ROBOT-AIDED NEURO-REHABILITATION IN STROKE: THREE-YEAR FOLLOW-UP

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Abstract

We are applying robotics and information technology to assist, enhance, and quantify neuro-rehabilitation. Our goal is a new class of interactive, user-affectionate clinical devices designed not only for evaluating patients, but also for delivering meaningful therapy via engaging "video games." Notably, the robot MIT-MANUS has been designed and programmed for clinical neurological applications, and has undergone extensive clinical trials for more than four years at Burke Rehabilitation Hospital. Recent reports showed that stroke patients treated daily with additional robot-aided therapy during acute rehabilitation had improved outcome in motor activity at hospital discharge, when compared to a control group that received only standard acute rehabilitation treatment. This paper will review results of a three-year follow-up of the 20 patients enrolled in that clinical trial. The three-year follow-up showed that:

- The improved outcome was sustainable over three years.
- The neuro-recovery process continued far beyond the commonly accepted 3 months post-stroke interval.
- Neuro-recovery was highly dependent on the lesion location.

Introduction

Over four million Americans suffer from disabilities and impairments as a result of the leading cause of permanent disability in the U.S.: stroke. Physical and occupational therapy provides a standard, presumably beneficial treatment, but it is labor-intensive, often requiring one or two therapists to work with each patient. Demand for rehabilitation services is also certain to increase in the coming decades due to the graying of the population.

The expected increase in the number of stroke patients will increase the nation's health care financial burden, which continues to grow above the rate of inflation (HCFA). Until recently, health care providers have attempted to reduce the costs of caring for patient's rehabilitation primarily by shortening inpatient stays. Once the practical limit of abbreviated inpatient stays is reached, further efficiencies will be attainable chiefly by addressing clinical practices themselves. Our research suggests that robotics and information technology can provide an overdue transformation of rehabilitation clinics from primitive manual operations to more technology-rich operations.

Claims that manipulation of the impaired limb influences recovery remains controversial. Therefore, we tested in a pilot study whether manipulation of the impaired limb influences recovery during the inpatient rehabilitation period. The results were positive and reported elsewhere (Aisen, 1997; Krebs, 1998). This paper describes our efforts to assess whether the previously reported improved outcome during inpatient rehabilitation was sustainable after discharge, or alternatively, whether manipulation of the impaired limb influenced the rate of recovery during the inpatient phase, but not the "final" plateau.

Methods

We used the novel robot MIT-MANUS, which has been designed for clinical neurological applications. Unlike most industrial robots, MIT-MANUS was designed to have a low intrinsic end-point impedance (i.e., be back-driveable), with a low and nearly-isotropic inertia and friction [Hogan, 1995; Krebs, 1998][1].

Twenty sequential hemiparetic patients were enrolled during 1995 and part of 1996 in the pilot study. Patients were admitted to the same hospital ward and assigned to the same team of rehabilitation professionals. They were enrolled in either a robot-aided therapy group (RT, N=10) or in a group receiving "sham" robot-aided therapy (ST, N=10). Both groups were described in detail elsewhere (Aisen, 1997; Krebs, 1998). Patients and clinicians were blinded to the treatment group (double blind study). Both groups received conventional therapy; the RT group received an additional 4-5 hours per week of robot-aided therapy consisting of peripheral manipulation of the impaired shoulder and elbow correlated with audio-visual stimuli, while the ST group had an hour of weekly robot exposure.

Twelve of these 20 inpatients were successfully recalled and evaluated almost three years post-stroke (of the remaining 8 patients, 4 could not be located, 1 died, 3 had a second stroke or other medical complications). Six patients in the RT and in the ST group were comparable in gender distribution, lesion size (RT = 53.8 ± 22.9 cm^3, ST = 53.9 ± 28.2 cm^3), and

[1]An overview of research efforts in rehabilitation robotics at MIT, the Palo Alto VA, the Rehab Institute of Chicago, and U.C. Berkeley can be found in Reinkensmeyer et al. (1999).

length of time from stroke to follow-up (RT: 1113.3 ± 59, ST: 960 ± 81 days). There was no control over patients' activities after hospital discharge.

