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Increasing productivity and quality of care: Robot-aided neuro-rehabilitation

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Abstract—This paper presents an overview of our research in robot-aided stroke neuro-rehabilitation and recovery. At the onset of this research we had to confront squarely (and solve!) a critical question: If anatomy is destiny, can we influence it? Our efforts over the last five years have been focused on answering this question and we will present a few of our clinical results from over 2,000 hours of robot-aided therapy with 76 stroke patients. To determine if exercise therapy influences plasticity and recovery of the brain following a stroke, we needed the appropriate "microscope" that would allow us to concomitantly control the amount of therapy delivered to a patient, while objectively measuring patient's performance. Back-driveable robots are the key enabling technology. Our results to date using common clinical scales suggest that robot-aided sensorimotor training does have a genuinely positive effect on reduction of impairment and the reorganization of the adult brain. Yet while clinical scales can help us to examine the impact in the neuro-recovery process, their coarse nature requires extensive and time-consuming trials, and on top of that they fail to show us details important for optimizing therapy. Alternative, robot-based scales offer the potential benefit of new finer measurements—and deeper insight into the process of recovery from neurological injury. We also plan to use present technology to establish the practicality and economic feasibility of clinician-supervised, robot-administered therapy, including classroom therapy. We feel quite optimistic that the march of progress will accelerate substantially in the near future and allow us to transfer this technology from the research realm to the everyday treatment of stroke survivors.

Key words: *robot, robot-aided neuro-rehabilitation, robot-aided stroke rehabilitation, stroke, stroke rehabilitation.*

INTRODUCTION

During his frequent testimony before Congress, the Federal Reserve Board Chairman, Alan Greenspan, attributed the longest period of economic expansion in American history to the information technology that is reshaping America. Unemployment rates are at a record low of a mere 4 percent, while inflationary pressure is clearly controlled, at less than 3 percent. This unheard-of growth and prosperity has puzzled more than a few economists and fortunetellers. To explain this anomaly, nothing is more appropriate than paraphrasing another moneyman, Paul Krugman of MIT: "Productivity isn't

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everything, but in the long run it is almost everything" (1). Yet, societal memory typically sells short and we forget the anguish of years in which many questioned if any real increase in productivity would ever occur despite technophile employees avidly spending working and nonworking hours entertaining themselves with the new puzzles offered by computers and networks. It paid off: After enduring their share of pain, "old industries" are reinventing themselves and productivity is soaring (competitiveness is an effect, not a cause).

Productivity has not increased at an equal pace across different industry sectors. Upheavals within the present health care system strongly suggest that it is moribund and may be the next "old industry" to undergo massive restructuring. In fact, it may well be the hardest and most regulated conversion. We cannot afford a temporary shutdown for restructuring but we may not be able to afford the present system either: The Health Care Financing Administration (HCFA) projected health care costs to surpass 16.6 percent of the total GNP in the year 2007 ($2.1 trillion).

This situation creates a pressing need and an opportunity, both of which motivate our research: The need is for new therapeutic strategies to increase productivity while optimizing the quality of care; the opportunity is to take advantage of recent dramatic advances in technology—especially in robotics, sensing, information processing, and telecommunications. In particular, our research goal is to develop innovative treatments that take advantage of robotics and information technology to enhance neuro-rehabilitation. Our approach is a departure from most prior work using robotics for rehabilitation; rather than developing rehabilitation robots to assist a person with disabilities, we are creating robot-aids to assist and support clinicians in their efforts to facilitate a disabled individual's functional recovery, while enhancing the healthcare system productivity.

There are three ways to increase productivity in the delivery of rehabilitation without sacrificing quality of patient care: a) develop evidence-based therapy (for example, deliver the optimal therapy to the particular patient's need), b) re-allocate personnel and tasks (for example, minimize paperwork, freeing more personnel to deliver care), and c) increase the productivity of each caregiver (for example, provide therapists with appropriate tools). Robotic aids can impact all these modes and increase productivity not only by introducing new efficiencies into certain routine physical and occupational therapy activities, but also by providing a rich stream of objective data to assist in patient diagnosis, prognosis, customization of therapy, assurance of patient compliance with treatment regimens, and maintenance of patient records.

This technology promises to have an impact on a broad range of neurological conditions, encompassing a large class (if not the entire gamut) of potentially disabling conditions. While millions of people in the U.S. acquire movement disabilities as the result of injury and disease—e.g., stroke CVA, traumatic brain injury (TBI), multiple sclerosis (MS), spinal cord injury (SCI), Parkinsons disease (PD)—it would be unrealistic to attempt to develop and evaluate the technology in all of these applications. For that reason we focused our initial efforts on stroke, the leading cause of disability in the U.S. with 700,000 new cases every year.

Notwithstanding the exciting possibilities of robotics and information technology, it is imperative to establish from the outset how well these technologies really work. Evidence-based healthcare casts a cynical (but scientifically appropriate) view on current rehabilitation practices, perhaps best captured by paraphrasing a remark attributed to Voltaire: "Physicians, nurses, and therapists are there to entertain the patient, while nature takes its course." It synthesizes the prevailing view that once a stroke patient arrives at a rehabilitation hospital there is little that can be done to impact outcome. If nature were the principal factor determining the stroke patient's outcome, the use of robots as "rehabilitators"[1] would be fundamentally flawed. Therefore, the critical question we addressed in the last 5 years was whether sensorimotor therapy influences brain recovery. In this paper we will summarize our results from over 2,000 hours of robot-aided therapy with 76 stroke patients.

Stroke

Stroke rehabilitation is labor-intensive, usually relying on one-on-one, manual interactions with therapists. The demand for physical and occupational therapy for stroke survivors is expected to increase because improvements in medicine and health care will continue to increase the life expectancy of the population, and the incidence of stroke is more prevalent among older adults. In fact, the relative incidence of stroke doubles with every decade after age 55 and the U.S. demographic patterns compound the problem; the leading edge of the "baby boom" will be 55 in a few years. Worldwide, the

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[1] To our knowledge, Steven Lehman (University of California, Berkeley) coined the term "rehabilitators."

World Health Organization (WHO) is predicting that the population over 65 years old will increase by 88 percent in the coming years. New treatments for stroke are being developed but their impact on the need for other forms of therapy is unclear. For example, as new pharmaceutical agents for neuro-protection (e.g., nerve growth factors, better receptor blockers, antioxidants, anti-inflammatory agents, and blood clot dissolving agents) come into widespread use, the percentage of people surviving a stroke may increase, but the percentage of stroke victims potentially requiring rehabilitation may increase as well.

