Subject Name: _____Last 4 SSN:_____ Date: _____

Title of Study: Neurophysiological and Kinematic Predictors of Response in Chronic Stroke (SRT5)_____

Principal Investigator: George Wittenberg, MD, PhD_____VAMC: Pittsburgh (646)

LAY TITLE: Predictors of Response to Therapy in Chronic Stroke (SRT5)

KEY ELEMENTS:
This is a research study to validate a formula that predicts how a person with a stroke will respond to an arm rehabilitation program. Your participation in this study is voluntary.

The study will involve the use of an arm robot, intensive arm training, magnetic resonance imaging (MRI) and transcranial magnetic stimulation (TMS). Each clinic visit will last 1-4 hours. Your total time commitment will be approximately 26 weeks with a maximum of 40 weeks to complete the study.

There are risks to this study that are described in this document. Some risks include: muscle soreness, breach of confidentiality, dislocations, headache and seizure. You may benefit from participating in this study. Direct benefits may include improvement in the movement and function of the arm affected by your stroke.

If you choose not to participate in this study, there may be other studies that you qualify for. Talk to your healthcare provider about such options. If you choose not to take part, your healthcare will not be affected.

If you are interested in learning more about this study, please continue reading below.

STUDY CONTACT INFORMATION:
If you have a general question about this research study, or if you have any concerns or complaints related to this research study, you may call **George Wittenberg, MD, PhD, Principal Investigator,** at **412-648-4178** or the Research Coordinator at **412-648-4179**. The address is 3520 Fifth Ave, Suite 201, Pittsburgh, PA 15213.

If you experience any illness, injury or other medical problem that you feel may be related to this study, please call George Wittenberg at 412-648-4178 or the Research Coordinator at 412-648-4179 and after-hours or on weekends call 1-866-785-9015 and tell the operator that you are a research subject from the Pittsburgh VA in Neurophysiological and Kinematic Predictors of Response in Chronic Stroke and need to speak with Dr. Wittenberg. Then give the operator a phone number where you can be reached. The operator will get in touch with Dr. Wittenberg.

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STUDY SPONSOR:
The Veterans Health Administration Rehabilitation Research and Development Service. Additional information regarding the study sponsor can be provided upon request.

PURPOSE OF THE RESEARCH STUDY:
The purpose of this research study is to validate a formula that predicts how a person with a stroke will respond to an arm rehabilitation program. The study will involve the use of an arm robot, intensive arm training, magnetic resonance imaging (MRI) and transcranial magnetic stimulation (TMS). TMS is a method of stimulating parts of the brain using magnetic pulses. You will be one of approximately 70 subjects asked to participate in this study.

You are being asked to participate because you have a history of a stroke affecting one side of your body that occurred at least 6 months ago. Also, you must have mild/moderate to severe arm dysfunction and be medically stable to participate in the study. You would not be eligible to participate if you are unable to give informed consent, have a serious complicating medical illness that would preclude participation, have joint deformities or orthopedic problems limiting range of joint motion in your affected arm, or have visual loss such that you would not be able to see the robot computer monitor. You would also not be eligible to participate if you had botulinum toxin ("Botox") to the affected arm within four months of baseline testing or received it during the study period or you are unable to comply with requirements of the study.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Website will include a summary of the results. You can search this Web site at any time.

DESCRIPTION OF THE RESEARCH STUDY:
If you sign the consent form, agree to participate and meet the eligibility criteria, you will complete the following: a neurological exam, three MRIs of the brain, TMS, questionnaires, cognitive testing, robot testing, arm activity monitoring, and arm function testing. The Stroke Impact Scale asks about your quality of life and arm function since your stroke and will take about 20 minutes. Baseline testing will be completed within a 6-week time frame. Two baseline sessions will be completed to examine arm strength,

range of motion, and the ability to perform various functional tasks. If the two differ by too much, a third baseline session may be done. If you do not have any exclusion criteria, one MRI and one TMS session will also be completed. Baseline evaluation visits are approximately two hours.

