A Randomized Controlled Comparison of Upper-Extremity Rehabilitation Strategies in Acute Stroke: A Pilot Study of Immediate and Long-Term Outcomes

Carolee J. Winstein, PhD, Dorian K. Rose, MS, Sylvia M. Tan, MS, Rebecca Lewthwaite, PhD, Helena C. Chui, MD, Stanley P. Azen, PhD

ABSTRACT. Winstein CJ, Rose DK, Tan SM, Lewthwaite R, Chui HC, Azen SP. A randomized controlled comparison of upper-extremity rehabilitation strategies in acute stroke: a pilot study of immediate and long-term outcomes. Arch Phys Med Rehabil 2004;85:620-8.

Objective: To evaluate the immediate and long-term effects of 2 upper-extremity rehabilitation approaches for stroke compared with standard care in participants stratified by stroke severity.

Design: Nonblinded, randomized controlled trial (baseline, postintervention, 9mo) design.

Setting: Inpatient rehabilitation hospital and outpatient clinic.

Participants: Sixty-four patients with recent stroke admitted for inpatient rehabilitation were randomized within severity strata (Orpington Prognostic Scale) into 1 of 3 intervention groups. Forty-four patients completed the 9-month follow-up.

Interventions: Standard care (SC), functional task practice (FT), and strength training (ST). The FT and ST groups received 20 additional hours of upper-extremity therapy beyond standard care distributed over a 4- to 6-week period.

Main Outcome Measures: Performance measures of impairment (Fugl-Meyer Assessment), strength (isometric torque), and function (Functional Test of the Hemiparetic Upper Extremity [FTHUE]).

Results: Compared with SC participants, those in the FT and ST groups had significantly greater increases in Fugl-Meyer motor scores ($P=.04$) and isometric torque ($P=.02$) posttreatment. Treatment benefit was primarily in the less severe participants, where improvement in FT and ST group Fugl-Meyer motor scores more than doubled that of the SC group. Similar results were found for the FTHEU and isometric torque. During the long term, at 9 months, the less severe FT group continued to make gains in isometric muscle torque, significantly exceeding those of the ST group ($P<.05$).

Conclusions: Task specificity and stroke severity are important factors for rehabilitation of arm use in acute stroke. Twenty hours of upper extremity–specific therapy over 4 to 6 weeks significantly affected functional outcomes. The immediate benefits of a functional task approach were similar to those of a resistance-strength approach, however, the former was more beneficial in the long-term.

Key Words: Disability evaluation; Randomized controlled trials; Rehabilitation; Stroke; Upper extremity.

STROKE IS THE LEADING cause of serious, long-term disability among American adults. Each year in the United States, approximately 730,000 people have strokes, and nearly 400,000 survive with some level of neurologic impairment and disability.[1] The cumulative total of stroke-affected Americans is over 4 million, and over $51.2 billion is the estimated annual burden from stroke-related disability.[2] Despite the enormity of these statistics, there have been few randomized controlled trials (RCTs) evaluating the effectiveness of poststroke rehabilitation interventions.[3]

Of all impairments that result from stroke, perhaps the most serious and most in need of rehabilitation effectiveness studies is hemiparesis of the upper limb. Population-based statistics indicate that between 73% and 88% of first-time strokes (infarctions only) result in an acute hemiparesis of the upper and/or lower limbs.[4,5] The upper limbs are of special concern because the impact of upper-extremity impairments on disability and health is so marked,[6,7] only limited attention has been given to upper-extremity rehabilitation after stroke, and functional recovery of the arm and hand are generally limited compared with that for the lower extremities.[8,9]

A 1997 critical review of stroke rehabilitation based on a meta-analysis reported that the published reports of constraint-induced movement therapy (CIMT) provided "the most promising evidence that motor recovery can be facilitated (after stroke).. . ."[10(p3)] Recent applications of CIMT for upper-extremity recovery have shown promise in chronic stroke,[11] acute stroke,[12] and with even less intensity in subacute stroke.[13] Others showed that repetitive training of isolated movements against resistance in 15-minute bouts twice a day for 4 weeks improved the outcome of motor rehabilitation of the paretic hand in subacute stroke.[14] However, little is known about how critical factors such as the focus of therapy (function vs strength), intensity of therapy, and stroke severity interact to impact the effects of rehabilitation therapy.

This study was designed as a small-scale (N=60) RCT to provide pilot data for feasibility of a larger, phase III multisite trial. The primary objective was to evaluate the posttreatment benefits and persistence 9 months after stroke of 2 different

From the Department of Biokinesiology and Physical Therapy (Winstein, Rose, Lewthwaite), Statistical Consultation and Research Center, Department of Preventive Medicine, Keck School of Medicine (Tan, Azen), and Department of Neurology, Keck School of Medicine (Winstein, Chui), University of Southern California, Los Angeles, CA; and Rancho Los Amigos National Rehabilitation Center, Downey, CA (Lewthwaite, Chui).

Presented in part at the American Physical Therapy Association, Combined Sections Meeting, February 17, 2001, San Antonio, TX; North American Stroke Association, August 17, 2001, San Diego, CA; American Physical Therapy Association, Combined Sections Meeting, February 23, 2002, Boston, MA; and International Stroke Symposium, April 27, 2002, Kansas City, MO.

Supported in part by the National Institute of Child Health and Human Development, National Institutes of Health (grant no. HD36212-02), and the Foundation for Physical Therapy (PODS scholarship award).

No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit upon the author(s) or upon any organization with which the author(s) is/are associated.

Reprint requests to Carolee J. Winstein, PhD, Dept of Biokinesiology and Physical Therapy, University of Southern California, Health Sciences Campus, 1540 E Alcazar St, CHP 155, Los Angeles, CA 90089-9006, e-mail: *Winstein@usc.edu.*

