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Multicenter Randomized Trial of Robot-Assisted Rehabilitation for Chronic Stroke: Methods and Entry Characteristics for VA ROBOTICS

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Abstract

Background—Chronic upper extremity impairment due to stroke has significant medical, psychosocial, and financial consequences, but few studies have examined the effectiveness of rehabilitation therapy during the chronic stroke period.

Objective—To test the safety and efficacy of the MIT-Manus robotic device for chronic upper extremity impairment following stroke.

Methods—The VA Cooperative Studies Program initiated a multicenter, randomized, controlled trial in November 2006 (VA ROBOTICS). Participants with upper extremity impairment 6 months poststroke were randomized to robot-assisted therapy (RT), intensive comparison therapy

(ICT), or usual care (UC). RT and ICT consisted of three 1-hour treatment sessions per week for 12 weeks. The primary outcome was change in the Fugl-Meyer Assessment upper extremity motor function score at 12 weeks relative to baseline. Secondary outcomes included the Wolf Motor Function Test and the Stroke Impact Scale.

Results—A total of 127 participants were randomized: 49 to RT, 50 to ICT, and 28 to UC. The majority of participants were male (96%), with a mean age of 65 years. The primary stroke type was ischemic (85%), and 58% of strokes occurred in the anterior circulation. Twenty percent of the participants reported a stroke in addition to their index stroke. The average time from the index stroke to enrollment was 56 months (range, 6 months to 24 years). The mean Fugl-Meyer score at entry was 18.9.

Conclusions—VA ROBOTICS demonstrates the feasibility of conducting multicenter clinical trials to rigorously test new rehabilitative devices before their introduction to clinical practice. The results are expected in early 2010.

Keywords

Stroke; Rehabilitation; Robotics; Randomized clinical trial; Health economics

Stroke is a leading cause of long-term disability in the United States, with a prevalence of approximately 5.8 million.¹ Of the 780000 incident strokes that occur annually in the United States, an estimated 80% of stroke patients survive 1 year beyond their acute event,¹ with upwards of 70% left with residual deficits.^{2–5} Up to 85% of strokes initially result in paresis of the arm and hand,^{3–5} and 67% of chronic stroke patients reported nonuse/disuse of the affected arm as a major problem even 4 years after stroke.⁶ The national financial and public health burdens of chronic stroke are significant and were estimated at \$65.5 billion in 2008 alone.¹

Post-acute stroke rehabilitation can restore functional ability for some and is recommended⁷; however, rehabilitation is not typically prescribed during the chronic stages of stroke care. This is due, in large measure, to the traditionally held belief that more than 90% of recovery from poststroke impairment occurs within the first 6 months,^{8,9} presumably leaving little potential for recovery later in the disease process. Nonetheless, recent studies of neurorecovery for chronic stroke motor impairments have begun to challenge this idea by demonstrating that intensive, function-oriented interventions can lead to significant improvements well beyond the first year poststroke.^{10,11}

With the lack of established rehabilitative therapies for chronic stroke, there is a need to develop and rigorously test new therapies to improve the functioning and quality of life of individuals with chronic stroke impairment. The Veterans Health Administration has recognized this need, and the Department of Veterans Affairs (VA) Stroke Quality Enhancement Research Initiative has identified improvement in stroke rehabilitation as one of its main objectives to help advance the quality of care for veterans.¹²

Recent advances in robot rehabilitation technologies, in combination with an increased understanding of the latent potential for stroke neurorecovery, make this an opportune time to conduct multicenter clinical trials in the field of neurorehabilitation. Robotic devices are

promising systems for the delivery of neurorehabilitation because of their capacity for consistent delivery of therapy and prolonged use. Single-center controlled studies with individual and combined MIT-Manus modules, one of the most tested robotic devices for upper extremity rehabilitation, have demonstrated significant motor benefits in stroke patients.^{13–25} Confirmation of these results in a multicenter, randomized, controlled clinical trial represents a necessary and important next step toward establishing the safety and clinical effectiveness of this innovative modality. Therefore, the VA Cooperative Studies Program in collaboration with the VA Rehabilitation Research and Development Service initiated Cooperative Study #558, Robots in Chronic Stroke (VA ROBOTICS) to evaluate robot-assisted upper extremity rehabilitation in veterans with chronic stroke using the MIT-Manus device. This article provides an overview of the study design and baseline characteristics of the participants.

