ACRM
AMERICAN CONGRESS OF REHABILITATION MEDICINE

Archives of Physical Medicine and Rehabilitation

journal homepage: www.archives-pmr.org

Archives of Physical Medicine and Rehabilitation 2013;94:817-21

ORIGINAL ARTICLE

Size Doesn't Matter: Cortical Stroke Lesion Volume Is Not Associated With Upper Extremity Motor Impairment and Function in Mild, Chronic Hemiparesis

Stephen J. Page, PhD, MS, MOT, OTR/L, FAHA,[a,b] Lynne V. Gauthier, PhD,[c] Susan White, PhD[a]

From the [a]School of Health and Rehabilitation Sciences, [b]Neuromotor Recovery and Rehabilitation Laboratory (the "RehabLab"), and [c]Department of Physical Medicine and Rehabilitation, The Ohio State University Medical Center, Columbus, OH.

Abstract

Objectives: To determine (1) the relationship between lesion volume and upper extremity (UE) motor impairment using the UE section of the Fugl-Meyer (FM) assessment; and (2) the relationship between lesion volume and UE functional outcomes using the Arm Motor Ability Test (AMAT) Functional Ability (FA) and Time scales.

Design: Secondary retrospective analysis of randomized controlled trial data.

Setting: Outpatient rehabilitation clinic.

Participants: Subjects with chronic stroke (N=139, 83 men; mean age ± SD of all subjects, 56.7±11.2y; mean time ± SD since stroke onset, 59.6±65.6mo; 90 subjects with right hemiparesis) and stable, active, distal UE movement.

Intervention: Data were collected related to subjects' lesion volume and UE movement before their participation in a multicenter, randomized controlled trial.

Main Outcome Measures: FM and AMAT.

Results: Neither age nor lesion volume was related to FM performance. The *P* value for the regression coefficient of lesion volume was .045 in the AMAT FA model and .016 in the AMAT Time model. Lesion volume accounted for only an additional 1.7% (AMAT FA) to 3.1% (AMAT Time) of the variability in motor function and was not clinically meaningful.

Conclusions: Data suggest no relationship between lesion volume and UE impairment, and a small, clinically insignificant relationship between lesion volume and UE motor function. Stroke causes metabolic changes in intact regions and diffuse structural loss in anatomically remote regions from the infarction. These other factors may account for variance in motor outcomes after stroke.

Archives of Physical Medicine and Rehabilitation 2013;94:817-21

Upper extremity (UE) hemiparesis remains one of the most common and devastating stroke-induced impairments.[1] Several rehabilitative approaches targeting stroke survivors with active, distal movement in their paretic UEs are efficacious.[2-4] However, the factors that predispose individuals with this level of movement to benefit from such approaches are not fully understood.

The characteristics of a lesion, including its volume, have been suggested to influence stroke recovery,[5] but equivocal evidence[6-8] supports this precept. In the acute phase (<1mo postictus), weak relationships are reported between lesion volume and UE outcome.[9-11] Furthermore, the ongoing and erratic nature of neurologic recovery during this phase diminishes the validity of using a single measurement point to characterize UE recovery. Since lesion volume remains relatively constant during the chronic phase (>6mo postictus),[12] others have examined the associations between lesion volume and response to UE interventions administered chronically.[13-15] However, conclusions from chronic stroke intervention studies are also limited because of relatively small subject numbers (eg, Sterr et al,[13] n=10; Riley et al,[14] n=23) and varied treatment parameters (eg, treatment session duration) and study criteria used in these trials. Other variations during the

Supported in part by Northstar Neuroscience and the National Institutes of Health (grant no. R01AT004454-04).

No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit on the authors or on any organization with which the authors are associated.

0003-9993/13/$36 - see front matter © 2013 by the American Congress of Rehabilitation Medicine
http://dx.doi.org/10.1016/j.apmr.2013.01.010

intervention period (eg, differences in subject compliance, variances in how the treatments are administered) may also affect treatment response and, thus, the validity of conclusions made by chronic UE intervention studies.

To overcome the above shortfalls and better understand factors affecting UE motor status, the purposes of this study were to determine (1) the relationship between lesion volume and UE motor impairment using the UE section of the Fugl-Meyer (FM) assessment; and (2) the relationship between lesion volume and UE functional outcomes using the Arm Motor Ability Test (AMAT). This study enrolled a well-defined cohort of 139 subjects with stable, mild, chronic UE hemiparesis. We enrolled people with mild UE hemiparesis given the proliferation of efficacious therapies targeting subjects exhibiting this level of UE motor impairment.[2-4] To our knowledge, this is the largest study examining relationships among lesion volume and chronic UE motor status.