The same standard assessment procedure used every other week to assess all patients during rehabilitation was used at recall three years post-hospital discharge (RT and ST groups). This assessment was performed by the same "blinded" rehabilitation professional. Patients' motor function was assessed by standard procedures including: the upper limb subsection of the Fugl-Meyer (F-M), Motor Power for shoulder and elbow (MP), Motor Status Score for shoulder and elbow (MS1), and Motor Status Score for wrist and fingers (MS2).

Results

The improved outcome observed in the first phase of the pilot study was sustained after three years.

Table I shows the change in scores for the twenty patients enrolled in the first phase of trial between admission and discharge from the rehabilitation hospital. Table II shows the same change in score during this first phase limited to the twelve patients successfully recalled (Volpe-a, 1999). This table also shows the change in scores between recall and discharge, as well as total change (between recall and admission to the rehab hospital).
This data should be interpreted with caution due to the small number of subjects. Nevertheless, the group of patients treated daily with additional robot-aided therapy during acute rehabilitation had improved outcome in motor activity at hospital discharge, when compared to a control group that received only standard acute rehabilitation treatment. Improved outcome was limited to the muscle groups trained in the robot-aided therapy, i.e., shoulder and elbow (Table II MS1 - Δ1 score). The improved outcome during inpatient rehabilitation was sustainable after discharge. Note that, comparing the overall recovery (between admission and recall) the MS1 for shoulder and elbow (which were the focus of robot training) of the experimental group improved twice as much as the control group (Table II MS1 - Δ3 score). Note also that both groups had comparable improvement between hospital discharge and three-year recall (period without robot-aided therapy, Table II - Δ2 score). Furthermore, eight out of twelve patients successfully recalled continued to improve substantially in the period following discharge (RT & ST subjects). This finding challenges the common perception that patients stop improving motor function after about 11 weeks post-stroke (e.g., Jorgensen, 1995, The Copenhagen Stroke Study). It suggests that there may be an opportunity to further improve the motor recovery of stroke patients by continuing therapy in the out-patient phase, for example, using the technology that is the focus of our project.

To tailor therapy to the patient's need, we must understand the process of neuro-recovery and systematically classify different strokes. Brain imaging technology allows us to classify strokes according to lesion site. For the patients recalled in the follow-up, CT scans showed 6 pure subcortical

Group	F-M (out of 66)	MP (Out of 20)	MS1 (Out of 40)	MS2 (Out of 42)
	Δ 1	Δ 1	Δ 1*	Δ 1
RT	14.1	3.9	9.4	5.5
ST	9.9	2.3	0.8	4

Table I. Change during Acute Rehabilitation (20 patients): Experimental (RT) vs Control (ST) Group

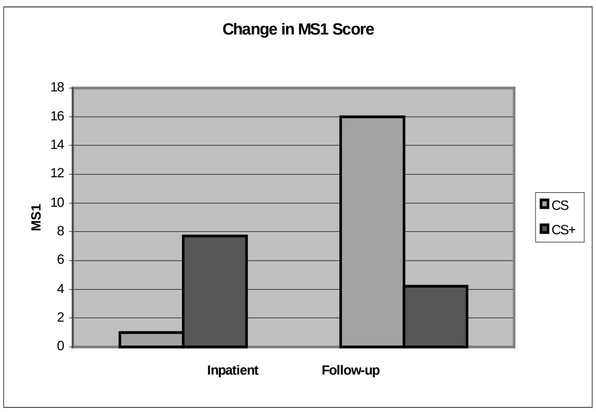
Group	F-M (out of 66)			MP (Out of 20)			MS1 (Out of 40)			MS2 (Out of 42)		
	Δ 1	Δ 2	Δ 3	Δ 1*	Δ 2	Δ 3	Δ 1*	Δ 2	Δ 3*	Δ 1	Δ 2	Δ 3
RT	15.3	5.0	20.3	4.5	4.6	9.1	12.0	9.4	21.4	8.2	8.3	16.4
ST	8.0	12.3	20.3	1.6	3.5	5.1	-1.0	10.2	9.2	3.7	8.0	11.7