Methods

Overview of Study Design

VA ROBOTICS was designed as a multicenter, randomized, controlled clinical trial to test the safety and efficacy of robot-assisted therapy (RT) compared with intensive comparison therapy (ICT) and usual care (UC) for upper extremity neurorehabilitation in individuals with chronic stroke. The target population was veterans with chronic (at least 6 months after their acute event) upper extremity impairment due to stroke. The experimental intervention (RT) was a 36-session protocol using 4 robotic modules for the upper extremity. There were 2 control groups: usual care and an intensity-matched therapy based on conventional therapy activities. The study duration was 33 months, with 24 months of recruitment and 9 months of follow-up. Participants were evaluated at 6, 12, 24, and 36 weeks. To maintain contact and improve retention, all study participants were followed by telephone between regularly scheduled clinic visits. On completion of the 36-week evaluation, UC participants were offered their choice of RT or ICT as compassionate care. To ensure consistency in the delivery of therapy and the assessment of outcomes, training was provided to study staff prior to the initiation of enrollment and periodically throughout the study. Four VA medical centers participated in the trial: Baltimore, Maryland; Gainesville, Florida; Seattle, Washington; and West Haven, Connecticut. The organizational structure and study personnel for the trial are listed in the Appendix.

The trial was monitored for efficacy and safety by an independent data and safety monitoring board (DSMB). The study protocol was approved by the institutional review boards at each participating site and the human rights committee at the coordinating center. All participants gave written informed consent prior to study participation. The study was registered on [ClinicalTrials.gov](https://clinicaltrials.gov) ([ClinicalTrials.gov](https://clinicaltrials.gov) identifier, NCT 00372411).

Study Hypotheses and Objectives

The primary study hypothesis was that RT, when compared with ICT and UC, leads to greater improvements in upper extremity function at 12 weeks as measured by the Fugl-Meyer upper extremity motor function score.²⁶ The secondary hypotheses were that RT, when compared with ICT and UC, leads to improved functional performance and improved

quality of life as measured by the Wolf Motor Function Test and the Stroke Impact Scale. Two other secondary objectives were to evaluate early (6 weeks) and late (24 and 36 weeks) effects on the primary and secondary outcomes.

Tertiary objectives included health economics and kinematics. The health economics analysis will evaluate the cost effectiveness of RT for poststroke rehabilitation if it is more effective than UC. Kinematic and kinetic submovement changes were also collected from the MIT-Manus on all participants in an effort to better understand the neuroscience of rehabilitation and motor recovery.

Treatment Regimens

Robot-assisted therapy—Participants assigned to RT received 12 to 14 weeks of therapy (three 1-hour sessions per week for a maximum of 36 sessions) followed by 24 weeks of usual care. The MIT-Manus robotic training consisted of 4 training blocks each lasting 3 weeks (9 training sessions per block) designed to train movements of the shoulder, elbow, wrist, and hand. The training consisted of point-to-point reaching movements corresponding to targets on a computer monitor that focused on isolated movements for proximal or distal upper extremity limb segments (the first 3 blocks) and then on whole arm training (final block). Each session included approximately 60 minutes of robot training consisting of 1024 movements. The first 3-week block employed a planar shoulder-and-elbow training robotic device; the second 3-week block used an antigravity shoulder and grasp/hand device; and the third 3-week block used the wrist robot. The final block included used all 3 devices to integrate proximal (shoulder) to distal (wrist and hand) training of the upper extremity. The robots were controlled with the well-studied performance-based algorithm that assisted on an “as needed” basis when the participant was not moving, moving slowly, or aiming poorly and then challenged the participant by reducing assistance during movements, except for designed and intentional unassisted attempts during kinematic testing.^{17,27}

Intensive comparison therapy—ICT was designed to match RT in intensity, duration, and frequency of arm movements using conventional rehabilitative therapeutic activities and to serve as an active control group. Similar to RT, participants assigned to ICT received 12 to 14 weeks of therapy (three 1-hour sessions per week for a maximum of 36 sessions) followed by 24 weeks of usual care. The detailed ICT regimen has been previously described.²⁸ Briefly, an ICT session consisted of 20 minutes of warm-up and assisted stretching focusing on the adductor/internal rotator groups of the shoulder girdle and elbow flexors using a Monark Rehab Trainer (881E; Monark Bodyguard, Quebec, Canada) and a Hemi-Glide for humeral elevation (never to exceed 90° of flexion and in 6- to 7-minute interspersed sessions). Next were exercises for scapular stabilization (5 minutes), then static stretching of the adductor/internal rotator groups of the shoulder girdle and elbow flexors and extensors (5 minutes), followed by goal-directed movements using a skateboard system (10 minutes). For the final 10 to 12 minutes, the activities required the use of the affected limb to maintain balance and support while reaching with the unaffected limb as well as performing tasks that required reaching with the affected limb.