The effects of stroke can be devastating, resulting in deficits of cognitive, affective, sensory, and motor functions. Motor deficits persist chronically in about one-half of stroke survivors (2). Damage to neural areas responsible for controlling movement and concomitant disuse and persistent abnormal posture of the impaired limb cause a host of centrally and peripherally based sensory and motor impairments. Common impairments are decreased passive range of motion, weakness (3), hyperactive reflexes (4), and incoordination, manifest in part as an inability to independently co-activate muscles (5). The biological processes that underlie recovery from neurological injury remain a topic of intensive research. A prominent theme of current neuroscience research into the sequelae of brain injury posits that activity-dependent plasticity underlies neuro-recovery. If that is the case, there is good reason to believe that neurological changes that may underlie recovery are facilitated by the standard practice of providing targeted sensorimotor activity.

Stroke patients commonly experience some spontaneous recovery, but are also treated with extensive physical and occupational therapy. Because the variability of brain injury following stroke is enormous, in many cases it is unknown which therapies best promote recovery; and because of the subjective nature of patient evaluation it is difficult to monitor treatment effects precisely. Different studies have reported positive outcomes with several approaches, including repetitive passive exercises (6), forced use of the paretic limb by restraining the contralateral limb (7–9), increased amounts of therapy including external manipulation (10,11), and biofeedback (12). On the other hand, comparative studies have generally shown little difference among different therapeutic techniques (13,14). In this paper, we will present one of these therapeutic approaches (our approach): robot-aided neuro-rehabilitation, which takes advantage of robotics and information technology to enhance neuro-rehabilitation (**Figure 1**).

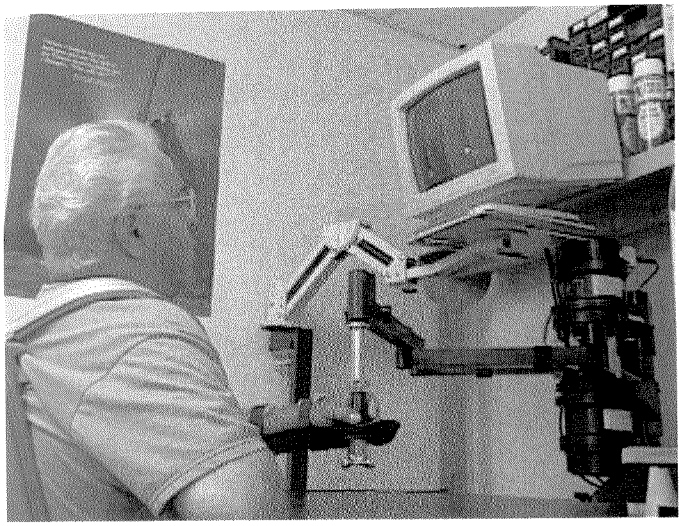


Figure 1.
A recovering stroke patient receiving upper extremity robot-aided neuro-rehabilitation therapy.

Back-driveable Robot: MIT-MANUS

To determine if exercise therapy influences plasticity and recovery of the brain following a stroke, we needed a tool that would allow us to control the amount of therapy delivered to a patient, while objectively measuring the patient's performance. Robotics can provide this tool. Yet, the requirements for rehabilitation of neurologically impaired patients impose unique constraints on robot design. The first requirement for interacting safely with humans (impaired or otherwise) is that the machine should be capable of gentle, compliant behavior. In engineering terms, it should be highly "back-driveable" (equivalently, it should have low intrinsic endpoint mechanical impedance). This requirement is difficult to satisfy with a commercial robot. While a commercial robot could exert forces on the patient's limbs, it shares current limitations of the industrial robot technology. Because of a typical robot's electromechanical design and control architecture, it is intrinsically a position-controlled machine and does not yield easily under the action of external forces. Active force feedback is needed to make the robot respond to the patients' actions, but that approach cannot (15) produce the "back-driveability" (low mechanical impedance) required to move smoothly and rapidly to comply with the patients' actions.

The second requirement derives from special characteristics of neurologically impaired patients, who often present abnormally low or (occasionally) high muscle tone. As a result, for abnormally low muscle tone, modest forces applied to the limbs can result in excessive relative motion of limb segments. Likewise, excessive muscle tone might misguide the clinician to apply very large robot forces to obtain the desired motion of limb segments. The problem is particularly acute for the shoulder where even the mild forces applied in standard therapy can injure the joint if applied improperly. Thus a neuro-rehabilitation robot capable of activating arm and hand motion must also be able to control the forces exerted on the shoulder. Furthermore it must do so while guaranteeing stable behavior despite almost complete ignorance of the dynamics of the neurologically impaired patient. That requirement can be satisfied by ensuring the robot exhibits passive impedance; hence impedance control is optimal.

To address the limitation of commercial robots, in 1989 we started to specifically design and build a novel low-impedance robot for clinical neurological applications capable of interacting safely and gently with humans: MIT-MANUS (16, **Figure 2**). Unlike most industrial robots, MIT-MANUS is configured for safe, stable, and compliant operation in close physical contact with humans. This is achieved using impedance control, a key feature of the robot control system that modulates the way the robot reacts to mechanical perturbation from a patient or clinician and ensures a gentle compliant behavior. Hogan (17) introduced impedance control, and it has been extensively adopted by other robotics researchers, especially those concerned with human-machine interaction. MIT-MANUS can move, guide, or perturb the movement of a subject's or patient's upper limb, and can record motions and mechanical quantities such as the position, velocity, and forces applied. An overview of the robot's main characteristics can be found elsewhere (18). This robot has been used daily for over 5 years with over 100 stroke patients at the Burke Rehabilitation Hospital (White Plains, NY). A second unit began operation in the fall of 1999 at the Spaulding Rehabilitation Hospital (Boston, MA), while a third unit is scheduled to begin operation shortly at the Burke Rehabilitation Hospital and a fourth unit at the Baltimore VA Hospital (Baltimore, MD). Our expectation is that these four units will substantially speed up the rate of research and permit us to significantly impact the way rehabilitation medicine is practiced.