0003-9993/04/8504-8239$30.00/0
doi:10.1016/j.apmr.2003.06.027

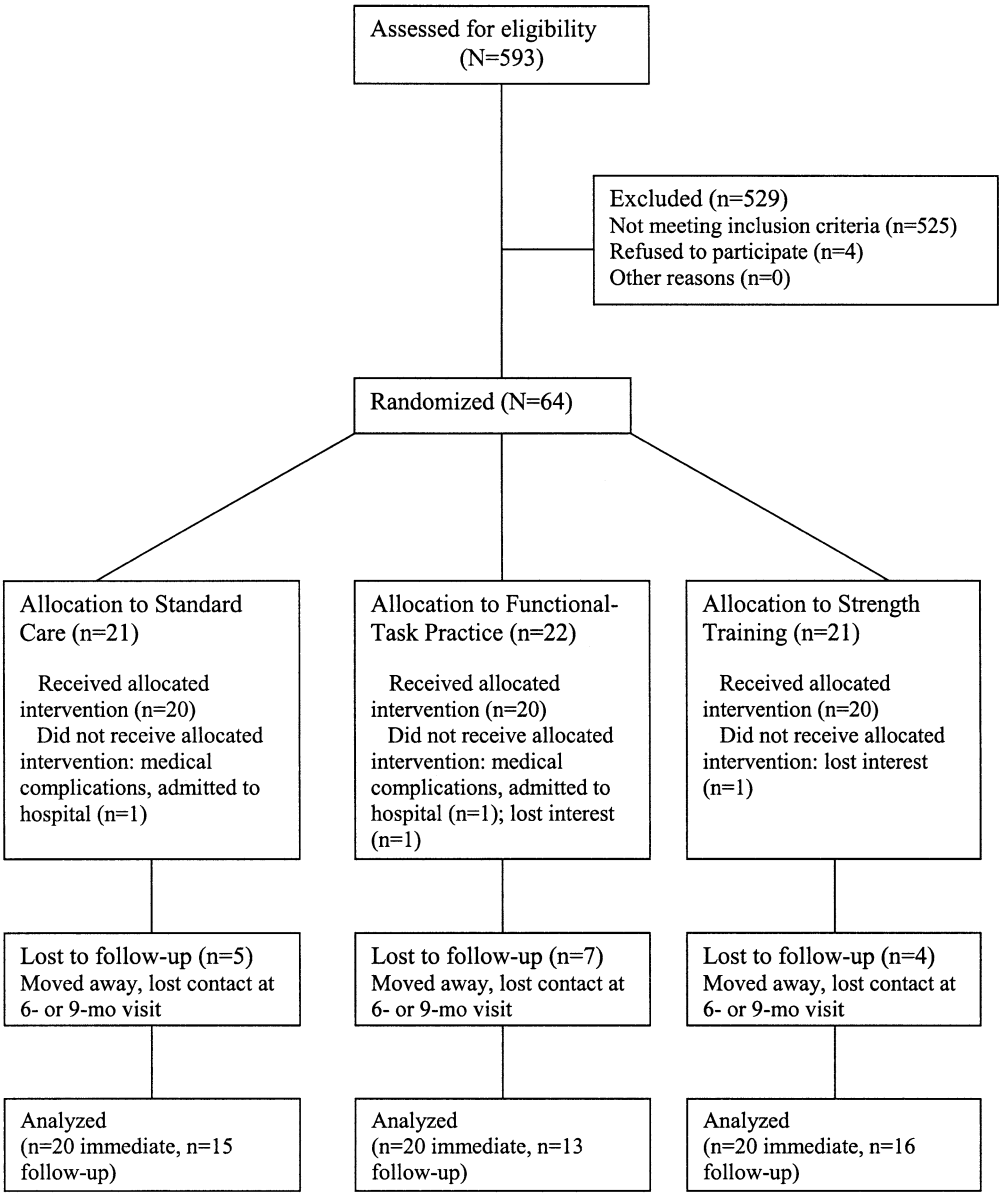

Fig 1. Flow of participants through each stage of the RCT.

treatment approaches applied in the acute phase, one that emphasized functional task practice, the other strength and motor control. Preliminary results of the present study were reported previously in abstract form.[15,16]

METHODS

Participants

Participants between the ages of 29 and 76 years were recruited from the Neuro-rehabilitation Service at Rancho Los Amigos National Rehabilitation Center (RLANRC) in Downey, CA. Medical charts of all new admissions were consecutively reviewed for eligibility. Eligibility criteria included first-time stroke from infarction in the anterior circulation confirmed by magnetic resonance imaging or computed axial tomography scan, onset of stroke from 2 to 35 days before study entry, and a FIM™ instrument[17] total score at admission of 40 to 80. Participants were excluded if they had peripheral nerve or orthopedic conditions that interfered with arm movement, had cardiac disease that limited function by exertional dyspnea, angina, or severe fatigue, or had subarachnoid hemorrhage without evidence of infarction, progressive hydrocephalus, previous history of brain injury, or severe aphasia, neglect, agitation, or depression that could limit participation. Early in the recruitment phase, we broadened our inclusion criteria to include patients with hemorrhagic or pontine stroke and a wider range of admission FIM scores. See figure 1 for details of how participants were allocated into randomized groups.

Study Design, Severity Index, and Outcome Measures

Eligible participants were randomized to groups within severity strata by means of the Orpington Prognostic Scale[18] (OPS), using a blocking factor that was not identified to study

personnel. This protocol guaranteed that the proportion of subjects in each group was similar across strata. Given the planned small sample size, we used a median split and categorized participants with OPS score between 1.6 and 4.1 as "less severe," and those with scores between 4.2 to 6.8 as "more severe." Individual treatment allocations were hand-delivered in sealed envelopes by the data manager (SMT) to the study coordinator (DKR). The next designated envelope was opened only on enrollment of the next eligible subject. The principle investigator (CJW) was blinded throughout the duration of the study.

Participants were tested by a single evaluator (DKR) on primary and secondary outcomes pretreatment (baseline), posttreatment, and at 6 and 9 months after stroke. Although the evaluator was not blinded to group membership, she was trained and her performance was standardized according to our Manual of Procedures for administration of each of the primary outcome measures. Primary outcome measures included the upper-extremity portion of the Fugl-Meyer physical assessment with motor, sensory and range of motion (ROM) sections[19]; isometric torque at the shoulder, elbow wrist[20]; grip and pinch force; and the Functional Test of the Hemiparetic Upper Extremity[21,22] (FTHUE). Secondary outcome measures included the self-care and mobility portions of the FIM.[17] Maximum isometric force was measured with a hand-held dynamometer from the flexor and extensor muscle groups of the shoulder, elbow, and wrist.[20] Lever arm, the distance from the joint center to dynamometer placement for each of the joints, was used to calculate torque. The 6 torque measures were summed for a composite isometric torque score that was used for analysis. For the FTHUE, we report the number of items successfully completed out of a 17-item hierarchically arranged battery of functional tasks (appendix 1).

Rehabilitation Interventions

The study protocol was approved by the University of Southern California Institutional Review Board (IRB) and the Los Amigos Research and Education Institute IRB. After eligible participants gave written informed consent, they were randomized to standard care (SC), task-specific functional training (FT) plus SC, or strengthening and motor control (ST) plus SC. Standard care for the upper extremity was delivered primarily by occupational therapists and could include muscle facilitation exercises emphasizing the neurodevelopmental treatment approach,[23] neuromuscular electric stimulation applied primarily for shoulder subluxation, stretching exercises, activities of daily living including self-care where the upper limb was used as an assist if appropriate, and caregiver training.