Usual care—Participants assigned to UC continued with whatever poststroke care they were currently receiving for the entire 36-week trial. Those in RT and ICT also continued with their usual care, and for all participants, the care received was not dictated by the study protocol but was documented. Typically, chronic stroke care includes medications (eg, antiplatelet agents, antihypertensive medications, and/or lipid-lowering medications) and recommendations for secondary stroke prevention (eg, smoking cessation, dietary modifications, and exercise), as well as follow-up visits or emergent visits as required. Ongoing rehabilitation was not expected to be included in chronic stroke care but was not prohibited; however, participants were requested to avoid any new arm rehabilitative approaches for the duration of the study.

Screening and Baseline Procedures

Individuals who had a verified diagnosis of stroke with resultant upper extremity paresis, by magnetic resonance imaging (MRI) or computed tomography (CT) neuroimaging, were screened for eligibility. Screening/baseline procedures included a review of medical conditions, a physical exam, and upper extremity assessments. If a participant was determined to be eligible, the following information was recorded: comorbidities from the Comorbidity Disease Index,^{29,30} stroke history (eg, type, location, and number of prior strokes), current medications, and behavioral and rehabilitation therapies used within the past month. Figure 1 lists the study inclusion and exclusion criteria.

Randomization and Blinding

Eligible participants were randomized to 1 of the 3 treatment groups stratified by site using a permuted block design. Randomization was performed centrally by the coordinating center. The treatment allocation ratio was 1:1:1 until the target sample size was reached for the RT versus UC comparison. Thereafter, the allocation was 1:1 for RT versus ICT until the end of the enrollment period. Although participants and investigators could not be blinded to treatment allocation, evaluators performing outcome assessments were blinded to treatment assignment.

Outcome Measures

The primary study outcome was the upper extremity motor function domain of the Fugl-Meyer Assessment of Sensorimotor Recovery after Stroke (FMA), a standard instrument for the quantitative clinical assessment of motor impairment and function.²⁶ The FMA upper extremity motor function domain assesses the severity of upper extremity motor impairment and consists of 22 items that are summed to produce an overall score, ranging from 0 (worst, completely plegic) to 66 (best, normal).

The secondary outcomes were the Wolf Motor Function Test (WMFT)^{31,32} and the Stroke Impact Scale, version 3.0 (SIS).³³ The WMFT is a function-based measure designed to provide an objective test of both proximal and distal control of the paretic arm for individuals after stroke. The WMFT consists of 17 items: 2 items measure strength (lifting and handgrip) and 15 measure speed to perform functional tasks. Speed is measured in seconds, with an upper limit of 120 seconds to accomplish a specific task. The SIS is a stroke-specific, clinically validated outcome measure that has been shown to be reliable,

valid, and sensitive to change. It is a self-reported measure that evaluates function and quality of life. SIS includes 59 items and assesses 8 clinically relevant domains. The specific domains of hand function, activities of daily living/instruments of daily living, and social participation were used for this trial.

For the health economics analysis, VA health care utilization and cost data were collected centrally through the VA electronic medical records system. Participant and therapist time were captured and will be used to estimate the intervention costs. Non-VA care and the Health Utilities Index (HUI) were collected by questionnaires at 12, 24, and 36 weeks. The HUI is a standardized multi-attribute utility instrument to assess an individual's health status. The health status scores were then converted into a utility score, which will be used in the quality adjusted life year calculation.^{34–36} The incremental cost-effectiveness ratio will be reported if RT is more effective than UC.

