entries are mean ± standard error of the mean
FM = Fugl-Meyer
FIM = Functional Independence Measure (self-care and transfers)
MSS = Motor Status Score (proximal sections)
Significant differences from control (*), bilateral (†), or unilateral(§)
All significance levels are P<0.05

Table 2. Average gains in clinical scores

	robot combined	robot unilateral	robot bilateral	control
post-treatment				
N	10	9	5	6
Ashworth prox	-0.7±0.7	0.9±0.6 *	-0.4±0.4	-1.3±0.7
Ashworth distal	-0.4±0.2	0.0±0.8	-1.0±0.6	0.7±0.6
FM proximal	5.3±1.2 *	4.3±1.4	2.4±1.5	2.5±0.6
FM distal	2.3±0.4	3.6±1.3	1.4±0.7	3.3±1.9
MSS movement	5.7±1.2	4.9±1.1	2.4±1.2	4.9±0.9
MSS synergy	4.0±1.0 *§	0.8±0.9	2.0±2.6	0.7±1.1
Motor Power	8.2±1.0 †	10.1±2.4 †	3.2±1.0	9.3±1.3 †
FIM	3.1±1.7	3.7±1.0 †	0.8±0.6	3.2±1.4 †
6-month follow-up				
N	6	7	5	5
Ashworth prox	-0.2±0.5	0.3±1.1	-2.0±0.8	0.2±0.8
Ashworth distal	-0.8±0.6	-0.6±0.6	-1.2±0.8	0.8±0.7
FM proximal	6.0±1.4	7.3±2.0	4.4±1.3	7.6±1.2
FM distal	3.0±1.0 §	8.9±2.1 †	3.0±1.5	6.2±2.5
MSS movement	8.8±2.3	8.3±2.5	6.3±1.6	7.6±1.7
MSS synergy	5.8±1.8	4.1±0.9	4.6±2.5	4.6±1.1
Motor Power	17.2±2.1	17.9±3.4	11.2±3.2	14.2±2.3
FIM	2.8±2.4	4.3±2.7	5.0±1.4	5.2±1.7

entries are mean ± standard error of the mean
FM = Fugl-Meyer
FIM = Functional Independence Measure (self-care and transfers)
MSS = Motor Status Score (proximal sections)
Significant differences from control (*), bilateral (†), or unilateral(§)
All significance levels are P<0.05

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