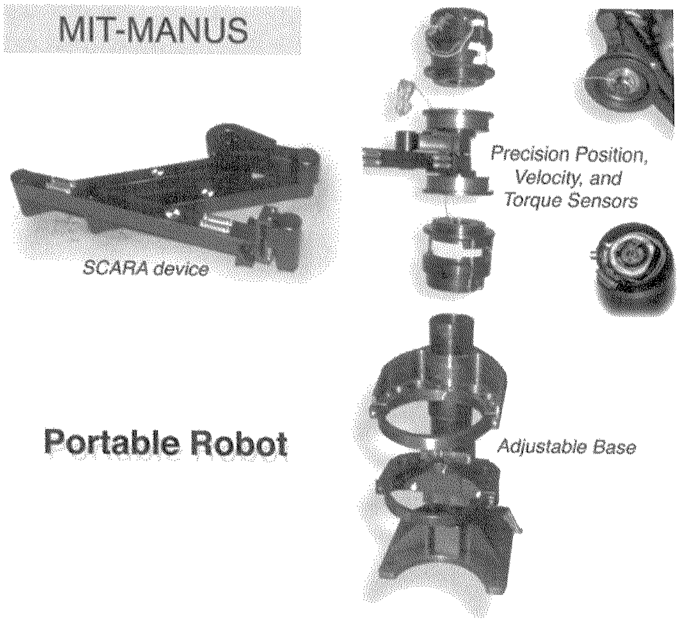


Figure 2.
Exploded view of two-degree-of-freedom robot module.

Evidence-based Rehabilitation: Robot-aided Neuro-rehabilitation Benefits

Evidence-based rehabilitation might sound like a managed-care "buzzword" to justify further pruning of rehabilitation expenses. Yet compassion alone cannot drive a high-quality efficient rehabilitation delivery system. Scientific evidence must qualify and quantify decisions that affect patient care. A common language that clinicians can understand is needed; therefore, we opted to make use of the existing standard clinical assessment scales to present admissible evidence to the clinician that indeed, sensorimotor training influences brain recovery.

Robot-aided Therapy

Seventy-six sequential hemiparetic patients were enrolled from 1995 to early 1999. Patients were admitted to the same hospital wards and assigned to the same team of rehabilitation professionals. They were enrolled in either a robot-aided sensorimotor therapy group (RT, N=40) or in a group receiving standard therapy plus "sham" robot-aided therapy (ST, N=36). Both groups are described in detail elsewhere (18-21). Patients and clinicians were blinded to the treatment group (a double-blinded study). Both groups received conventional therapy; the RT group received an additional 4 to 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.

The sensorimotor motor training for the RT group consisted of a set of "video games" and typically lasted for six weeks. Patients were required to move the robot end-effector according to the game's goals (**Figure 3**). If the patient could not perform the task, the robot assisted and guided the patient's hand. The robot was controlled by an impedance controller, which produced a constant isotropic end-point stiffness and damping. Coupled to our highly back-driveable design, the stability of this controller is extremely robust to the uncertainties due to physical contact (22,23). The training for the ST group was similar to the RT group. Half of the one hour session consisted of playing the video games with the unimpaired arm and half the session with the impaired arm while the robot passively supported the arm and provided the video-game visual feedback (position feedback). If the patient could not perform the task, he/she used the unimpaired arm to assist the impaired arm and complete the game (self-ranging), or the clinician assisted.

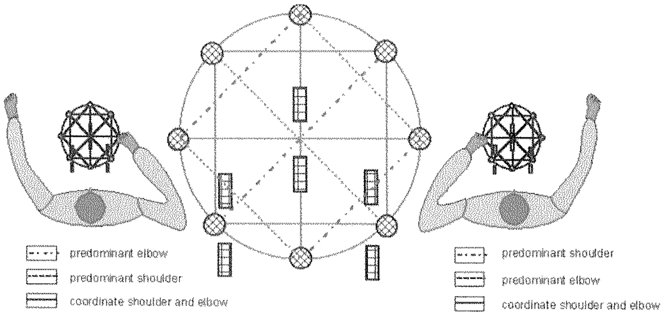


Figure 3.
Robot-aided neuro-rehabilitation task. Targets were arranged so that diagonal paths required predominantly elbow or shoulder motions, while vertical, horizontal or curved paths (circle) required coordination of both.

A standard assessment procedure was used every other week to assess all patients during rehabilitation and during the recall post-hospital discharge (robot-aided therapy group and control group). This assessment was always performed by the same "blinded" rehabilitation professional. Each patient's motor function was assessed by standard procedures including: the Functional Independence (FIM), 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).

In-patient Benefits

Table 1 presents the composite results of two trials with 76 patients (initial study with 20 patients, see references 18–20; replication study with 56 patients, see reference 21).

Table 1.
Change during acute rehabilitation (76 patients)

Group	F-M	MP	MS1	MS2
	Δ1	Δ1*	Δ1*	Δ1
RT (40 patients)	9.25±1.36	3.99±0.43	8.15±0.79	4.16±1.16
ST (36 patients)	*7.1±1.20*	*2.0±0.32*	*3.42±0.62*	*2.64±0.78*

Experimental (RT) vs. Control (ST) Group--Δ1: score change from rehabilitation hospital admission to discharge; one-way t-test that RT>ST with $p<0.05$ for statistical significance (*).

The F-M and MS2 show no statistically significant difference between groups. The MS1 and MP for shoulder and elbow show a statistically significant improvement: the experimental group responding to therapy with about twice the score improvement of the control group over a comparable period. Our replication study confirmed and strengthened our initial pilot study (19). Note that results for the additional 56 patients were of the same order of magnitude as the ones in the initial study (21). The difference between the results with the different measures may be in part due to differences in the resolution of these instruments and what they measure. For example, the F-M measures motor behavior most sensitively from the acute injury (a time when the affected limb may be flaccid) to a point when the limb is developing tone and reflex changes and synergy. For that reason we adopted the MSS scale, which was developed at the Burke Rehabilitation Hospital for a previous study. The MSS scale takes the F-M measures and focuses the motor analysis on the movement about the shoulder, elbow, wrist, and fingers.

The MSS for elbow and shoulder (MS1) consists of a sum of scores (0 to 2) given to 10 shoulder movements and 4 elbow/forearm movements. The MSS for wrist and fingers (MS2) consists of a sum of grades for three wrist movements and 12 hand movements (19–21). The Motor Power Score includes the standard six-point scale assessing muscle power in biceps, triceps, and anterior and lateral deltoid muscles, and is sometimes referred to as the Oxford Scale (21). A notable feature of these results is that although the MS1 is capable of detecting a significant advantage of robot therapy for shoulder and elbow, the MS2 for wrist and fingers shows no significant difference between experimental and control groups. As it is unlikely that the lack of statistical significance is due to inadequate resolution of this measure, the result suggests that the benefit of robot-administered sensorimotor training (and perhaps human-administered sensorimotor training, too) is specific to the muscle groups or limb segments exercised and does not generalize broadly.