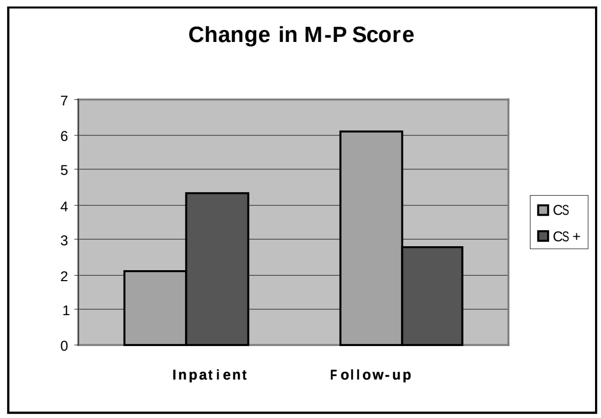
Table II. Change during Acute Rehabilitation & Follow-Up (12 patients): Experimental (RT) vs Control (ST) Group.

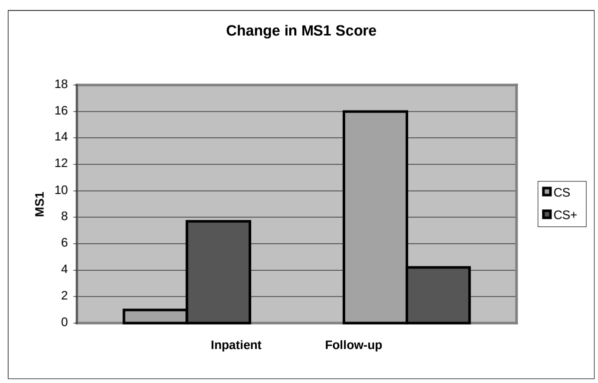
Both Tables: Δ1 admission to discharge of rehabilitation hospital; Δ2 discharge to follow up; Δ3 admission to follow up; one-way t-test that RT > ST with $p < 0.05$ for statistical significance (*).

and 6 subcortical plus cortical lesions. We excluded a pure thalamic lesion from the subcortical group. The comparison of outcome for 5 patients with corpus striatum lesions (CS) versus 6 patients with corpus striatum plus cortex (CS+) is shown in Fig.1. (Volpe-b, 1999). These patients had comparable demographics and were evaluated by the same therapist on hospital admission (19 days ± 2 post-stroke), discharge (33 days ± 3 later), and follow-up (1002 days ± 56 post discharge). The CS group had smaller lesion size (CS = 13.3 ± 3.9cm^3, CS+ = 95.1 ± 25.2cm^3, $p < 0.05$).

Although the CS group had smaller lesion size, recent report suggested that patients with stroke confined to basal ganglia (CS) have diminished response to rehabilitation efforts compared to the patients with much larger lesion (CS+). Miyai et al. suggested that isolated basal ganglia strokes may cause persistent corticothalamic-basal ganglia interactions that are dysfunctional and impede recovery (Miyai, 1997). Our results are consistent with Miyai's observation. Note in Fig.1. that the CS+ group outperformed the CS group during inpatient rehabilitation. However, note also in Fig.1. that the CS group outperformed the CS+ group between discharge to follow-up. In fact, the CS group outcome is superior at follow-up. Our results are consistent with studies suggesting that transneural degeneration follows a stroke in the basal ganglia and once the degeneration is completed, recovery proceeds (e.g., Saji, 1997). As stated earlier, motor recovery during inpatient rehabilitation may not be completed and understanding motor recovery will require longitudinal studies beyond the inpatient period.