Task-specific functional training focused on the systematic and repetitive practice of tasks that could be performed within the level of available voluntary motion. Tasks were progressively arranged and customized to account for any unique proximal-to-distal recovery patterns of reaching and grasping actions. All tasks were designed to be standard, repeatable, and to have some functional goal (eg, pointing, grasping, stirring). The principles of motor learning were applied as the physical therapists systematically provided knowledge of results and progressed task difficulty to keep the participants challenged, motivated, and engaged.[24] Doable tasks were ordered randomly during practice to facilitate learning and to mimic real-world activities.[25] For FT task training, none of the items contained in the FTHUE were chosen as tasks for systematic practice.

Strengthening and motor control training used resistance to available arm motion to increase strength. Exercises were performed using either eccentric, isometric, or concentric muscle contractions, and concentric exercises were performed in a gravity-lessened position or against gravity, if possible. These exercises were progressed to repetitions against resistance using free weights, Theraband strips, or grip devices for the fingers. Progression of exercises used a protocol of high-intensity progressive resistance training of shoulder, elbow, wrist, and hand motions. If, during the resistance phase, undesired associated movements or an increase in muscle tone was evident, the training bout was interrupted for a short period and then resumed after muscle tone was reduced or undesired associated movements were diminished. This strengthening program was implemented on alternate days for 3 days a week. On other days, the same exercises were performed with less resistance and greater speeds. As with the FT intervention, knowledge of results (eg, load, number of repetitions) was provided systematically during the therapy.

Therapy Dose

Basing our decision on practical concerns pertaining to the inpatient setting and previous findings with humans[14,26] and primates,[27] we chose 1h/d, 5d/wk for 4 weeks (20h) as an effective and tolerable dose for this trial. Because the average inpatient stay was less than 4 weeks (23.1 ± 11.1d), the additional time needed to fulfill the 20 hours stipulated by the trial was completed in an outpatient setting. Two experienced physical therapists, each a board-certified neurologic clinical specialist, applied the 20 hours of treatment to the FT and ST groups over 4 to 6 weeks. This treatment regimen was separate (ie, it was added to the standard dose of occupational and physical therapy).

Statistical Analyses

Demographics, stroke history, and baseline functional evaluations were compared across randomized groups. We used analysis of variance (ANOVA) for means and chi-square procedures for proportions. Analyses of the study end points were conducted for all evaluable participants (ie, with a baseline and at least a posttreatment evaluation). To evaluate treatment differences in functional performance across the 3 treatment arms, we used analyses of covariance (ANCOVAs) procedures. For posttreatment outcomes at discharge, the dependent variable was the change in each functional evaluation (posttreatment baseline), and the covariate was the baseline score. For the long-term (9-mo) treatment outcomes, the dependent variable was the change in each functional evaluation (9-mo poststroke posttreatment); the covariates were both baseline and posttreatment scores. In cases for which the distribution of the change score was nonnormal, log-transformations were performed. When significant differences across the treatment groups were found, multiple comparisons were conducted using the Tukey adjustment procedure. Treatment group by time interactions were evaluated using repeated-measures ANOVA.

We also conducted 2 planned subgroup analyses. First, we contrasted outcomes between the SC group and the combined FT and ST group at both time points (posttreatment, long term). This allowed us to contrast the effects of standard care with those of a focused upper-extremity treatment program. Further, we contrasted outcomes (across all 3 treatment arms, and between the SC vs FT+ST groups) according to stroke severity classification using "less severe" or "more severe" baseline OPS. For these subgroup analyses, we used similar statistical methods to assess treatment benefits. All statistical analyses used SAS[a] and were conducted at the .05 significance level.

RESULTS

To achieve the planned sample size of 60 evaluable participants (20 per treatment arm), a total of 64 participants were

Table 1: Baseline Demographics, Stroke History, and Functional Evaluations

Characteristic	SC (n=20)	FT (n=20)	ST (n=20)	*P* Value*
Gender				
Men	12 (60)	9 (45)	12 (60)	.68
Women	8 (40)	11 (55)	8 (40)	
Age group (y)				
<35	2 (10)	0 (0)	0 (0)	.32
35–75	18 (90)	19 (95)	20 (100)	
≥75	0 (0)	1 (5)	0 (0)	
Type of stroke				
Ischemic	16 (84)	16 (84)	19 (100)	.23
Intracerebral hemorrhage	3 (16)	3 (16)	0 (0)	
Subarachnoid hemorrhage	0 (0)	0 (0)	0 (0)	
Side of lesion				
Left	12 (60)	13 (65)	16 (80)	.47
Right	8 (40)	7 (35)	4 (20)	
Location of lesion				
Cortical	1 (6)	2 (13)	2 (12)	.93
Subcortical	15 (94)	13 (81)	15 (88)	
Both	0 (0)	1 (6)	1 (6)	
Pontine stroke	2	4	2	
Time since onset (d)	15.4±5.5	15.5±6.0	17.3±10.6	.70
Length of inpatient stay (d)	25.2±14.9	22.4±6.9	21.8±10.8	
OPS				
Less severe (1.6–4.1)	14±70	12±60	14±70	.83
More severe (4.2–6.8)	6±30	8±40	6±80	
FIM				
Admission total	61.35±15.54	59.55±14.30	62.50±15.46	.74
Mobility subtotal	11.20±6.56	10.50±4.54	12.20±5.41	.62
Self-care subtotal	17.05±4.66	16.20±4.32	19.10±5.59	.16
Upper-extremity Fugl-Meyer				
ROM	23.25±1.21	23.60±0.82	22.55±2.39	.12
Pain	22.40±2.50	22.40±2.09	21.65±3.33	.60
Sensory	9.95±3.65	8.60±4.10	9.60±3.72	.52
Motor function	23.55±22.31	18.70±16.40	19.85±19.56	.72
FTHUE	5.40±6.52	4.30±5.35	5.15±5.97	.83
Isometric torque (kg/cm)	361.17±462.09	305.30±302.10	419.34±557.25	.73
Grasp and pinch force (kg)				
Grip	2.10±6.83	0.85±3.80	2.20±6.80	.73
Palmar pinch	0.83±1.94	0.25±0.66	0.83±1.92	.44
Lateral pinch	1.00±1.99	0.73±1.45	1.55±2.86	.48

NOTE. Values are frequency (column %) or mean ± standard deviation (SD).
*Chi-square exact for proportions, ANOVA for continuous variables.

recruited and randomized (see the CONSORT flow diagram, fig 1). Four participants were inevaluable because they withdrew from the study before completing the 20-hour treatment period. No significant differences existed between the evaluable and inevaluable participants in demographics, stroke history characteristics, and functional performance measures. Table 1 summarizes the demographic and stroke history characteristics for each treatment arm, including severity strata and baseline measures. No significant differences existed across the treatment groups in demographic or stroke history characteristics. Overall, 33 (55%) participants were men, and only 3 (5%) participants were younger than 35 or older than 75 years. The most prevalent type of stroke was ischemic (85%). The majority of strokes occurred on the left side and resulted in right hemiparesis (68%). The most prevalent location of lesion was subcortical (72%). The average time since onset ± standard deviation (SD) was 16.1±7.7 days.