All serious adverse events and only nonserious adverse events that were related to participation in the trial were recorded. Additional safety measures included pain using the 10-point numerical rating scale for both general pain and arm specific pain, and spasticity using the Modified Ashworth Scale.³⁷

Sample Size

The trial was designed to test the superiority of RT when compared with ICT and UC; thus, a 1-sided type I error of .025 was used for the 2 primary treatment comparisons. Sample size was calculated for a 2-sample *t* test assuming: 90% power, a common standard deviation of 5, a mean difference of 3 units on the FMA between RT and ICT, a mean difference of 5 units between RT and UC, and a loss rate of 10%. A sample size of 26 participants per treatment group was required to detect the hypothesized 5-unit difference between RT and UC, whereas a sample size of 66 participants per treatment group was required to detect the hypothesized 3-unit difference between RT and ICT. Therefore, the total target sample size for the study was 158 participants.

The rationale for selecting the effect sizes for the sample size calculations was based on a 3-unit change on the FMA as representing the minimal clinically meaningful change. This threshold was established using data from the Kansas City Stroke Study database,³³ which showed that a 3-unit change on the FMA equated to a 20-point mean change on the SIS. Previous validation studies for SIS³⁸ showed that SIS changes in this range represented a change of sufficient magnitude to differentiate individuals based on their modified Rankin disability categories. Because RT was hypothesized to be much more effective than usual care, a 5-unit difference was deemed to be clinically relevant for this comparison.

Interim Monitoring and Analytical Plans

Interim monitoring—Interim monitoring of the “maximum information” $[(\text{variance}/n)^{-1}]$ for each treatment group and the 2 treatment comparisons was performed. The initial estimate of the FMA variance used in the sample size calculation was based on a relatively modest amount of prior information, whereas the estimated effect sizes were based on what was considered to be minimally clinically important differences. Therefore, information was

monitored based on the sample variance, with the goal of adjusting the sample size, if necessary, to achieve the maximum information for each treatment group and treatment comparison (ie, a type of adaptive design).

Treatment differences were monitored using an information-based group sequential trial^{39–43} with a flexible error spending approach based on sloped boundaries.⁴⁴ The unadjusted treatment differences for the primary outcome were monitored to terminate the trial early for efficacy or futility. East software, version 5.1 (Cytel, Inc, Cambridge, MA) was used to create the stopping boundaries.

The first interim analysis was conducted at 1 year; subsequently, enrollment into UC was terminated because the required information had been attained for the RT versus UC comparison. The second analysis was conducted just prior to the end of recruitment at 2 years. At that time, the DSMB recommended that the study continue until its scheduled conclusion with no sample size adjustment.

Analysis—The effect of treatment on the primary endpoint, that is, change on the FMA, will be analyzed by an analysis of covariance model, adjusted for site; the Comorbidity Disease Index^{29,30}; and the baseline FMA score. For participants missing the 12-week outcome, the most recent posttreatment assessment will be used, if available. Planned subgroup analyses include stroke location and presence or absence of multiple strokes. Subgroup effects will be evaluated via treatment by covariate interactions, although the power to detect them will be limited because of the small sample size. Secondary analyses will evaluate the early (6 weeks) and late effects (24 and 36 weeks) of treatment using longitudinal methods,⁴⁵ and the relationship between number of treatment sessions attended and outcome (dose response). Longitudinal models will be fitted using the method of maximum likelihood, which is valid when missing data are ignorable. In addition, sensitivity analyses will be conducted using multiple imputation techniques to impute missing values under different missingness mechanisms.^{46,47} The same analytic approach will be used for the secondary outcomes.

Results

Between November 6, 2006, and October 31, 2008, 200 veterans were screened and 127 were randomized: 49 to RT, 50 to ICT, and 28 to UC (Figure 1); 37 participants were enrolled at Gainesville, 36 at West Haven, and 27 at both Baltimore and Seattle. The most common reasons for exclusion included a FMA score out of the acceptable range of 7 to 38 (78% of those excluded), an upper extremity fixed contracture, joint pain, or other medical condition that would interfere with the therapy (14%); inability to complete the entire 36-week study due to a medical condition, transportation, or for other reasons (12%); and no verification of stroke via an MRI or CT Scan (6%).