Transcranial magnetic stimulation involves the use of a magnet to stimulate the parts of the brain that control movement. We will ask you to wear a headband or glasses so that we can keep track of where to put the magnet. Small sensors with wires attached to them will be placed on your arms and legs to record the electricity coming out of your muscles. When the magnet is used, it will be gently placed on top of your head and you will hear a tapping sound and feel tingling on your scalp. Your body may move after each tap. We will move the magnet to different places on your scalp and repeat the process up to 1000 times, each time measuring the electricity from your muscles and how it affects the movements that you make.

After completion of the baseline evaluations, the intervention phase of the study will begin. During this time, you will complete up to a total of 36 intervention sessions of robot and transition to task (TTT) arm training. These will occur 3 times per week for 12 weeks. If scheduling conflicts arise, changes will be allowed with sessions occurring up to 4 times per week or up to but not exceeding 18 total weeks. The intervention sessions will be one hour in duration. During each session, you will complete 45 minutes of robotic intervention followed by 15 minutes of repetitive arm exercises using objects and materials you would use in your daily life. You will progress through 3 robot programs sequentially, first focusing on the wrist/forearm, then focusing on the elbow/shoulder, then alternating between the two areas each session. You will receive periodic arm movement evaluations throughout the course of the intervention. At the beginning and end of the intervention period, and after a 12-week period without appointments, you will be asked to wear sensors on both wrists for 3-5 days to measure your arm movement activity outside of the laboratory.

After the final training session and after a 12-week period without appointments you will be brought back for evaluations including questionnaires and arm and robot evaluations. If you do not have any exclusion criteria, TMS evaluation and an MRI of the brain will also be completed at that time. Follow-up testing will be completed within a 4-week time frame. Evaluation and test procedures may need to be repeated if there are technical difficulties with collection equipment. Your total time commitment will be approximately 26 weeks with a maximum of 40 weeks to complete the study.

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RISKS AND BENEFITS:
Robot: This risk of robot injury is minimized by the design of the robot and supervision from staff who can stop the robot if there is any potential for injury. The robot has never caused such injuries; however, it is possible that it could cause dislocations, or bone fractures.

MRI: Some people experience anxiety (claustrophobia) when they get into the MRI scanner. If this happens to you we ask that you notify one of the investigators with a wave of one of your hands and we will remove you from the scanner. The MRI scanner is loud. The risk of hearing loss from the scanner is minimized by having you wear earplugs or headphones. It is possible that the MRI may identify problems in your head that will require follow up from a doctor. The investigators will notify you if this occurs. You will be asked about any implants or metal in your body that would prevent you from safely receiving the MRI. Although there are no known biological effects of MRI on fetuses, safety has not yet been established. We recommend that you do not participate or continue participation in the MRI portions of the study if there is any chance you may be pregnant.

TMS: You may get a headache or feel uncomfortable during parts of the study. Permanent side effects have never been reported after magnetic stimulation or robotic arm training. Magnetic stimulation over your head feels like a tap on your scalp, may cause some tingling in your scalp or other parts of your body, and may make a part of your body move. There is an extremely small risk of the stimulation causing a seizure. That risk is so small that no seizures have occurred with this type of stimulation in people who do not have seizure disorder. There is also the risk of skin irritation at the site of the EMG electrodes used for TMS data collection and the chance of electrical current (DC) less than what would be experience with a nine-volt battery.

Other: There are general risks associated with using any piece of equipment and with any exercise involving moving, standing, sitting, or lying in place for prolonged periods of time. These risks include skin wounds like abrasions, pinching, bruises, or irritations; body stiffness, soreness, aches, and trembling; and general symptoms like upset stomach, chills, fatigue, mood changes, light-headedness, and dizziness.

In addition, it is possible that there might be risks that have not yet been identified. The study doctor will tell you as soon as possible if any new information becomes available that could affect your health or welfare or willingness to stay in this study.

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You may benefit from participating in this study. Direct benefits may include improvement in the movement and function of the arm affected by your stroke.