No significant baseline differences were found across the treatment groups in OPS, FIM, upper-extremity Fugl-Meyer, FTHUE, isometric torque, or grasp and pinch force (see table 1). Overall, the majority of participants (40 participants, 67%) were categorized as less severe on the OPS. The 2 OPS groups differed at baseline for clinical tests of impairment, function, and disability, with the less severe group upper-extremity Fugl-Meyer motor capability (impairment) significantly higher (27.25±19.94) than that for the more severe OPS group (7.60±8.66) (*t* test, $P<.0001$). Consistent with the greater upper-extremity motor capability, the less severe group also had less pain (Fugl-Meyer pain score: less severe group, 22.65±2.26; more severe group, 21.15±3.17; $P=.04$), greater sensory perception (Fugl-Meyer sensory score: less severe group, 10.78±2.27; more severe group, 6.60±4.71; $P=.001$), and could accomplish, on average, the first 7 items on the FTHUE, which included stabilizing a package (FTHUE score: less severe group, 7.03±6.18; more severe group, 0.80±1.32; $P<.0001$), whereas the more severe group, on average, could not accomplish even the second item of bringing the hand into the lap. The 2 OPS groups also differed on the overall admis-

Table 2: Posttreatment Change From Baseline Scores in Functional Performance: All Evaluable Participants

Characteristic	SC (n=20)	FT (n=20)	ST (n=20)	FT+ST (n=40)	*P* Value*	*P* Value†
FIM						
Mobility	14.10±7.58	15.00±6.22	15.00±7.14	15.00±6.61	.86	.62
Self-care	17.00±5.17	15.85±5.21	16.15±5.81	16.00±5.45	.74	.54
Upper-extremity Fugl-Meyer						
ROM	−0.60±1.93	−1.90±2.02	−0.75±2.00	−1.33±2.07	.14	.16
Pain	−0.60±1.79	−1.60±2.80	−0.70±2.30	−1.15±2.57	.36	.36
Sensory	0.75±1.33	0.75±2.99	1.30±2.23	1.03±2.62	.35	1.00
Motor function‡	9.05±7.60	16.50±13.74	18.20±13.54	17.35±13.49	.08	.04
FTHUE	3.35±3.63	4.70±4.27	4.25±4.33	4.48±4.25	.61	.34
Isometric torque (kg/cm)‡	220.58±260.26	369.29±367.90	353.53±296.25	361.41±329.79	.05	.02
Grasp and pinch force (kg)						
Grip	1.50±4.38	1.25±6.70	1.70±3.45	1.48±5.27	.96	.98
Palmar pinch	1.00±1.65	1.35±1.95	1.45±1.82	1.40±1.86	.66	.36
Lateral pinch	1.74±2.29	1.72±2.09	1.28±2.03	1.50±2.05	.65	.67

NOTE. Values are mean ± SD.
*Assessing overall group differences; *P* value obtained from ANCOVA (covariate=baseline value).
†Assessing differences in combined treatment (FT+ST) versus standard care; *P* value obtained from ANCOVA (covariate=baseline value).
‡Normalizing log-transformations.

sion FIM score, with the less severe group's score (67.08±13.51) being significantly higher than that for the more severe group (50.10±11.82; $P<.0001$). This difference in disability level was similarly reflected in the FIM mobility score (less severe, 13.13±5.72; more severe, 7.75±2.38; $P<.0001$) and FIM self-care score (less severe, 19.13±4.78; more severe, 14.10±3.43; $P<.0001$).

Posttreatment Outcomes

The prescribed intervention for the FT and ST groups was 20 hours over a 4- to 6-week period (≈1h/d, 5d/wk). Compliance was nearly perfect with only 1 exception, a participant in the FT group who, after discharge and because of travel distance from home to the training site (RLANRC), completed only 15 of the 20 hours of the intervention. Table 2 presents the posttreatment changes in functional performance for the 3 treatment arms. ANCOVAs revealed significant differences across the treatment groups in isometric torque ($P=.05$) and marginally significant differences in Fugl-Meyer motor scores ($P=.08$). However, no significantly different pairwise differences were detected using the Tukey procedure. In contrast, subgroup analyses revealed (table 2) that, compared with those in the SC group, participants in the FT and ST groups had significantly greater improvements in Fugl-Meyer motor scores ($P=.04$) and in composite isometric torque ($P=.02$).

Table 3 presents the change in functional performance posttreatment for participants with less severe OPS score. Significant differences in Fugl-Meyer motor score improvement were found across the 3 treatment groups ($P=.02$). Multiple comparisons revealed that the FT and ST groups improved significantly more than the SC group (Tukey, $P<.05$). Subgroup analyses revealed that participants in the FT and ST groups had a 22-point improvement in the upper-extremity Fugl-Meyer motor score compared with a 9.4-point improvement for the SC group ($P=.005$). Also, there was nearly a 90% greater improvement in the average change score for the FTHUE in the

Table 3: Posttreatment Change From Baseline Scores in Functional Performance: Participants With Less Severe OPS Score

Characteristic	SC (n=14)	FT (n=12)	ST (n=14)	FT+ST (n=26)	*P* Value*	*P* Value†
FIM						
Mobility	15.79±7.11	17.50±5.84	15.64±4.63	16.50±5.20	.79	.49
Self-care	17.00±4.37	17.58±5.63	17.50±5.73	17.54±5.57	.50	.52
Upper-extremity Fugl-Meyer						
ROM	−0.29±1.33	−1.42±1.44	−0.43±1.40	−0.88±1.48	.16	.20
Pain	−0.36±1.86	−1.17±1.70	−0.29±2.27	−0.69±2.04	.55	.46
Sensory	0.43±1.09	0.83±2.17	0.50±1.09	0.65±1.65	.61	.35
Motor function‡‖	9.36±8.05*†	21.75±13.57*	21.71±14.44†	21.73±13.77	.02	.005
FTHUE	3.14±3.53	6.42±4.50	5.43±4.67	5.88±4.53	.12	.05
Isometric torque (kg/cm)‡	250.46±276.79	495.47±427.51	407.46±312.54	448.08±364.98	.10	.03
Grasp and pinch force (kg)						
Grip	2.21±5.12	2.08±8.70	2.43±3.94	2.27±6.43	.98	.99
Palmar pinch	1.32±1.87	2.25±2.09	2.07±1.86	2.15±1.93	.42	.19
Lateral pinch	2.26±2.47	2.71±2.19	1.82±2.22	2.23±2.21	.65	.99