Methods

Study design

This study was a secondary analysis of data from the Everest randomized controlled trial of implanted cortical stimulation for UE movement in chronic stroke.[16] Outcome measures had been administered before and after intervention as part of the above trial. However, the current study focused solely on lesion volume and values obtained on the FM and AMAT before randomization or before any interventions had taken place. The study had been approved by all participating centers' institutional review boards or by outside institutional review boards.

Participants

Participants were recruited for the intervention trial from across the United States using several recruitment strategies, including print advertisements (eg, pamphlets) placed in clinics near enrolling sites, radio advertisements in the markets of enrolling sites, and print advertisements placed in national magazines whose primary subscribers were survivors of stroke. As volunteers came forward, inclusion and exclusion screening criteria were applied.

Inclusion criteria were as follows: (1) subjects must have had an ischemic vascular lesion (ie, stroke), as documented by computed tomography (CT) or magnetic resonance imaging (MRI) and occurring above the level of the midbrain; (2) stroke occurred >4 months before study enrollment; (3) subjects were medically and neurologically stable, as determined by medical history and documented neurologic examination; (4) score on the UE section of the FM assessment (described later) was ≥28 and ≤50, and there was active extension in the affected wrist of at least 5°; (5) age ≥21 years at time of enrollment; (6) for women of childbearing potential, a negative serum beta-human chorionic gonadotropin pregnancy test within 2 weeks of study entry and a willingness to practice adequate contraception during the study, because of the unknown potential impact of the surgery used in the trial on the fetus; and (7) the ability to comply with the study rehabilitation protocol.

Exclusion criteria were as follows: (1) hemorrhagic stroke; (2) >1 stroke; (3) any neurologic condition (beyond the stroke) or physical condition that impaired function of the affected arm; (4) history of seizure disorder or a spontaneous seizure that had occurred 1 month or longer from stroke, because of the possible impact of cortical stimulation on seizure activity; (5) neurologic condition that would likely reduce the safety of study participation, including central nervous system vasculitis, intracranial tumor, intracranial aneurysm, multiple sclerosis, or arteriovenous malformations; (6) moderate to severe hemispatial neglect and/or anosognosia involving the affected arm, because of the potential impact of this condition on ability to participate in the rehabilitative therapies provided during this trial; (7) severe sensory deficit including, but not limited to, a score of 2 on part 8 of the National Institutes of Health Stroke Scale (NIHSS); (8) inability to understand, cooperate, or comply with the study procedures; (9) severe spasticity, defined as an Ashworth score of 4 in any region of the affected arm; (10) change in oral spasticity medications occurring 2 weeks before enrollment, or botulinum toxin A injections in the affected arm 4 months before enrollment; (11) major active psychiatric illness that may interfere with treatment; (12) untreated or inadequately treated depression, defined by a score of ≥19 (out of 63) on the 21-question version of the Beck Depression Inventory; (13) modified Rankin score ≥4; (14) a substantial cardiopulmonary or metabolic disorder, which includes a current serum creatinine >3.0mg/dL, a total serum bilirubin >2.0mg/dL, or advanced chronic obstructive pulmonary disease; (15) increased risk for myocardial infarction or other major medical complications of general anesthesia or surgery; (16) terminal illness associated with survival of <12 months, because of the projected duration of the study; (17) inability to discontinue antithrombotic therapy (eg, antiplatelet agents or anticoagulants) perioperatively for device implantation and removal; (18) introduction in the 2 months before enrollment of a potentially confounding central nervous system drug (eg, amphetamines, antiepileptics, anxiolytics, antidepressants); (19) history of spinal cord injury, traumatic brain injury, or spontaneous subdural or epidural hematoma that has resulted in a neurologic deficit; (20) current abuse of alcohol or drugs, as this may have an influence on study compliance; (21) contraindication to MRI (eg, implanted metallic or electrical devices); (22) nursing a child, pregnancy, or intent to become pregnant during the study, given the unknown impact of cortical stimulation on the fetus and on breast milk; (23) participating in another trial within 30 days of enrollment in this study; and (24) any other condition that, in the opinion of the investigators, would interfere with study compliance or safety.

With the use of the aforementioned study criteria, 139 subjects were included in the current analysis (83 [57.6%] men; mean age ± SD of all subjects, 56.7±11.2y; mean time ± SD since stroke onset for subjects in sample, 59.6±65.6mo; 90 subjects with hemiparesis affecting their right UEs; 80 subjects [57.6%] with hemiparesis affecting their dominant UEs). The demographics of the subjects are shown in table 1.

Outcome measures

Lesion volume was obtained from the original medical record and verified by at least 2 independent neurologist-observers for each subject by manually tracing the perimeter of the area of abnormal

List of abbreviations:

AMAT	**Arm Motor Ability Test**
CT	**computed tomography**
FA	**functional ability**
FM	**Fugl-Meyer**
MRI	**magnetic resonance imaging**
NIHSS	**National Institutes of Health Stroke Scale**
UE	**upper extremity**