Long-term Benefits

To test whether motor advantages conferred on the robot-trained group would persist, we recalled patients enrolled in the first pilot clinical trial (20 patients) 3 years after hospital discharge. If the improved outcome was not sustainable, one might conclude that manipulation of the impaired limb influenced the rate of recovery during the inpatient post-stroke phase, but not at the "final" plateau. Twelve of these 20 inpatients were successfully recalled and evaluated by the same "blinded" therapist (of the remaining 8 patients, 4 could not be located, 1 had died, and 3 had a second stroke or other medical complications). Six patients in the RT and in the ST groups were comparable in gender distribution, lesion size (RT=53.8±1113.3±59, ST: 960±81 days). There was no control over patients' activities after hospital discharge. Results are shown in **Table 2** and were described elsewhere (20,25). Summarizing, the improved outcome during inpatient rehabilitation was sustained after 3 years post discharge; and the improvement was again confined to the muscle groups trained in the robot-aided therapy, i.e., shoulder and elbow.

This data should be interpreted with care due to the small number of subjects. Nevertheless, comparing the overall recovery (between admission and 3 years after discharge) the MSS for shoulder and elbow (which were the focus of robot training) of the experimental group improved twice as much as that of the control group (MS1 - Δ3 score), whereas the MSS of wrist and fingers (which were not robot trained) improved by essentially the same amount for both groups (MS2 - Δ3 score). Note also that both groups had comparable improvement between hospital discharge and 3-year recall (period without robot-aided therapy, Δ2 score). These results corroborate our inpatient studies (**Table 1**), indicating that the benefits of robot training are specific to the muscle groups or limb segments exercised. Furthermore, it is striking that eight out of twelve patients who were successfully recalled continued to improve substantially in the period following discharge (RT and ST subjects).

If this finding is corroborated in the recall of the replication study group (56 patients—recall in progress), it would challenge the common perception that patients stop improving after about 11 weeks post-stroke (e.g., The Copenhagen Stroke Study, see reference 26). Our results suggest the possibility that the use of unsuitably coarse scales may misjudge patients' potential and that there may be an opportunity to further improve the motor recovery of some stroke patients by continuing therapy in the outpatient phase.

Neuro-recovery Time History Changes with Lesion Territory

The fundamental mechanisms underlying neurorecovery are understood poorly at best. The so-called "activity-dependent plasticity" that is posited to drive recovery may be due, in part, to the unmasking of preexisting connections, focal synaptic changes, or neosynaptogenesis—the growth of new connections. Experimental support for this idea derives primarily from measurements of synaptic branching and cortical thickness in rats raised in enriched environments and deprived environments (e.g., 27–31) and in monkeys recovering from ischemic injury (e.g., 32). One challenge is to understand whether the neurobiologic mechanism for the changed motor behavior is based on reorganization of normal cortex that surrounds the injury, or of more distant supplemental motor circuits (in the supplemental motor area, the basal ganglia, or cerebellum), or of the unaffected hemisphere (33–35). Another (and probably related) mechanism involves assumption of lost function by adjacent areas of undamaged brain tissue. Reorganization of cortical maps has been demonstrated in the motor system (36,37), sensory system (38,39), visual system (40), and auditory system (41). A further mechanism of recovery of function post stroke involves the homologous regions of

Table 2.
Change during acute rehabilitation and follow-up (12 patients)

	F-M (out of 66)			MP (out of 20)			MS1 (out of 40)			MS2 (out of 42)		
	Δ1	Δ2	Δ3	Δ1*	Δ2	Δ3	Δ1*	Δ2	Δ3	Δ1	Δ2	Δ3
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

Experimental (RT) vs. Control (ST) Group - Δ1: score change from rehabilitation hospital admission to discharge; Δ2: score change from discharge to follow up; Δ3: score change from admission to follow up; one-way t-test that RT>ST with $p<0.05$ for statistical significance (*).

the unaffected contralateral cerebral hemisphere substituting for the infarcted brain tissue (42–44). A mechanism by which motor function may be controlled by the unaffected ipsilateral hemisphere may be through the 25 percent (45) of pyramidal tract fibers that are uncrossed.

Activity-dependent cortical plasticity has been found to accompany motor learning, and rehabilitation and training after injury have also been reported to influence the pattern of reorganization. These findings suggested that at least some aspects of the recovery of motor behavior in stroke patients should exhibit characteristics normally associated with motor learning. Our own results to date are consistent with this hypothesis. To the extent that sensorimotor training facilitates a process akin to motor learning, its benefits should be specific to the limb segments involved in the training, and that is what we have observed. Whereas the arm and forearm, which are the focus of our robot training, show significant reduction of impairment, the wrist and fingers, which are not a focus of this training, show no significant benefit of robot training.

Given this state of knowledge, the best predictors of outcome remain a topic of research. Intuitively one might expect that larger lesions would lead to poorer outcomes, but Miyai and colleagues showed that while lesion size is an important variable in predicting stroke outcome, lesion territory might be even more important. They showed that patients with stroke confined to basal ganglia (CS) with smaller lesions have diminished response to rehabilitation efforts compared to patients with much larger lesions that involve both the basal ganglia and cortical territories (CS+; reference 46). They suggested that isolated basal ganglia strokes might cause persistent corticothalamic-basal ganglia interactions that are dysfunctional and impede recovery. At face value, it would seem that sensorimotor therapy would have little benefit for this (CS) group. However, we must go beyond the inpatient phase and track the whole process to fully understand the process of neuro-recovery.

For the patients recalled in the follow-up described above, CT scans showed six pure subcortical and six subcortical plus cortical lesions. The comparison of outcome for 5 patients with corpus striatum lesions (CS) *versus* 6 patients with corpus striatum plus cortex (CS+) is shown in **Table 3** and **Figure 4** (one patient with rapid motor recovery after an isolated thalamic injury was excluded; see reference 25). 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 (1,002 days + 56 post-discharge). As in the study by Miyai et al., the CS group had smaller lesion size (CS=13.3±3.9 cm^3, CS+=95.1±25.2 cm^3, $p<0.05$).