NOTE. Values are mean ± SD.
*Assessing overall group differences; *P* value obtained from ANCOVA (covariate=baseline value).
†Assessing differences in combined treatment (FT+ST) versus standard care; *P* value obtained from ANCOVA (covariate=baseline value).
‡Normalizing log-transformations.
‖Means noted with the same symbols differ significantly from each other at .05 (Tukey multiple comparison procedure).

Table 4: Long-Term Change From Posttreatment Scores in Functional Evaluations: All Randomized Participants

Characteristic	SC (n=15)	FT (n=13)	ST (n=16)	FT+ST (n=29)	*P* Value*	*P* Value†
FIM						
Mobility	5.67±5.47	4.54±5.78	2.44±1.82	3.38±4.15	.61	.36
Self-care	6.07±4.62	6.38±5.59	2.75±4.34	4.38±5.19	.39	.39
Upper-extremity Fugl-Meyer						
ROM	−0.33±1.45	−0.46±2.76	−2.13±2.96	−1.38±2.94	.10	.14
Pain	−1.00±2.88	−1.23±2.42	−1.19±4.00	−1.21±3.33	.83	.54
Sensory	0.07±1.03	0.69±2.36	0.25±0.68	0.45±1.64	.66	.41
Motor function‡	8.33±11.26	5.77±4.49	5.38±9.11	5.55±7.29	.30	.24
FTHUE	2.53±3.36	2.15±2.41	2.38±4.10	2.28±3.39	.96	.91
Isometric torque (kg/cm)	368.83±298.87	393.57±338.59	165.86±298.34	267.93±331.81	.10	.26
Grasp and pinch force (kg)						
Grip	2.47±8.59	8.31±8.86	3.25±6.65	5.52±7.99	.41	.40
Palmar pinch‡	1.03±1.26	2.12±2.00	1.44±1.85	1.74±1.92	.45	.38
Lateral pinch	1.55±1.76	2.50±2.35	1.94±2.52	2.19±2.41	.51	.36

NOTE. Values are mean ± SD.
*Assessing overall group differences; *P* value obtained from ANCOVA (covariates=baseline and discharge values).
†Assessing differences in combined treatment (FT+ST) versus standard care; *P* value obtained from ANCOVA (covariates=baseline and discharge values).
‡Normalizing log-transformations.

FT and ST groups than in the SC group ($P=.05$). Finally, there was nearly an 80% greater improvement in the average change score for composite isometric torques in the FT and ST groups compared with that for the SC group ($P=.03$).

No treatment differences were found for participants with more severe OPS scores across the 3 treatment arms or between the SC and combined FT+ST group (data not shown). There were no treatment group differences in the self-care or mobility FIM scores overall, or by severity subgroups.

Long-Term Outcomes

A total of 44 (73%) participants (15 in the SC group, 13 in the FT group, 16 in the ST group) completed the 9-month follow-up. Overall, there were no significant differences across the treatment arms (table 4). However, marginally significant differences were noted for upper-extremity ROM and isometric torque (both $P=.10$), primarily due to changes in the ST group that exhibited a greater decrease in ROM score and smaller increase in composite torque than that of the other 2 groups.

For the less severe participants (table 5), significant differences existed in improvement across the 3 treatment groups in isometric torque ($P=.02$) and palmar pinch force ($P=.03$). Marginally significant differences in improvement across the 3 treatment groups were found in Fugl-Meyer motor scores ($P=.07$) and lateral pinch force ($P=.07$). Multiple comparisons revealed that the FT group improved significantly more than the ST group in composite isometric torque (Tukey, $P<.05$) during this interval and showed similar (although nonsignificant) trends for Fugl-Meyer motor scores and palmar pinch. The FT group improved significantly more than the SC group in palmar pinch (Tukey, $P<.05$) and showed similar (although nonsignificant) trends for lateral pinch. Subgroup analyses revealed that, compared with participants in the SC group, participants in the FT and ST groups had significantly greater

Table 5: Long-Term Change From Posttreatment Scores in Functional Performance: Patients With Less Severe Orpington Score

Characteristic	SC (n=11)	FT (n=9)	ST (n=12)	FT+ST (n=21)	*P* Value*	*P* Value†
FIM						
Mobility	4.18±5.42	2.33±2.69	2.92±1.38	2.67±2.01	.92	.68
Self-care	6.00±4.34	6.33±5.61	2.92±3.58	4.38±4.76	.21	.20
Upper-extremity Fugl-Meyer						
ROM	−0.64±1.29	0.11±1.97	−1.58±3.06	−0.86±2.73	.44	.50
Pain	−1.00±2.86	−0.44±1.88	−1.42±4.06	−1.00±3.27	.83	.86
Sensory	−0.18±0.75	0.00±1.00	0.17±0.58	0.10±0.77	.52	.27
Motor function‡	4.82±6.93	6.44±4.56	2.08±3.70	3.95±4.56	.07	.44
FTHUE	1.45±2.25	1.56±2.19	0.58±0.67	1.00±1.55	.35	.93
Isometric torque‖	336.04±306.34	558.92*±261.31	140.19*±334.33	319.65±365.89	.02	.56
Grasp and pinch force (kg)						
Grip	2.73±10.09	12.00±8.25	4.33±7.43	7.62±8.52	.20	.22
Palmar pinch‡‖	0.95*±1.06	3.06*±1.67	1.75±1.99	2.31±1.93	.03	.05
Lateral pinch	1.16±1.65	3.22±2.17	2.13±2.82	2.60±2.56	.07	.06

NOTE. Values are mean ± SD.
*Assessing overall group differences; *P* value obtained from ANCOVA (covariates=baseline and discharge values).
†Assessing differences in combined treatment (FT+ST) versus standard care; *P* value obtained from ANCOVA (covariates=baseline and discharge values).
‡Normalizing log-transformations
‖Means noted with the same symbols differ significantly from each other at .05 (Tukey multiple comparison procedure).

improvement in palmar pinch ($P=.05$) and marginally greater improvement in lateral pinch ($P=.06$).

