University of Massachusetts Medical School/ UMass Memorial Health

Pilot Randomized Controlled Study of the Impact of MedRhythms' MR-010 in Acute Stroke

Protocol Number: Version 1.0

Name of Investigational Product:	MedRhythms' MR-010
Indication:	Acute Ischemic Stroke
Sponsor:	UMass Memorial Healthcare 55 Lake Avenue North Worcester, MA 01655 Tel: 508-334-5989
Principal Investigator:	Brian Silver, MD
Protocol Version:	1.0
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H00021940: Pilot Randomized Controlled Study of the Impact of MedRhythms' MR-010 in Acute Stroke

Clinical Protocol Element	Description
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Protocol Number / Title	H00021940: Randomized Controlled Study of the Impact of MedRhythms' MR-Stride Plus In Acute Stroke
Device Risk	The investigational device does not meet the criteria of significant risk device as defined in 21 CFR 812.3(m), because the intended use and technological basis for Stride Plus does not meet the following criteria (paraphrased): 1. intended as an implant 2. purported or represented for use in supporting or sustaining human life 3. is for use of substantial importance in diagnosing, curing, mitigating, or treating disease or otherwise preventing impairment of human health, or 4. otherwise represents a potential for serious risk to health, safety or welfare of the Participant.
Device Manufacturer	*MedRhythms, Inc.* 183 Middle Street, Suite 300 Portland, ME 04101

Institutional Review Board	The applicable Institutional Review Board (IRB) will review and approve the study protocol and informed consent documents prior to enrolling Study Participants into this study
Investigational Device Description	Device Name: MedRhythm's MR-Stride Plus The following materials will be provided: 1. Access to *Stride Plus* patient application. 2. Mobile Devices. 3. Motion Sensors. 4. Headphones. The MedRhythms MR-Stride Plus includes a patient application and sensors with commercially available headphones and smartphones. The *MR-Stride Plus* is a device intended to improve gait metrics and improve walking speed. This technology uses embedded audio cues to facilitate improvements in walking speed based on Rhythmic Auditory Stimulation. When using the system, patients walk with sensors that are attached to their shoes and collect gait parameters, including the following measurements: speed, stride length, symmetry (temporal and spatial), and cadence. The algorithm uses data from the sensors to inform changes made to the audio cues. These cues, which are embedded in time-shifted music, are delivered back to the users who aim to walk to the beat. Research shows that walking to an external rhythmic stimulus globally engages the brain, coupling the auditory and motor regions. For stroke survivors with damage to the motor system, this dual engagement has the effect of establishing new neural connections to the motor region. Furthermore, this has the potential to make walking certain distances, which may ordinarily be onerous or impossible tasks, achievable for these individuals. As a result of neuroplasticity, repeating these audio-cueing exercises on a consistent basis can change one's brain composition, allowing walking improvements made with the device to manifest without the engagement of the intervention.
Enrollment and Consent	Study Participants will be enrolled into the study by a study staff member at participating study sites. Once informed consent is received, Study Participants will be screened for enrollment into the study.
Study Objectives	The purpose of this clinical study is to evaluate the effects of the Stride-Plus on tolerability, biomechanics and walking speed in the acute stroke care setting in addition to its impact on length of stay. The study will also look at the impacts of the intervention on falls and cost of care over a 90-day period post-discharge from acute care setting.
Study Design	This study will be a single site, prospective, randomized controlled clinical study. Approximately 40 individuals will be enrolled per the inclusion/exclusion criteria. Participants will be randomized using simple randomization into one of two arms. It is expected that study participants will be approximately equally distributed to either arm (20/20). All interested, potential study participants will participate in the screening study phase. A member of the study team will seek informed consent and review inclusion and exclusion criteria to determine eligibility. Individuals who qualify for enrollment will be randomized into one of two arms: Arm A: Standard of Care + MR-Stride Plus Intervention Arm B: Standard of Care