Our results are consistent with the observation of Miyai et al. (46) for the time period that covered the acute rehabilitation phase. Note in **Table 3** that the CS+ group outperformed the CS group during inpatient rehabilitation. However, the follow-up reinforced the old clinical truism that anatomy is destiny: It revealed that patients with smaller lesions eventually fare better. Specifically, note that the CS group outperformed the CS+ group between discharge to follow-up. In fact, the CS group outcome is far superior at follow-up. This clinical result bears some resemblance to the important problem of delayed neuronal degeneration. There are several animal models in which initial injury in the basal ganglia are accompanied by neuronal degeneration in neurons distant from the initial injury and occurring over longer periods of time (e.g., 47–49). This further reinforces the impression that motor recovery during inpatient rehabilitation may not be complete.

Understanding motor recovery will require longitudinal studies beyond the inpatient period. Otherwise we might wrongly conclude that therapy should be discontinued to patients with stroke confined to the CS territories, because they appear not to respond. In fact, the CS group in our study outperformed the CS+ following hospital discharge. For cost reasons, extending inpatient

Table 3.
Change during acute rehabilitation and follow-up

Group	F-M (out of 66)			MP (out of 20)			MS1 (out of 40)			MS2 (out of 42)		
	Δ1	Δ2*	Δ3*	Δ1	Δ2	Δ3	Δ1	Δ2*	Δ3*	Δ1	Δ2*	Δ3*
CS	9.3	25.0	34.3	2.1	6.1	8.2	1.0	16.0	17.0	10.0	14.5	24.5
CS+	10.7	-1.3	9.4	4.3	2.8	7.1	7.7	4.2	11.9	3.3	3.2	6.5

Lesion Site Classification--Δ1: score change from rehabilitation hospital admission to discharge; Δ2: score change from discharge to follow up; Δ3: score change from admission to follow up; one-way t-test CS>CS+ with $p<0.05$ for statistical significance (*).

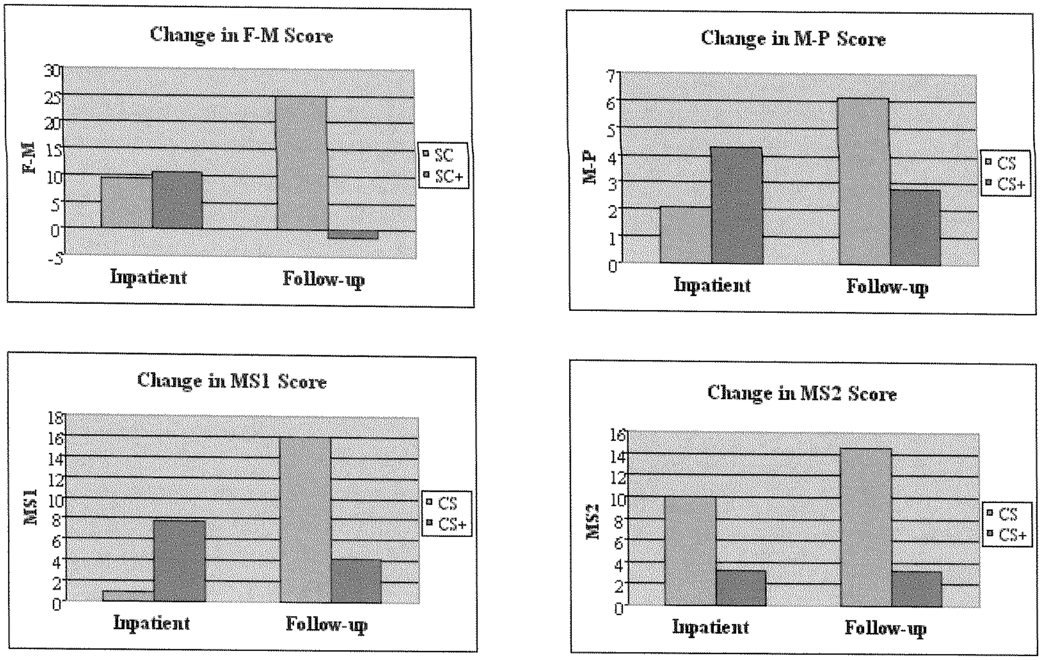


Figure 4.
Change during acute rehabilitation and follow-up: Lesion site classification.

rehabilitation is unlikely to be practical. However, the robotic neuro-rehabilitation technology might facilitate the extension of therapy for neuro-rehabilitation far beyond the inpatient phase. For example, it may enable robot-assisted self-therapy in a home setting. Connection to the Internet may permit low-cost periodic evaluation by appropriate clinical personnel, or interactions with other patients at similar stages of recovery.

Robot-aided Therapy Interacts with Lesion Anatomy

Our repeated finding that patients who received robotic training enjoyed significantly improved motor outcome is encouraging. However to assess the true potential of robot-aided neuro-rehabilitation, we need to understand the biological basis of recovery. As outlined above, our initial approach is to examine the relation between lesion anatomy and the effects of therapy. Does lesion territory determine functional outcome? More succinctly, is anatomy destiny? Lesion anatomy is clearly a critical factor—for instance, the absence of any lesion would surely obviate the need for therapy—but perhaps the more definitive question is whether lesion anatomy dictates the effectiveness of robot therapy.

Consider patients with middle cerebral artery lesions (MCA) involving the pre-motor area (PMC), or sparing it. **Table 4** and the top row of **Figure 5** show the motor power scores of 33 of these patients (14 patients with lesion involving the PMC and 19 patients with spared PMC). Reclassifying our patients according to whether the PMC and the subcortical efferents from the PMC were damaged suggested that those patients with spared PMC were better at the first and final evaluation on the MP scale. Similar results were obtained for the other scale of impairment of the shoulder and upper arm muscles, the MS1 (data not shown). In particular, they demonstrated the facilitator effect PMC sparing had on shoulder and upper-arm motor function.