The mean age of participants was 64.6 years (SD = 11.3); 96% were male and 78% were white (Table 1). The vast majority (85%) of participants had an ischemic stroke (for their index stroke), and the stroke occurred most frequently in the anterior circulation (58%); only 12% involved the posterior circulation. Although 20% of participants reported a clinical

history of a stroke in addition to their index stroke, 33% had a second stroke identified by MRI or CT imaging. The average time from the index stroke to enrollment was 56 months, ranging from 6 months to almost 24 years. The majority of participants (52%) had 3 comorbidity domains on the Comorbidity Disease Index, whereas only 13% had 1 domain (Table 1).

At entry, 81% of the participants were taking a lipid-lowering agent, 80% an antihypertensive agent, and 80% an aspirin or an antiplatelet agent. Behavioral activities to reduce stroke risk, such as exercising and dieting, were reported by 43% and 31% of participants, respectively. Seventeen percent reported receiving occupational and/or physical therapies, and 24% reported an average of 3.3 hours of arm therapy, defined as any prescribed rehabilitative therapy for improved arm functioning. The mean FMA score at entry was 18.9 (Table 1).

Discussion

VA ROBOTICS is the first multicenter, randomized, controlled clinical trial to assess the safety and efficacy of a technologically advanced robotic device for rehabilitation of the upper extremity. The study was designed using 1-sided testing because robot-assisted therapy was expected to be superior to both comparison groups and not worse than either one. Because usual care is highly variable and rarely includes rehabilitative therapy, an active control group (ICT) was added to match the contact time and movements in robot-assisted therapy.

The study also included assessments at the midpoint of the intervention phase (6 weeks) to examine the effect of a smaller treatment dose. At the time this study was designed, there was little information about the variability of the FMA to determine sample size relative to the data available for determining clinically relevant effect sizes. Therefore, we used an adaptive design strategy for sample size re-estimation based on the sample variance and not the effect size.

Although upper arm impairment with chronic stroke is relatively common, recruitment for VA ROBOTICS was difficult. Although nearly two thirds of eligible participants were enrolled in the study, the target enrollment was not achieved at the end of the planned enrollment period. Two major barriers to recruitment were the time demands placed on participants (activity-based treatments required three 1-hour sessions at the VA weekly over a 12–14 week period) and the related transportation difficulties in getting to and from the research sites. Because of these barriers, potential participants could only be drawn from a limited geographic area surrounding the participating sites. In addition, the therapy and evaluation sessions occurred during normal working hours; therefore, only those participants who were either not working or had flexible work schedules could attend these sessions. Because the study was limited to veterans only, this further restricted the eligible pool of potential enrollees.

Although representative of the gender ratio for the veteran population, a limitation of the study population is the small percentage of women. However, one would expect that if robot

therapy is effective in men, it would also be effective in women based on the results of past controlled single-center studies showing no gender effect on outcome.^{17,24,28} There is also no strong plausible mechanism to support the belief that these therapies would have a different effect in men when compared with women.

A number of participants had multiple strokes identified by either self-report (20%) or neuroimaging (33%), a finding that is comparable to the US stroke population where 23% of strokes that occur annually are reported as recurrent.¹ In contrast, prior single-center controlled trials using comparable robotic devices enrolled participants with a single clinical stroke, purposefully excluding patients with more than 1 stroke, and therefore, it is not known how individuals with multiple strokes would respond. The ability of any new therapy to improve recovery in individuals with multiple strokes would have a greater impact for the general stroke population. Thus, findings from VA ROBOTICS may provide more realistic implications for clinical practice.

Prior to study inception, it was believed that chronic stroke survivors would not be engaged in arm rehabilitation; however, nearly one quarter of the cohort reported an average of 3 or more hours of ongoing arm therapy per week and nearly one fifth reported receiving physical and/or occupational therapies. These findings are greater than expected and may be partially explained by the self-selection of highly motivated individuals or by greater access to rehabilitative services within the VA compared with the private sector. Rehabilitation therapy use in chronic stroke has not been widely reported in the literature. A 2005 Centers for Disease Control and Prevention survey showed that approximately 31% of stroke survivors received outpatient rehabilitation, but it did not distinguish when rehabilitation occurred (acute, subacute, chronic).⁴⁸

Although the VA ROBOTICS cohort was relatively young at the time of their index stroke (mean age 60 years), predominately male with at least a high school education, and consisted of long-term stroke survivors (average 5 years poststroke), their demographics are comparable with other studied veteran cohorts.^{30,49,50} The cohort is also representative of the general VA population who suffer primarily from ischemic strokes and with many comorbid illnesses. Moreover, it is similar to the national stroke survivor population on a number of sociodemographic and stroke-related characteristics, including race, stroke type, and prevalence rate of recurrent strokes.¹ Thus, the results of this trial should be generalizable to both the veteran and national stroke survivor population.