Group	F-M (out of 66)			MP (Out of 20)			MS1 (Out of 40)			MS2 (Out of 42)		
	Δ 1	Δ 2*	Δ 3*	Δ 1	Δ 2	Δ 3	Δ 1	Δ 2*	Δ 3*	Δ 1	Δ 2*	Δ 3*
SC	9.3	25.0	34.3	2.1	6.1	8.2	1.0	16.0	17.0	10.0	14.5	24.5
SC+	10.7	-1.3	9.4	4.3	2.8	7.1	7.7	4.2	11.9	3.3	3.2	6.5

Δ1 admission to discharge of rehab hospital; Δ2 discharge to follow-up; Δ3 admission to follow-up; one-way t-test SC > SC+ with $p < 0.05$ for statistical significance (*).

We evaluated the overall patient performance using standard assessment procedures. Yet those are limited. To understand the functional motor consequences of the neuro-recovery process, a facility to measure and manipulate the motor system is needed. Robotic technology can serve this purpose. Figure 2 shows examples of reaching movements made by patients with CS (8.9 cm^3) and CS+ (109.9 cm^3) lesions. The left column shows a plan view of the patients' hand path attempting a point-to-point movement. The right column shows the tangential speed of the hand. Comparing the two patients, note that the CS patient appears to move exceptionally slowly. Yet, the hand path is generally well aimed towards the target. In contrast, the CS+ patient appears to make a faster movement, but poorly aimed. The CS+ patient's mis-aiming appears to be consistent with observations that activity of populations of motor cortical neurons are correlated with the intended direction of reaching movements (Georgopoulos, 1984).

We compared the speed-accuracy tradeoff of aimed movements by using the first successful attempt of six patients (3 CS patients w/ mean lesion size 12.6 cm^3 and 3 CS+ patients w/ mean lesion size 92.1 cm^3). Patients were asked to hit eight outboard

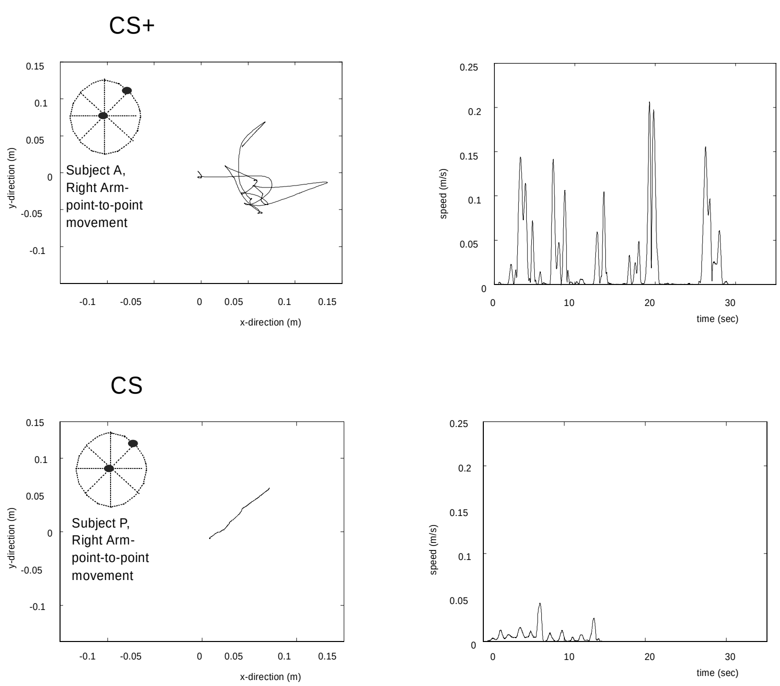


FIG.2. Examples of reaching movements made by patients with CS (8.9 cm^3) and CS+ (109.9 cm^3) lesions. The left column shows a plan view of the patients' hand path attempting a point-to-point movement. The right column shows hand speed.

targets, equally spaced around a horizontal 2D circle of 10cm diameter, and presented in a clockwise fashion starting at 12 o'clock position. The "inner" home target was presented following each the outboard targets. For all patients, kinematic measures demonstrated diminished speed-accuracy performance. CS patients had a predominantly speed impairment, while CS+ patients had a predominant aiming impairment (Aisen, 1998).