	For all Study Participants, standard of care will be followed in both the acute care setting and in the discharge setting. Data required to evaluate the study objectives will be collected from record review and participant interviews. Participants will not be required to physically visit the study facility for study-specific procedures once they have been discharged from the acute care setting. Participants will be contacted by telephone to answer study assessment questions (e.g., mRS) intended at Days 45 (+/-2 Days), and 90 (+/-7 Days). For those Study Participants enrolled into Arm A, study staff will review the intended walking intervention therapy schedule with the study participant. The Stride Plus is intended to be used for thirty (30) minutes a day, three (3) times a week. Participants will complete the following intervention phases related to use of the Stride Plus: **Intervention Phase 1** (within 24 hours from admission): In addition to standard of care therapy, study participants will complete at least one (1) walking therapy session with the Stride Plus while an inpatient in the acute care setting. Additional study therapy sessions will continue until the Study Participant is discharged from the acute care setting. **Intervention Phase 2** (Day 1 post-discharge to Day 90): In addition to standard of care therapy, study participants will complete a series of three (3) remote walking therapy sessions a week with the Stride Plus following discharge from acute care setting. Participants will schedule their sessions according to their preference and needs. Intervention Phase 2 will continue until the Study Participant is 90 days since discharge or earlier if the study participant is withdrawn from the study therapy. Participants will complete a walking test using the Stride Plus at discontinuation to determine the walking speed. **Post-Intervention Phase**: Participants will be followed from discontinuation of the Stride Plus until Day 90. At Day 90 (+7 days), participants will complete a walking test using the Stride Plus to determine walking speed. For those study participants in Arm B, the control group, only standard of care therapy will be provided. Participants will complete a 6-meter walk test (approximately 20 feet) to measure gait speed at baseline, biweekly post- discharge from acute care to day 90 (+/-7 days) following discharge.
Primary Endpoint	The primary study objectives are as follow: 1) Change in gait speed (m/s) from baseline to study completion (90 days following discharge from acute care or earlier if study participant withdraws); 2) time-to-functional change in gait speed from baseline to study completion 3) adherence to the MR-Stride Plus therapy schedule.
Secondary Endpoint	The secondary study objective is to assess the median length of stay in acute stroke hospital and the percent of readmission during the 90 (+/-7) days following discharge.
Participant Population	No age, race, education or geographical restrictions apply. All individuals who meet the inclusion/exclusion criteria at participating study sites will be considered.
Inclusion Criteria	To be enrolled and randomized into the study, potential Study Participants must meet *all* of the following inclusion criteria: 1.0 Must be 18 years of age or older. 2.0 Must be able to read and speak English fluently. 3.0 Be within 24 hours from admission for confirmed stroke event.