The VA ROBOTICS cohort also has similarities to the EXCITE cohort.⁵¹ The age and racial distributions were comparable. However, as expected in a veteran population, VA ROBOTICS had a much greater proportion of male participants than EXCITE (96% vs 64%). In both studies, the most prevalent stroke type was ischemic (85% in VA ROBOTICS vs 98% in EXCITE), and the incident stroke affected the dominant limb in less than 50% of the participants. One major difference between the studies was that EXCITE only enrolled subjects with a new, first-time subacute stroke (ie, within 3–9 months of their first stroke), whereas in VA ROBOTICS, participants' strokes were chronic and up to one third of participants had an additional stroke besides the index stroke per clinical history or by neuroimaging report. Another difference is that VA ROBOTICS enrolled participants with

moderate to severe upper extremity impairment (mean FMA = 18.9), whereas the EXCITE study population had milder upper extremity impairment (mean FMA = 41.8).

In summary, VA ROBOTICS is the first multicenter, randomized, clinical trial to test a robotic device for upper extremity neurorehabilitation of individuals with chronic stroke. This study demonstrates that well-designed clinical trials in the field of rehabilitation are feasible. The results are expected in early 2010.

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Appendix

The following persons participated in the VA ROBOTICS Study: *Planning Committee*—C. Bever, L. Brass,[†] P. Duncan, P. Guarino, H. Krebs, A. Lo, P. Peduzzi, R. Ringer, S. Stratton,[†] B. Volpe, T. Wagner; *Executive Committee*—A. Lo (chair), C. Bever, D. Bravata, P. Duncan, D. Federman, P. Guarino, J. Haselkorn, H. Krebs, P. Peduzzi, L. Richards, R. Ringer, B. Volpe, G. Wittenberg, T. Wagner; *Data and Safety Monitoring Board*—D. Good (chair), B. Dobkin, P. Lachenbruch, L. Lennihan, B. Turnbull; *VA Cooperative Studies Program Human Rights Committee, West Haven, CT*—R. Marottoli (chair), H. Allore, D. Beckwith, W. Farrell, R. Feldman, R. Mehta, J. Neiderman, E. Perry, S. Kasl, M. Zeman; *VA Site Investigators, Coordinators, Therapists and Evaluators—Baltimore, MD*: G. Wittenberg, J. McMorris-Marrow, S. Conroy, T. DeHaan, T. Jenkins, R. Asbury, R. Vanapalli; *Gainesville, FL*: L. Richards, S. Nadeau, C. Hanson, M. Wellborn, S. Davis, S. Arola, A. Sethi; *Seattle, WA*: J. Haselkorn, J. Powell, R. Frost, M. Donahue, I. Reep, V. Short, D. Blazey, A. Sloan; *West Haven, CT*: D. Federman, D. Bravata, N. Ranjbar, E. Billingslea, M. Laut, M. Dallas, J. Fawcett; *Consultants—The Burke Medical Research Institute, White Plains, NY*: B. Volpe, D. Lynch, A. Rykman; *Massachusetts Institute of Technology, Cambridge, MA*: H. Krebs; *Study Chair's Office VA Connecticut Healthcare System, West Haven, CT, and VA Medical Center, Providence, RI*—A. Lo (study chair), B. Corn, A. Maffucci; *VA Cooperative Studies Program Coordinating Center, VA Connecticut Healthcare System, West Haven, CT*—P. Peduzzi (director), M. Antonelli, (associate director of operations), L. Durant, P. Guarino, E. Jobes, S. Joyner, K. Kirkwood, V. McBride, M. Perry, J. Russo, J. Scholl, S. Stratton[†]; *VA Cooperative Studies Program Clinical Research Pharmacy Coordinating Center, Albuquerque, NM*—M. Sather (director), B. Del Curto, R. Ringer; *VA Cooperative Studies Program Site Monitoring, Auditing and Review Team, Albuquerque, NM*—C. Haakenson, D. Krueger, J. Taylor; *VA Cooperative Studies Program Health Economics Resource Center, VA Palo Alto Healthcare System, Menlo Park, CA*—T. Wagner; *VA Office of Research and Development, Clinical Science R&D, Washington, DC*—T. O'Leary (director), G. Huang (deputy director, Cooperative Studies Program); *VA Rehabilitation Research & Development Service, Washington DC*—M. Selzer (director), P. Dorn (deputy director).