Repeated-measures ANOVA for participants in the less severe group who completed the 9-month follow-up revealed a significant group by visit interaction for the Fugl-Meyer motor score ($P=.0001$), composite isometric torque ($P=.006$), palmar pinch force, and FTHUE (both $P=.02$). Figure 2 illustrates the longitudinal pattern of change in these performance measures.

For participants in the more severe group, there were also significant differences in improvement across the 3 treatment groups in isometric torque ($P=.004$, data not shown). Multiple comparisons for composite isometric torque revealed that the FT and ST groups showed significantly less improvement than the SC group ($P<.05$). These results, however, need to be interpreted with caution because of the small sample (n=4/group) and the relatively large SDs, especially for isometric torque.

There were no adverse events reported for the total cohort of randomized participants.

DISCUSSION

Previous research[11,28,29] on the benefits of focused therapy on functional outcomes has focused on chronic stroke, partly because "spontaneous recovery" is viewed as a confound for interpretation of treatment effects. Here, we show that spontaneous recovery and the "natural history" of upper-extremity recovery can be modified by an appropriate intervention applied during the acute rehabilitation phase after stroke. Nakayama et al[9] concluded that recovery of upper-extremity function in the majority of patients is achieved only by compensation using the unaffected upper extremity. Recently, Shelton et al[30] showed that admission motor impairment can guide treatment aimed at reducing motor impairment better than use of compensatory techniques.

How can we determine which patients might respond to a focused upper extremity-specific therapy program? Our study used the OPS[16] to stratify subjects by severity. For the most part, only those in the less severe group showed positive effects from the focused upper-extremity therapy program using outcomes of paretic limb performance. Indeed, the self-care portion of the FIM was insensitive to the focused therapy and its functional consequences. The importance of severity of arm impairment and response to therapy is emphasized in the recent literature,[30-33] but it is not routinely considered in rehabilitation practice.[34] Our present results provide evidence for the validity and usefulness of the OPS to guide upper-extremity rehabilitation treatment after stroke.

Compared with participants who received only standard care, less severely impaired participants who received functional task-specific training or resistance and strength training (ie, 20 additional hours of upper extremity–specific therapy distributed over 4 to 6wk beginning ≈2.5wk poststroke) had better immediate posttreatment functional outcomes. An additional round of specialized therapy was more effective than standard care therapy for reducing both impairment (Fugl-Meyer motor; composite isometric torque) and functional (FTHUE) contributors of disablement. One interpretation of these short-term results is that the essential therapeutic element was the extra round (20h) of therapy and not the content of the therapy (function vs strength). Several recent studies[31,32,35,36] showed the importance of intensity and duration of therapy for rate or magnitude of recovery. However, examination of the long-term results provides a compelling argument against a simple dose-response explanation of these therapeutic effects. At the 9-month follow-up visit and despite participant subject attrition in the less severe cohort, the FT group outperformed the ST group in improvement of upper-extremity isometric torque. The performance of the ST group approached the level of the SC group while the FT group accelerated its gain in

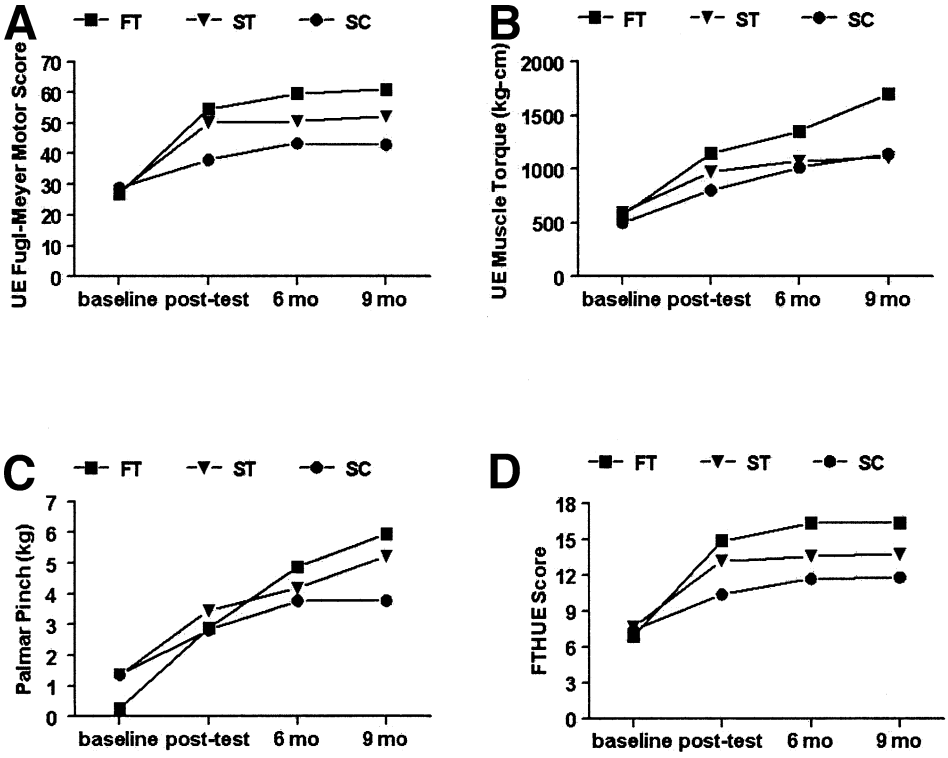

Fig 2. Time series plots comparing group means for the less severe cohort across the 4 evaluation points: (A) upper-extremity (UE) Fugl-Meyer motor score, (B) upper-extremity muscle torque—composite score, (C) palmar pinch, and (D) FTHUE.

upper-extremity isometric torque output over the posttreatment to 9-month interval. This difference at the 9-month point suggests that task specificity or its correlates—and not simply therapy dose—was critical to the treatment effect.

Interestingly, the FT group demonstrated better performance than the ST group on a strength (isometric torque) measure. One explanation for this counterintuitive result may be that functional task practice provided a more favorable and meaningful context for continued strength gains that were mediated through daily activity than did the resistance exercise training. There is evidence that intervention strategies that provide context-relevant, meaningful engagement in activities and promote self-management are more beneficial for skill acquisition and transfer than rote exercises or passive modalities.[37-39] This interpretation is supported in part by the FTHUE data. At 9 months poststroke, the SC group was able to complete an average 11.8±5.9 of the FTHUE tasks; whereas the ST and FT groups were able to complete an average 13.7±5.7 and 16.4±1.0 tasks, respectively (group by visit, $P=.02$).