	4.0 Currently able to walk at a speed greater or equal to 0.4m/s, but less than 1.0m/s, as determined by a 6-meter walk test (approximately 20 feet) for comfortable walking speed (the average of three trials). 5.0 Demonstrates some level of asymmetry in gait. 6.0 Is expected to be discharged from the acute care setting requiring physical therapy per standard of care and participant has verbally committed to receiving at least one therapy session. 7.0 Able and willing to consent with proposed study schema (verbal commitment), including consent to participate in communication with the treating clinician (as needed) during the study period. 8.0 Score ≤1 on question 1b and a 0 on question 1c on the NIH Stroke Scale. 9.0 Able to safely participate in protocol-defined walking therapy sessions of 30-minute duration as determined by the Investigator.
Exclusion Criteria	In addition, any Study Participant that meets the following criteria will be excluded from study enrollment. 1.0 Participant unable or unwilling to provide informed consent. 2.0 Has a known history of neurologic (excluding stroke) injury. 3.0 Has severe aphasia and/or a speech/language disorder, limiting ability to express needs and comprehend instructions. 4.0 Has an external lower limb prosthetic ("artificial limb"). 5.0 Has a hearing impairment. 6.0 Had orthopedic surgery in the last year. 7.0 Has co-morbidities that prevent participation in exercise (for example: musculoskeletal, cardiovascular, pulmonary and neurological – other than stroke). 8.0 Vulnerable populations as deemed inappropriate for study by site Principal Investigator.
Procedures	**<u>ARM A: STANDARD OF CARE + MR-STRIDE PLUS</u>** For Study Participants randomized into Arm A, therapy sessions will begin within twenty-four (24) hours of enrollment. Intervention Phase 1 of the study requires a minimum of one (1) therapy session with the possibility of additional sessions until discharge; however, no more than 3 therapy sessions should occur during a given week. Intervention Phase 2 of the study requires 3 independent, remote therapy sessions a week regardless of discharge setting (e.g., rehabilitation hospital or home). Therapy will continue until day 90 (+/-7) following discharge from acute care. Therapy sessions with the MR-Stride Plus should not replace standard of care physical therapy, but be used in addition to standard of care physical therapy. Participants may be contacted by the study staff to collect data on the number of standard of care physical therapy services provided and occurrence of readmission to acute care. Participants will be able to schedule their three (3) sessions a week therapy according to their needs. Participants will be allowed to miss sessions if they are unable to make them up on a different day in the week. Participants therapy activity will be monitored remotely by the study team. If participants are unable to maintain the therapy schedule, the study will contact the participants to gauge willingness to continue. At investigator discretion and participant agreement, the number of sessions a week may be reduced or the participant may withdraw from therapy. If the participant is withdrawn from therapy, participants will be asked if they are willing to participate in a gait speed assessment using the MR-Stride Plus at day 45 and 90 post-discharge if they have not already been completed. The 6-meter walk test (approximately 20 feet) will be conducted to evaluate gait speed at screening and biweekly thereafter until study completion. Gait speed will also be assessed at

	the time of withdrawal from study therapy if withdrawal occurs before Day 90 (+/-7) post discharge. At the initial therapy session, Study Participants will be provided with all necessary equipment (pre set-up) and instruction for using the MR-Stride Plus. Study staff will provide appropriate oversight of the Participant during their initial walking therapy session in acute care to ensure safety; study staff will not be required to provide any instruction on use of the device. Participants will conduct 30 minutes of walking therapy at the participant's self-selected pace in a space (e.g., track or hallway) that limits the amount of stops and/or pivot turns in order to optimize velocity. Participants may choose to take breaks as needed, or when investigators believe that a rest break is necessary. The use of an overhead harness system is prohibited in this study. If technical or medical issues arise, the training session should be terminated to allow for adequate resolution. For independent, remote therapy sessions following discharge from the acute care hospital, it is not required that a participant be under the supervision of clinical staff or a caregiver (depending on discharge setting), but participants may choose to according to their preference. Participants should perform their therapy sessions in an environment that limits safety hazards and, in a space, e.g., track or hallway, that limits the amount of stops and/or pivot turns in order to optimize velocity. Participants will perform their 30 minutes of walking therapy at their self-selected pace. *MR-Stride Plus Procedure*: Study staff and participants will be required to follow the Instructions For Use (IFU) provided by MedRhythms. The IFU will detail all procedures required for proper operation of the system. Study Participants will be trained in utilizing the Stride Plus by the study staff. Mobile devices that have the MedRhythms Stride Plus application installed will be provided for use during therapy sessions. Participants will be provided with a pre-established username and password. No personally identifiable patient information will be recorded or stored in the Stride Plus application. **ARM B: STANDARD OF CARE** For Study Participants randomized into Arm B, clinical standard of care will be followed with no intervention provided using the MR-Stride Plus. Participants will also complete the 6MWT at screening, baseline and biweekly post-discharge from acute care and at days 45 and 90 (+/-7 days) following discharge. All participants will be followed for 90 days following discharge from acute care facility for initial stroke event and discharge date, discharge setting, number of physical therapy services and occurrence of readmission to acute care will be collected.
Minimizing Bias	The study is not blinded because the primary outcome measure of gait speed renders the likelihood of a placebo benefit unlikely. However, Study Participants will be blinded to the results of the 6-meter walk test (approximately 20 feet). No results will be provided to the Study Participant at any time during participation in the trial.
Study Visits	All key assessments will be conducted at the study site and remotely via telecommunication, as applicable.
Study Duration	Each Participant is required to complete a screening visit. For Participants who are randomized into Arm A (MR-Stride Plus Intervention), therapy sessions will take approximately forty-five (45) minutes for set-up and therapy. After the first therapy session in