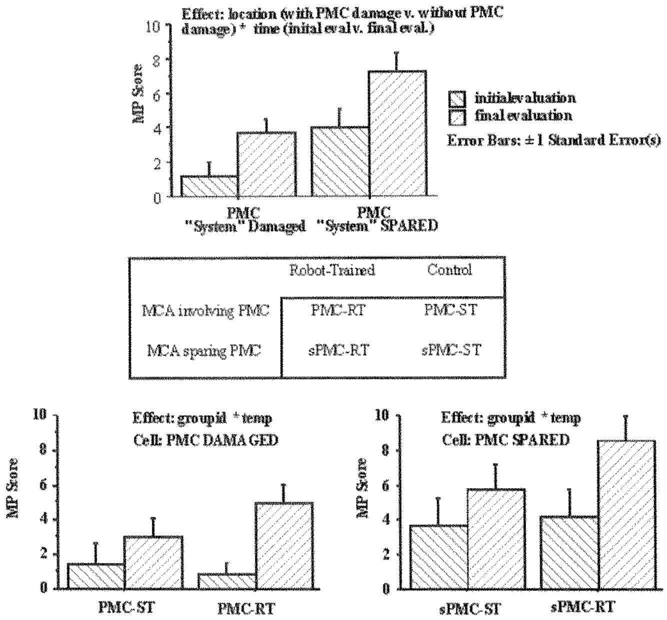
These results are in agreement with recent studies indicating that patients for whom the PMC was spared (sPMC) recover significantly better than the ones with lesion foci that includes the PMC (50). Patients with cortical and subcortical damage of comparable volume had different functional outcome depending on whether the PMC was damaged. Results from other investigators using a variety of functional cerebral imaging techniques have also pointed to the PMC as a crucial region of activation during motor recovery (51,52). The emerging importance of the PMC in motor recovery finds additional support in the *in vivo* experimental literature.

Because we are also interested in the effect of robot training, these data were further analyzed consid-

Table 4.
Motor power scores

(out of 20)	PMC (14 patients)	sPMC (19 patients)
MP-admission	1.19±0.83	3.95±1.10
MP-discharge	3.66±0.86	7.24±1.02

Motor power scores at admission and discharge of patients with MCA lesion including or excluding the premotor territories (PMC or sPMC, respectively; ANOVA for groups being different; p-value 0.0027).



	Robot-Trained	Control
MCA involving PMC	PMC-RT	PMC-ST
MCA sparing PMC	sPMC-RT	sPMC-ST

Figure 5.
Positive interaction robot training and PMC status.

ering such training as an additional independent variable (bottom row of **Figure 5**). While the sample size was small, there was a clear trend in both the PMC-spared and -damaged groups for the robot training to positively impact the outcome, i.e., patients in the robot-aided sensorimotor training program, independent of PMC status, improved more than the subjects in the control group. This finding further suggests that while lesion anatomy is clearly the critical factor, it does not dictate the effectiveness of robot therapy.

One must take the above results with the appropriate caveats: Anatomy may not be destiny, but it appears to be a close relative. Understanding motor recovery will allow us to best challenge fate. For example, in the 56-patient replication study, a histogram of the number of patients per lesion volume (bins of 25 cm^3) suggested a bimodal distribution, indicating two distinct classes of patients: one with lesion volume smaller than 100 cm^3 (N=42) and another with lesions larger than 100 cm^3 (N=14). While an analysis of whether the differences in motor outcome might result from lesion volume alone were unrevealing, of those in the group of 42 patients with smaller lesion volume, the ones exposed to the robot sensorimotor training outranked the remaining ones not exposed to this kind of focused exercise (MP and MS1 scales).

Robot-based Measurements

A common language facilitates communication. Therefore in the previous sections, we refrained from using any measurement but standard clinical scales to make the point to the clinical community that our results to date indicate that exercise therapy has a genuine positive effect on brain recovery following a stroke. Yet while we might be able to impact the neuro-recovery process, we have only touched the tip of the iceberg and harder questions lie ahead. Of particular importance is how to tailor and optimize therapy to the particular patient's need. While clinical scales alone can help us trace the big picture, their coarse nature requires extensive and time-consuming trials and on top of that they fail to show us details important for optimizing therapy. Our goal in this section is twofold: First, we want to emphasize that robotic technology offers the potential benefit of new measurements—and deeper insight—into the process of recovery from neurological injury; and second, we want to emphasize the importance of back-driveable robots not only for delivering therapy, but also for measurement.

To that end we will revisit the example depicted in **Figure 6** (18), which shows the movements of a recovering stroke patient attempting to draw a circle in a horizontal plane. At week 6 post-stroke, the patient had just regained the control of the elbow extension and can perform the task; the movement is rather uncoordinated and jerky. By week 11 the path is more nearly circular and the speed fluctuations have diminished and it would appear eminently reasonable to conclude that the movement at week 11 is superior to the movement at week 6. Nevertheless, the standard clinical measures failed to indicate any difference; in fact, the most sensitive of these clinical measures for shoulder and elbow, the Motor Status Score for shoulder and elbow (MS1), indicated the same score value.

Another example of the insight that may be acquired from robot data is presented in **Figure 7**, which shows

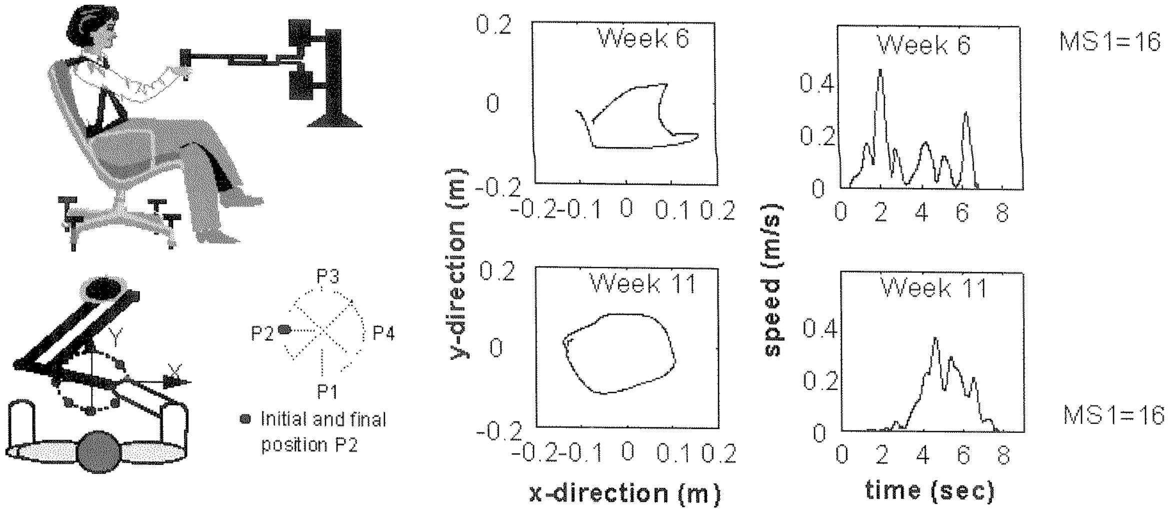


Figure 6.
Movements of a recovering stroke patient attempting to draw a circle in a horizontal plane. The left column shows a plan view of the patient's hand path. The right column shows the tangential speed of the hand along the path plotted against time. Note that the scored value for MS1 (shoulder and elbow) was the same.