In contrast to the less severe cohort, the more severe FT and ST groups showed significantly less improvement in isometric torque and Fugl-Meyer motor scores and marginally less improvement in ROM than the SC group; however, the small group sample limits credibility and warrants replication with a larger sample.

Our results run counter to those of Sunderland et al[40] who found little evidence after 1 year of the benefits of "enhanced treatment" on recovery of arm function after stroke; however, their treatment resembled more that of the ST group than the FT group in our study and showed long-term outcome similar to that of our ST group. Our results appear contrary to several recent reports[29] that have used CIMT and stressed the importance of "massed practice" for effectiveness. The functional task training used here is similar in some ways to that used in CIMT programs; however, there are differences between the 2 approaches, including the inclusion criteria, dose, intensity, timing, and conceptual foundation. These differences preclude comparison and warrant further research for several reasons. First, the impairment level of participants in this trial and even among those designated as less severe by OPS criteria, was more severe than that of typically recruited for CIMT trials. Further, we did not restrict inclusion based on subjective arm-use questionnaire ratings. Rather, we restricted inclusion for reasons related to the ability to participate in the therapy (eg, medically stable). Second, the amount of therapy was approximately 33% (20h) of a typical CIMT dose (60h). Third, the intensity was considerably reduced (≈1h/d) compared with approximately 6 hours a day of CIMT. Fourth, the timing of this intervention was much earlier postonset than most of the previous CIMT therapy trials (but see Dromerick et al[12] for recent exception). Finally, the fundamental principles of training are derived from a motor learning and skill acquisition perspective where the participant is challenged to solve the movement problem through practice of functional and meaningful tasks. Therefore, the principles of training underlying the FT protocol are derived from a framework of information processing and task specificity,[41] not an operant conditioning framework that supports behavioral "shaping" to progress practice.

Further research is needed to shed light on the essential ingredients underlying the effectiveness of these specialized, focused retraining programs for upper-extremity recovery after stroke hemiparesis. How critical is the constraint that is used in CIMT? How important is the problem-solving context for task practice compared with the behavioral shaping approaches of CIMT? Van der Lee et al[11] compared the effectiveness of an upper-extremity CIMT program with a bilateral neurodevelopmental therapy (NDT) training approach in a single-blind RCT in chronic stroke patients. Overall, the CIMT program was more effective 1 week after the last treatment session in some outcome measures; other outcome measures did not improve more for the CIMT group compared with the bimanual NDT group. Indeed, both groups improved to a similar degree, suggesting that there are some common essential elements that need further controlled clinical trials.

Further research is needed to understand the dose, intensity, and timing of training. In the present study, we applied an additional 20 hours of therapy specific to the upper extremity and distributed it over a 4- to 6-week period beginning 16 days after stroke to effect long-term changes in the less severely impaired participants. Current approaches using CIMT recommend 60 hours of training over a 10-day period but later after stroke (chronic, subacute). A reduced dosage and intensity of CIMT has recently been shown to be effective in a case report[13]; however, a larger scale systematic examination is needed to understand more fully the optimal dose, intensity, and timing of training.

Our trial was limited in scope because of its small sample size and was designed as a feasibility trial in preparation for a larger-scale, single-blind, multisite phase III RCT. Because of limited resources for personnel, our evaluator was also our recruiter and eligibility screener and therefore was not blinded to intervention group, which may be a source of bias. However, our data manager determined the group assignment and our evaluator used standard and reliable methods for all assessments. Both procedures contributed some degree of rigor to this phase I RCT.

CONCLUSIONS

Our RCT suggests that specificity of training and stroke severity are important factors for recovery and rehabilitation of arm use in the acute rehabilitation stage. An additional 20 hours of therapy specific to the upper extremity and distributed over 4 to 6 weeks positively influenced both immediate and long-term outcomes only for the less severe cohort. Although the immediate benefits of a protocol specific to a functional task were similar to those of a strength and motor control protocol, and both were superior to standard care immediately posttreatment, the functional-task protocol was most beneficial 9 months after stroke.

Acknowledgments: We gratefully acknowledge the work of primary physical therapists Walter Weiss, MPT, NCS, and Arlene Yang, MPT, NCS, who applied the majority of the investigational protocols with skill and enthusiasm. We also thank the physical therapists who assisted in the provision of the investigational therapy: Daniel Corey, DPT, Lisa Haubert, MPT, Betsy King, DPT, Patricia Pate, MPT, NCS, Christine Pekar, PT, William Robinson, MPT, and Julie Tilson, DPT. We thank the physicians of the Neurology Service of RLANRC including, Drs. Lily Atalla, Ziyad Ayyoub, Ginte Jasulaitis, Noopur Kapadia, Henry Levenson, David Saperia, Michael Scott, Jocely Sumcad, and Harvey La Tourette for their support of this clinical trial. We also thank the occupational therapy and physical therapy departments of RLANRC and Kathleen Gross, MA, OTR, director of occupational therapy, and Jorge R. Orozco, PT, NCS, director of physical therapy, for contributions to the study logistics, classification of standard care therapy, and daily tracking of therapeutic activities.

APPENDIX 1: FUNCTIONAL TEST OF THE HEMIPARETIC UPPER EXTREMITY[21,22]

Hierarchically progressed tasks

1. Associated reaction
2. Place hand into lap

3. Abduct shoulder
4. Hold a pouch
5. Stabilize a pillow
6. Stabilize a jar
7. Stabilize a package
8. Wring a rag
9. Hold a pan lid
10. Hook and zip a zipper
11. Fold a sheet
12. Blocks and box
13. Place box on shelf
14. Put coin in coin gauge
15. Form a cat's cradle
16. Screw in a light bulb
17. Remove rubber band