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Figure 1. Flow of Participants in the Study

Note: MRI, magnetic resonance imaging; CT, computed tomography; UC, usual care; ICT, intensive comparison therapy; RT, robot-assisted therapy.

Table 1**Overall Study Design and Study Participation (N = 127)**

Entry Characteristic	
Age, mean (SD), min-max, years	64.6 (11.3), 28–95
Male sex, n (%)	122 (96)
Race, ^a n (%)	
White	99 (78)
Black or African American	28 (22)
Other	3 (2)
Hispanic ethnicity, n (%)	3 (2)
Education, n (%)	
Less than high school graduation	8 (6)
High school graduation	37 (29)
Some college	38 (30)
College graduation or advanced degree	44 (35)
Body mass index, mean (SD)	28.6 (4.8)
Blood pressure	
Systolic, mean (SD), mm Hg	130 (18)
Diastolic, mean (SD), mm Hg	75 (11)
At goal: systolic <140 and diastolic <90, or systolic <130 and diastolic <80 for diabetics, n (%)	76 (60)
Smoking status, n (%)	
Current	18 (14)
Former	72 (57)
Never	37 (29)
Medical history, n (%)	
Musculoskeletal problems	41 (32)
Diabetes	36 (28)
Emotional problems	35 (28)
Sleep disorder	32 (25)
Glaucoma or cataract	30 (24)
Myocardial infarction	25 (20)
Congestive heart failure	22 (17)
Cancer	20 (16)
Peripheral vascular disease	13 (10)
Chronic pain syndrome	13 (10)
Angina	8 (6)
Chronic obstructive pulmonary disease	7 (6)
Comorbidity Disease Index, n (%)	
1 Domain	16 (13)
2 Domains	45 (35)
3 Domains	66 (52)
Index stroke type, n (%)	

Entry Characteristic	
Ischemic	108 (85)
Hemorrhagic	19 (15)
Index stroke location, n (%)	
Anterior circulation (<1/3 of hemisphere)	48 (38)
Anterior circulation (>1/3 of hemisphere)	26 (20)
Small deep infarct	38 (30)
Posterior circulation	15 (12)
Handedness (self-report)/upper extremity affected by index stroke, n (%)	
Right/left	63 (50)
Right/right	42 (33)
Left/right	14 (11)
Left/left	4 (3)
Ambidextrous/right	3 (2)
Ambidextrous/left	1 (1)
Additional non-index stroke identified by imaging, n (%)	42 (33)
Additional non-index stroke identified by self-report, n (%)	26 (20)
Residual upper extremity impairment	11 (9)
Residual lower extremity impairment	12 (9)
Residual impairment of activities of daily living	9 (7)
No residual impairment	19 (15)
Months from index stroke to enrollment, mean (SD), min-max	56 (52), 6–283
Concomitant medications use, n (%)	
Lipid-lowering agents	103 (81)
Aspirin or antiplatelet agents	102 (80)
Antihypertensive agents	101 (80)
Warfarin	34 (27)
Antidepressants	48 (38)
Antianxiety agents	16 (13)
Prescription pain medications	24 (19)
Baclofen	14 (11)
Tizanidine	6 (5)
Other muscle relaxants	12 (9)
Behavioral interventions (self-report), n (%)	
Exercise (3 × per week for 20 minutes)	55 (43)
Dietary management	39 (31)
Upper extremity therapy	30 (24)
Occupational therapy	22 (17)
Physical therapy	21 (17)
Speech therapy	11 (9)
Smoking cessation	3 (2)
No therapy	34 (27)
Hours of upper extremity therapy per week, mean (SD)	3 (3)

Entry Characteristic		
Outcome assessments, mean (SD)		
Fugl-Meyer Upper Extremity Motor Function Score		18.9 (9.5)
Wolf Motor Function Test (seconds)		77.1 (33.1)
Stroke Impact Scale		49.4 (14.7)

^aMore than 1 race indicated by 3 participants.

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