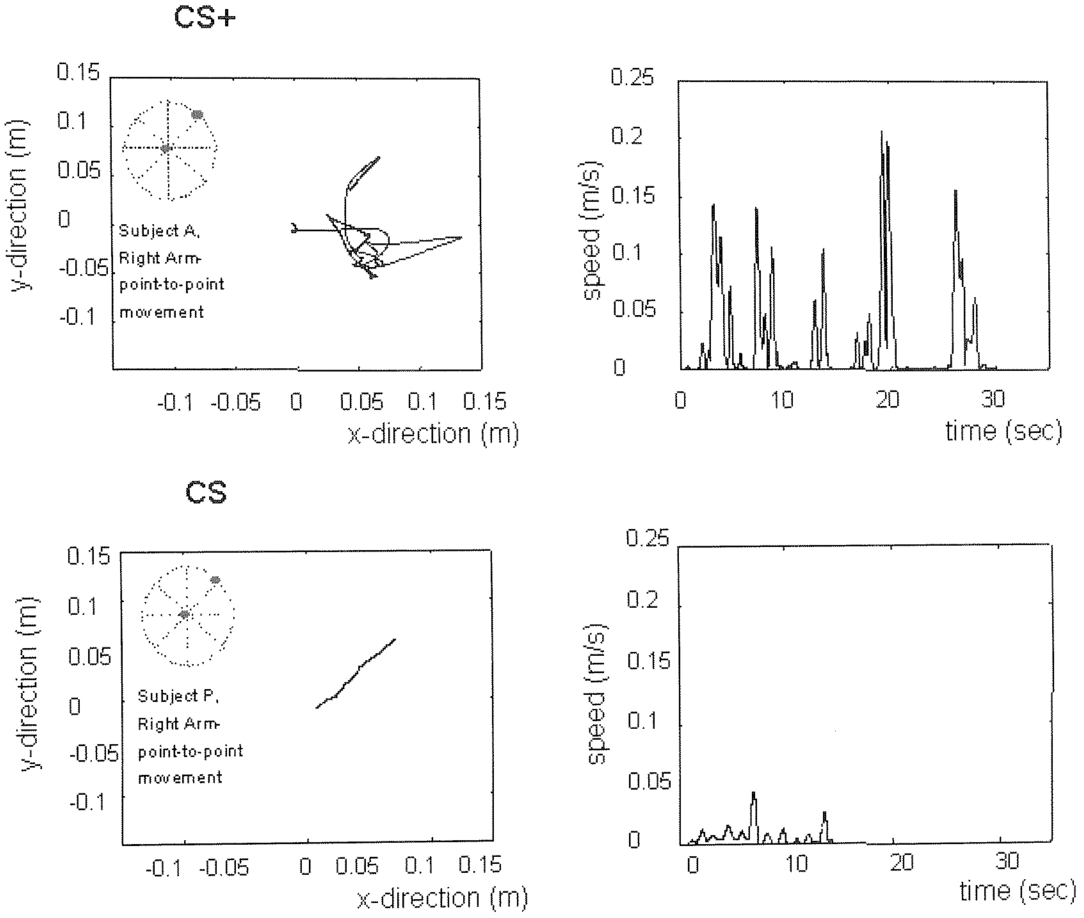


Figure 7.
Reaching movements made by patients with corpus striatum lesion—CS (8.9 cm^3) and corpus striatum plus cortex—CS+ (109.9 cm^3) lesions. The left column shows a plan view of the patients' hand path attempting a point-to-point movement. The right column shows hand speed.

representative reaching movements made by two patients with different brain lesions. The left column shows a plan view of the patient's hand path when attempting to move from one position to another, as indicated. The right column shows the tangential speed of the hand along the path plotted against time. The top two rows were recorded from a patient with a single ischemic infarct in the motor cortex. The bottom two rows were recorded from a patient with a single ischemic infarct in the basal ganglia outside the internal capsule. Comparing the two patients, note that the patient with the basal ganglia lesion appears to move exceptionally slowly; however, the hand path is generally well aimed towards the target position. In contrast, the patient with the motor cortical lesion makes a series of moves with much higher peak speeds (approaching the movement speeds of unimpaired subjects) but each of these movements appears to be poorly aimed at the target position (53). The cortical patient's mis-aiming appears to be consistent with the observation (e.g., 54) that activities of populations of motor cortical neurons are correlated with the intended direction of reaching movements.

Observations such as these are the basis for our belief that robot-based instrumentation can provide finer-grained, higher-resolution measures of recovery. In fact, borrowing from a century-old conjecture (55), we have been developing techniques for movement analysis based on the concept of segmentation of apparently continuous movement (submovements). By studying the kinematics of movements made by patients with neurological injury, we may have discovered the kinematic profile of a primitive unit action (56). This temporal motor primitive is in line with Woodworth's conjecture that a repertoire of movement primitives constitutes the fundamental building blocks of complex motions. The fact that we have identified a precise mathematical characterization of submovement kinematics provides the key information that makes it possible to de-convolve continuous movements objectively and reliably into their component submovements. That is, it changes a "hard inverse problem" into a filtering problem.

These examples illustrate the potential benefit of better measurements that afford deeper insight into the process of neuro-recovery. Furthermore, they illustrate the importance of back-driveable robots not only for delivering therapy, but also for concomitantly measuring patient behavior. As with the design of any instrument, we must ensure that the measurement process does not corrupt the quantity to be measured. In this case, to avoid suppressing dynamic details of patient movement the robot should not encumber the patient; it should have minimal mechanical impedance (ideally zero). This is not a trivial requirement. To be specific, the data shown in **Figures 6** and **7** and also shown in Krebs et al. (56) could not have been obtained using a typical commercial robot, even with active force feedback, because that approach cannot produce the "back-driveability" required to move smoothly and rapidly to comply with the patient's actions.

Increase in Productivity

One common misperception is that robot therapy would ultimately replace human-administered therapy. To those afraid of this kind of technology, we offer a quote by Isaac Asimov "I do not fear computers, I fear the lack of them." Just as word processors opened the door to markedly increased efficiencies for office workers, robot assistants promise the same for rehabilitation clinicians. We envision the role of the therapist evolving from delivering repetitive labor-intensive manual treatment to a more supervisory decision-making capacity. Productivity will soar if the concept of robot-aided classrooms lives up to its promise, i.e., delivering individual therapy to more than one patient at a time without compromising quality or dosage. **Figure 8** shows a composite illustrating the concept of a classroom in which a therapist oversees four patients either directly or via a robot-aided workstation, as each patient interacts with a robot.