References

1. Kelly-Hayes M, Robertson JT, Broderick JP, et al. The American Heart Association Stroke Outcome Classification. Stroke 1998;29: 1274-80.
2. American Heart Association. Heart and stroke statistics—2003 update. Dallas: AHA; 2002.
3. Wagenaar RC. Effects of stroke rehabilitation. In: Kaufman T, editor. Rehabilitation of the geriatric patient. New York: Churchill Livingstone; 2000. p 130-4.
4. Foulkes MA, Wolf PA, Price TR, Mohr JP, Hier DB. The Stroke Data Bank: design, methods, and baseline characteristics. Stroke 1988;19:547-54.
5. Duncan PW, Goldstein LB, Horner RD, Landsman PB, Samsa GP, Matchar DB. Similar motor recovery of upper and lower extremities after stroke. Stroke 1994;25:1181-8.
6. Ostwald SK, Snowdon DA, Rysavy SD, Keenan NL, Kane RL. Manual dexterity as a correlate of dependency in the elderly. J Am Geriatr Soc 1989;37:963-9.
7. Olsen TS. Arm and leg paresis as outcome predictors in stroke rehabilitation. Stroke 1990;21:247-51.
8. Wade DT, Hewer RL, Wood VA, Skilbeck CE, Ismail HM. The hemiplegic arm after stroke: measurement and recovery. J Neurol Neurosurg Psychiatry 1983;46:521-4.
9. Nakayama H, Jorgensen HS, Raaschou HO, Olson TS. Recovery of upper extremity function in stroke patients: the Copenhagen stroke study. Arch Phys Med Rehabil 1994;75:394-8.
10. Duncan PW. Synthesis of intervention trials to improve motor recovery following stroke. Top Stroke Rehabil 1997;3:1-20.
11. van der Lee JH, Wagenaar RC, Lankhorst GJ, Vogelaar TW, Deville WL, Bouter LM. Forced-use of the upper extremity in chronic stroke patients: results from a single-blind randomized clinical trial. Stroke 1999;30:2369-75.
12. Dromerick AW, Edwards D, Hahn M. Does the application of constraint-induced movement therapy during acute rehabilitation reduce arm impairment after ischemic stroke? Stroke 2000;31: 2984-8.
13. Page SJ, Sisto S, Johnston MV, Levine P, Hughes M. Modified constraint-induced therapy in subacute stroke: a case report. Arch Phys Med Rehabil 2002;83:286-90.
14. Butefisch C, Hummelsheim H, Denzler P, Mauritz KH. Repetitive training of isolated movements improves the outcome of motor rehabilitation of the centrally paretic hand. J Neurol Sci 1995;130: 59-68.
15. Winstein CJ, Rose DK, Chui HC, et al. Recovery and rehabilitation of arm use after stroke [abstract]. J Stroke Cerebrovasc Dis 2001;10:197.
16. Rose DK, Winstein CJ, Tan SM, Azen SP, Chui HC. Comparison of upper extremity intervention strategies at six and nine months post-stroke [abstract]. Neurol Rep 2001;25:130.
17. Hamilton BB, Granger CV. Disability outcomes following inpatient rehabilitation for stroke. Phys Ther 1994;74:494-503.
18. Kalra L, Crome P. The role of prognostic scores in targeting stroke rehabilitation in elderly patients. J Am Geriatr Soc 1993;41:396-400.
19. Sanford J, Moreland J, Swanson LR, Statford PW, Gowland C. Reliability of the Fugl-Meyer assessment for testing motor performance in patients following stroke. Phys Ther 1993;73:447-54.
20. Bohannon R, Smith MB. Assessment of strength deficits in eight paretic upper extremity muscle groups of stroke patients with hemiplegia. Phys Ther 1987;67:522-5.
21. Wilson DJ, Baker LL, Craddock JA. Functional test for the hemiparetic upper extremity. Am J Occup Ther 1984;38:159-64.
22. Wilson DJ, Baker LL, Craddock JA. Protocol—functional test for the hemiplegic/paretic upper extremity. Downy (CA): Los Amigos Research and Education Institute; 1984.
23. Davies PM. Steps to follow: a guide to the treatment of adult hemiplegia. Berlin: Springer; 1985.
24. Winstein CJ. Motor learning considerations in stroke rehabilitation. In: Duncan PW, Badke MB, editors. Stroke rehabilitation: the recovery of motor control. Chicago: Year Book Medical; 1987. p 109-34.
25. Hanlon RE. Motor learning following unilateral stroke. Arch Phys Med Rehabil 1996;77:811-5.
26. Lincoln NB, Parry RH, Vass CD. Randomized, controlled trial to evaluate increased intensity of physiotherapy treatment of arm function after stroke. Stroke 1999;30:573-9.
27. Nudo RJ, Wise BM, SiFuentes F, Milliken GW. Neural substrates for the effects of rehabilitative training on motor recovery after ischemic infarct. Science 1996;272:1791-4.
28. Tangeman PT, Banaitis DA, Williams AK. Rehabilitation of chronic stroke patients: changes in functional performance. Arch Phys Med Rehabil 1990;71:876-80.
29. Taub E, Miller NE, Novack TA, et al. Technique to improve chronic motor deficit after stroke. Arch Phys Med Rehabil 1993; 74:347-54.
30. Shelton FD, Volpe BT, Reding M. Motor impairment as a predictor of functional recovery and guide to rehabilitation treatment after stroke. Neurorehabil Neural Repair 2001;15:229-37.
31. Parry RH, Lincoln NB, Vass CD. Effect of severity of arm impairment on response to additional physiotherapy early after stroke. Clin Rehabil 1999;13:187-98.
32. Partridge C, Mackenzie M, Edwards S, et al. Is dosage of physiotherapy a critical factor in deciding patterns of recovery from stroke: a pragmatic randomized controlled trial. Physiother Res Int 2000;5:230-40.
33. Barreca S, Wolf SL, Fasoli S, Bohannon R. Treatment interventions for the paretic upper limb of stroke survivors: a critical review. Neurorehabil Neural Repair 2003;17:220-6.
34. De Weerdt W, Feys H. Assessment of physiotherapy for patients with stroke [comment]. Lancet 2002;359:182-3.
35. Keith AR. Treatment strength in rehabilitation. Arch Phys Med Rehabil 1997;78:1298-304.
36. Kwakkel G, Wagenaar RC, Twisk JW, Lankhorst GJ, Koetsier JC. Intensity of leg and arm training after primary middle-cerebral artery stroke: a randomized trial. Lancet 1999;354:191-6.
37. Lin KC, Wu CY, Tickle-Degnen L, Coster W. Enhancing occupational performance through occupationally embedded exercise: a meta-analytic review. Occup Ther J Res 1997;17:25-47.
38. Watson G. Neuromuscular physiotherapy: encouraging self-management. Physiotherapy 1996;82:352-7.
39. Ma HI, Trombly CA, Robinson-Podolski C. The effect of context on skill acquisition and transfer. Am J Occup Ther 1999;53:138-44.
40. Sunderland A, Fletcher D, Bradley L, Tinson D, Hewer RL, Wade DT. Enhanced physical therapy for arm function after stroke: a one year follow-up study. J Neurol Neurosurg Psychiatry 1994; 57:856-8.
41. Winstein CJ, Wing AM, Whitall J. Motor control and learning principles for rehabilitation of upper limb movements after brain injury. In: Grafman J, Robertson I, editors. Plasticity and rehabilitation. Vol 9. Amsterdam: Elsevier Science; 2003. p 77-137.

Supplier

a. SAS Institute Inc, 100 SAS Campus Dr, Cary, NC 27513.