ALTERNATIVES TO PARTICIPATION:
Your alternative is to not take part. If you choose not to take part, your healthcare at the VA Pittsburgh Health Care System (VAPHS) will not be affected and you could receive physical therapy as part of your routine medical care, if applicable. There may be other studies that you qualify for. Talk to your provider about such options.

NEW FINDINGS: You will be informed of any significant new findings during the course of the study, which may affect your willingness to continue to participate.

INVESTIGATOR INITIATED WITHDRAWAL: The investigator(s) may stop your participation in this study without your consent for reasons such as: it will be in your best interest; failure to follow instructions of the research staff; if you are no longer able to perform the tasks described in the protocol; inability to contact you for follow-up visits; and repeatedly missing appointments without contacting study staff. The sponsor can also end the research study early. The study doctor will tell you about this and you will have the chance to ask questions if this were to happen.

VOLUNTARY PARTICIPATION/RIGHT TO WITHDRAW: Your participation in this study is voluntary. You do not have to take part in this study, and your refusal to participate will involve no penalty or loss of rights to which you are entitled. You may withdraw from this study at any time without penalty or loss of VA or other benefits to which you are entitled.

Your doctor may also be involved as an investigator in this research study. As both your doctor and a research investigator, he is interested both in your medical care and the conduct of this research study. You are under no obligation to participate in this or any other research study offered by your doctor. Before you agree to participate in this research study, or at any time during your participation in this study, you may discuss your care with another doctor who is not associated with this research study.

If you decide to stop taking part, if you have questions, concerns, or complaints, or if you need to report a medical injury related to the research, please contact the investigator listed on the first page. There are no

adverse consequences (physical, social, economic, legal, or psychological) of your decision to withdraw from the research. A written withdrawal is requested and should be sent to the Principal Investigator and address listed on the first page of this document. If you withdraw from this study, already collected data may not be removed from the study database.

MEDICAL TREATMENT: In the event that you sustain injury or illness as a result of your participation in this VA approved research study, conducted under the supervision of one or more VA employees, all medical treatment (emergent as well as medical treatment beyond necessary emergent care) will be provided by the VA. Except in limited circumstances, the necessary medical care must be provided in VA medical facilities.

If there is a medical emergency, an AED is available on site and the 911 emergency medical system would be activated by the research team. If 911 is activated, you would be taken to the nearest available hospital for care.

However, if such injury or illness occurred as a result of your failure to follow the instructions for this study, you may not be eligible for free care unless you have independent eligibility for such care under Federal Law.

FINANCIAL COMPENSATION: If you sustain an injury or illness as a result of participating in this research study, you may be eligible to receive monetary compensation for your damages pursuant to applicable federal law. If you believe that you are injured as a result of participation in this study, please contact the Principal Investigator. If compensation is available the Principal Investigator will provide you with an explanation as to what that compensation consists of, or where you can obtain further information regarding it.

COST AND PAYMENTS: You or your insurance will not be charged for any costs related to the research. You will be not be compensated for time away from work. However, if you are receiving medical care and services from the VA that are not part of this study, and you are a veteran described in federal regulations as a "category 7" veteran, you may be required to make co-payments for the care and services that are not required as part of this research study. Payment of $20 per visit will be made once a month while you are enrolled in the study. Except in limited circumstances, payments issued through VA are generated by Electronic Funds Transfer (EFT). Therefore, in order to receive payment associated with

your participation in this study, you must be willing to receive EFT and to provide banking information to VA, if that information has not already been provided. If you are not able to receive payment through EFT, the Direct Express Debit MasterCard may be issued. The Direct Express Debit MasterCard is a prepaid debit card. Please refer to the flyer that study personnel has provided for more information about which services may require a fee if using your Direct Express Debit MasterCard. In addition, due to limitations in the Financial Management System, payments made to you will generate Internal Revenue Service (IRS) Form 1099 regardless of amount. Payments will be reported to the IRS as income and your social security number will be used for this purpose. If you are a Veteran eligible for Beneficiary Travel, please speak with the research team to understand how research visits may impact your ability to receive Beneficiary Travel.