Conclusions

These findings suggest that (a) manipulation of the impaired limb influences recovery, (b) the improved outcome was sustained after three years, (c) the neuro-recovery process continued far beyond the commonly accepted 3 months post-stroke interval, and (d) neuro-recovery was highly dependent on the lesion location.

We just completed a second clinical trial with a larger pool of patients of 60 patients. The objective of this second trial was to address the main limitation of the first study, i.e., small sample size. At the time of writing this paper, we are analyzing data. Nevertheless, it might be not far fetched to conclude that, while few persons will pass through life unaffected directly or indirectly by the consequences of stroke, now however, the benefits of technology that have so deeply penetrated other medical sectors might be available to help the victims of debilitating stroke maximize their potential for recovery.

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References

Aisen, M.L., Krebs, H.I., McDowell, F., Hogan, N., Volpe, N., The effect of robot assisted therapy and rehabilitative training on motor recovery following stroke, *Archives of Neurology,* 54(1997), pp.443-446.

Aisen, M.L., Krebs, H.I., Hogan, N., Volpe, N., Lesion location and speed-accuracy tradeoff in stroke patients, *Proc. 1998 Am. Acad. Neur.*, (1998).

Georgopoulos, A.P., Kalaska, J.F., Crutcher, M.D., Caminiti, R., Massey, J.T., The representation of movement direction in the motor cortex: single cell and population studies. In: *Dynamic Aspects of Neocortical Function. John Wiley & Sons*, (1984).

Hogan, N., Krebs, H.I., Sharon, A., Charnnarong, J., Interactive robotic therapist, *U.S. Patent #5,466,213, MIT.*

Jorgensen, H.S., Nakayama, H., Raaschou, H.O., Vive-Larsen, J., Stoier, M., Olsen, T.S., Outcome & time course of recovery in stroke, I: Outcome, II: Time course of recovery, Copenhagen Stroke Study, *Arch. Phys. Med. Rehab.*, 76:5(1995), pp.399-412.

Krebs, H.I., Hogan, N., Aisen, M.L., Volpe, B.T., Robot-aided neuro-rehabilitation, *IEEE Trans. on Rehab. Eng*, 6:1(1998), pp.75-87.

Miyai, I., Blau, A.D., Reding, M.J., Volpe, B.T., Patients with stroke confined to basal ganglia have diminished response to rehabilitation efforts, Neurol., 48(1997), pp.95-101.

Reinkensmeyer, D.J., Hogan, N., Krebs, H.I., Lehman, S.L., Lum, P.S., Rehabilitators, robots, and guides: new tools for neurological rehabilitation, In: *Biomechanics and Neural Control of Movement, Spr-Verlag,* 1999 (in press).

Saji, M., Endo, Y., Miyanishi, T., Volpe, B.T., Ohno, K., Behavioral correlates transneuronal degeneration of substantia nigra reticulata neurons are reversed by ablation of subthalamic nucleus, *Behavioral Brain Research*, 84(1997), pp. 63-71.

Volpe, B.T., Krebs, H.I., Hogan, N., Edelstein, L., Diels C., Aisen, M.L., Robot-Training Enhanced Motor Outcome in Patients with Stroke Maintained in Three Year Follow-up, *Proc 1999 Am Acad Neur*, (1999, sub).

Volpe, B.T., Krebs, H.I., Hogan, N., Edelstein, L., Diels C., Aisen, M.L., Comparison of the Motor Recovery in Patients with Subcortical and Cortical Stroke: Inpatient Rehabilitation to Three Years Post Stroke, *Proc. 2nd World Cong Neur Rehab* (1999, sub).