In keeping with our caution against raising premature and/or unrealistic clinical expectations, our initial objective is to establish that robot therapy can be equivalent in quality to traditional methods, but it will deliver therapy at reduced cost and with increased institutional controls. We therefore are working to identify patterns of use for the device, together with all underlying reimbursement mechanisms, to confirm that from an efficiency-minded clinic's point of view, robot therapy confers the benefits of desirable technology innovations: the accomplishment of everyday tasks more efficiently, and with increased precision. Toward that end, we are identifying how Burke's patient census translates into daily hours of usage of the device, as well as the nature of those hours (e.g., diagnostic *versus* therapy delivery). We are also identifying the sources of reimbursement for robot therapy—Medicare, private payor, fee for service—and how those sources may affect the daily hours of use of the device. As an ancillary issue, we are identifying patients who may be amenable to commencing robot therapy at the clinic, and then continuing with a home-based therapy.

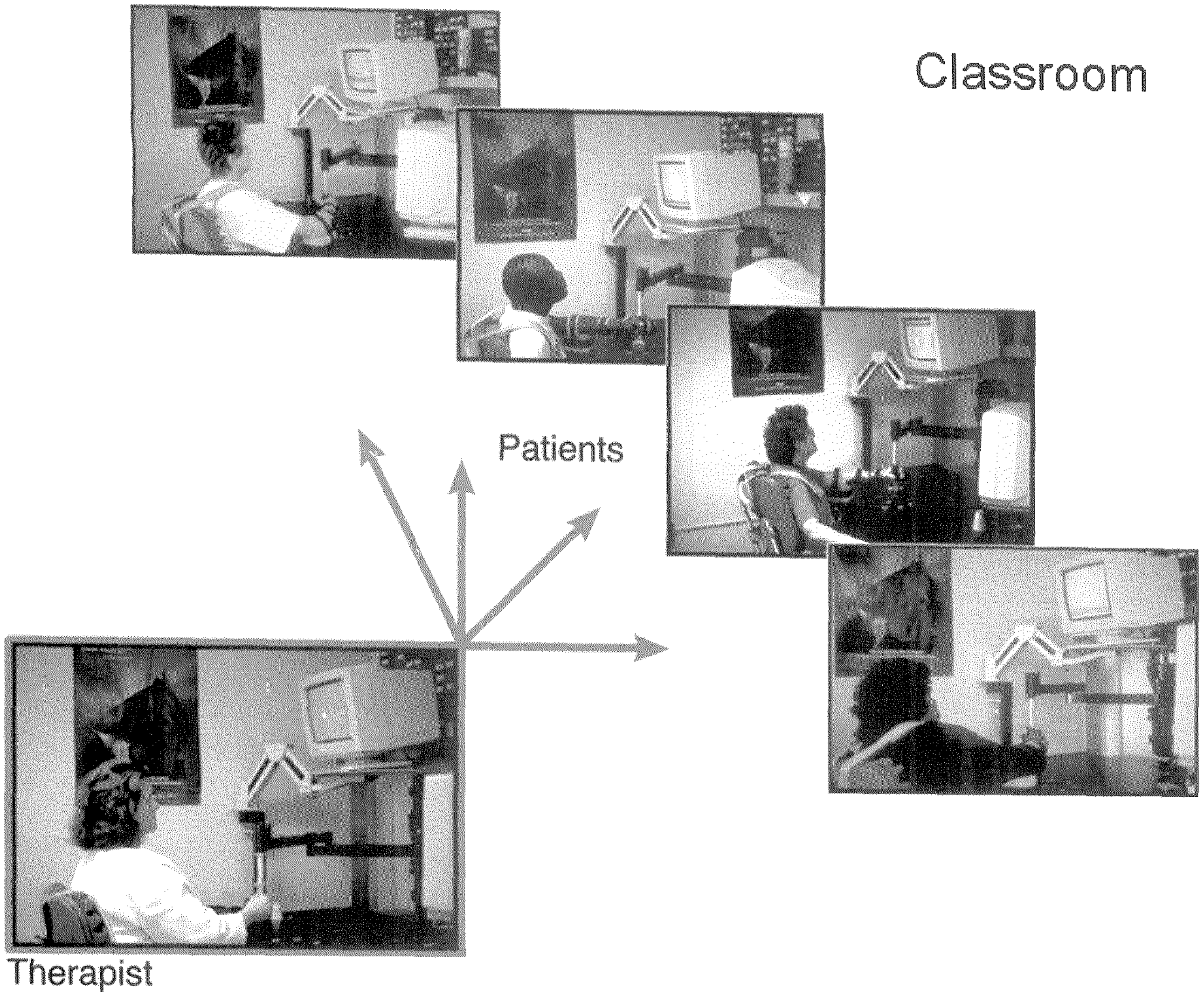


Figure 8.
Robot-aided classroom.

CONCLUSION

At the onset of this research we had to confront squarely (and solve!) a critical question: If anatomy is destiny, can we influence it? This research question has been the focus of our concern over the last 5 years, and in presenting a few of our clinical results of over 2,000 hours of robot-aided therapy with 76 stroke patients, we have barely scratched the surface. Nevertheless, all of the indications to date suggest that robot-aided sensorimotor training does have a genuinely positive effect on reduction of impairment and the reorganization of the adult brain. Our results are in agreement with one of the prominent themes of current neuroscience research into the sequelae of brain injury or trauma, which posits that activity-dependent plasticity underlies neuro-recovery. In other words, there is good reason to believe that neurological changes that may underlie recovery are facilitated by the standard practice of providing targeted sensorimotor activity, and that this can be accomplished using robot technology.

Nevertheless, the fundamental mechanisms underlying neuro-recovery following a stroke remain poorly understood. Considerable further study is needed to understand the biological basis of recovery and to optimize treatment to meet a particular patient's needs. To that end, we need the appropriate "microscope." Back-driveable robots are the key enabling technology that allow us concomitantly to control the amount of therapy delivered to a patient while objectively measuring the patient's performance. We also plan to use present technology to establish the practicality and economic feasibility of clinician-supervised, robot-administered therapy, including classroom therapy. We feel quite optimistic that the march of progress will accelerate substantially in the near future and allow us to transfer this technology from the research realm to the everyday treatment of stroke survivors.

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