RECORD RETENTION: Your research records will be retained in accordance with the Veterans Health Administration (VHA) Records Control Schedule, or longer, if required by other Federal regulations.

CONFIDENTIALITY AND USE AND DISCLOSURE OF DATA: There are rules to protect your private health information. Federal and State laws and the Federal medical law, known as the HIPAA Privacy Rule, also protect your privacy. By signing this form, you provide your permission called your 'authorization', for the use and disclosure of information protected by the HIPAA Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including information from your medical records such as: diagnoses, progress notes, medications, lab or radiology findings and demographic information such as name, age, date of birth, race. You may also be asked to fill out questionnaires, surveys, and/or a subject diary.

The research team may also need to disclose your health information and the information it collects to others as part of the study progress. Others may include the University of Pittsburgh IRB, The Veterans Health Administration Research and Development Service, and the University of Pittsburgh Magnetic Resonance Research Center. In addition, Institutional Review Board, Food and Drug Administration, Office (FDA), Office of Human Research Protections (OHRP), the VA Office of Research Oversight (ORO), and the Government Accountability (GAO) may have access to your research records. Your health information disclosed pursuant to this authorization may no longer be protected by Federal laws or regulations and may be subject to re-disclosure by the recipient.

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Finally, you consent to the publication of the study results or release of the data when published, so long as the information about you is anonymous and/or disguised so that your identity will not be disclosed.

Confidentiality risks and precautions to decrease risk:

Every effort will be made to make sure that the information about you obtained from this study will be kept strictly confidential. As private information is collected about you as part of this study, there is a risk to your privacy and confidentiality. The research staff will take every precaution to protect your identity and the confidentiality of the information collected about you. Any electronic or hard/paper copies of the information collected about you will be stored in a secured location. Any copies of data that contain information that could be used to identify you (such as your name, address, and social security number) will be stored separately from any information that does not contain identifiers. Only those individuals who are authorized to review your information will have access to it.

Revocation: You can revoke this authorization, in writing, at any time. To revoke your authorization, you must write to the Principal Investigator at the address below. Your request will be valid when the Release of Information Office receives it. If you revoke this authorization, you will not be able to continue to participate in the study. This will not affect your rights as a VHA patient to treatment or benefit outside of the study.

George Wittenberg
3520 Fifth Ave, Suite 201
Pittsburgh, PA 15213

Treatment, payment or enrollment/eligibility for benefits cannot be conditioned on you signing this authorization. This authorization will expire at the end of the research study unless revoked prior to that time.

RESEARCH SUBJECTS' RIGHTS: You have read or have had read to you all of the above. Dr. George Wittenberg or his authorized representative has explained the study to you and answered all of your questions. The risks, discomforts, and possible benefits of this research study, as well as alternative treatment choices, have been explained to you.

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A description of the study has been provided to you, including an explanation of what this study is about, why it is being done, and the procedures involved. You have the right to ask questions related to this study or your participation in this study at any time. You should be giving your consent only under conditions in which you (or the person representing you) have sufficient opportunity to carefully consider whether or not to participate in this study. Your consent should not be given under conditions that pressure you or try to influence your decision in any way.

Your rights as a research subject have been explained to you, and you voluntarily consent to participate in this research study. You will receive a copy of this signed consent form.

If you have any questions about your rights as a participant in this study, or wish to speak more about the study with someone not associated with the research study, you can call the Associate Chief of Staff for Research and Development at (412) 360-2394.

As long as the study is renewed as required by the IRB, your signature on this document is valid for the duration of the entire research study. Should any changes occur during the course of the study that may affect your willingness to participate, you will be notified.

By signing this form, you agree to participate in this research study.

_____	_____	_____
Subject's Signature	Date	Time
_____	_____	_____
Investigator/Person Obtaining Consent*	Researcher (Print)	Date

Version Date 12/03/2019