	the acute care setting, participants should be able to complete the setup and therapy session with the MR-Stride Plus independently. Collection of data related to study adherence (for participants in the MR-Stride Plus Intervention), gait speed assessment, standard of care administration, discharge and readmission will be performed by study staff remotely through review of medical records, MR-Stride Plus database, and by contacting the participant over the phone. Once participants have reached 90 days following discharge from the acute care facility for the initial stroke event, no follow-up or subsequent Participant involvement is required.
Study Discontinuation, Drop Out, Withdrawal and Replacement	Participants may discontinue their participation in the study at any time. A Participant may be withdrawn from the study at any time at the discretion of the Investigator. Participants who are withdrawn or drop out prior to the study endpoint will still have data that was collected up until the withdrawal/drop out eligible for analysis. These Participants will be analyzed in an Intent-To-Treat analysis.
Benefits / Risks	*Benefits* This project will facilitate the development and clinical translation of targeted gait interventions that can improve walking ability, including the development of new technology that extends the abilities of clinicians. *Risks* There are some risks to participating in this study. We have categorized them below as *Possible, Less Likely,* and *Rare* risks. In summary, the expected risks include: **<u>Possible risks:</u>** • Fatigue • Nausea • Shortness of breath • Muscle or joint soreness • Minor muscle cramps • Loss of balance or fall *Fatigue; Muscle or joint soreness* – Depending on participants' level of disability, sessions will be mildly to moderately strenuous. The participant may become fatigued, or experience joint soreness in their hip, knee, ankle or foot. *Fatigue; Nausea; Shortness of breath; Muscle cramps or muscle soreness* – As with any exercise, there is the possibility that abnormal responses could occur. These include nausea, shortness of breath, fatigue, muscle cramps or soreness (lasting into subsequent days after testing). *Loss of balance or fall:* There is a risk of falling to the ground. Participants who typically wear an ankle brace may be asked to walk without the brace. When walking without the brace, the foot and ankle may not be as stable and there is an increased risk of ankle sprains during walking and falling. *<u>Less Likely Risks:</u>* • Muscle strain/tear • Injury due to fall (ankle sprain, twisted knee, etc.) • Abnormal physiological response to physical activity • Irregular heart rate • Fainting • Bruising and bleeding

	Muscle strain/tear; Injury due to fall : Injuries such as muscle strains and tears are also possible due to exercise activities. Injuries due to falling are also possible. *Abnormal physiological response; Irregular heart rate; Fainting:* As with any exercise, there is the possibility that abnormal responses could occur. These abnormal responses include unexpected changes in blood pressure, irregular heart rate, fainting, or joint injury. This risk is increased in the post stroke population. *Bruising and bleeding :* Participants who are taking anticoagulants may be at increased risk for bruising and bleeding due to a fall. <u>*Rare Risks:*</u> • Heart problems • Hospitalization • Anxiety • Heart attack • Stroke • Death *Heart and lung problems; Hospitalization:* As with any exercise, there is the possibility that abnormal responses could occur. Rare risks associated with exercise could include heart problems or hospitalization and in very rare cases, stroke and death. There is also a risk of pulmonary embolism. *Anxiety :* There also is a potential risk for Study Participants to become anxious. Many of the investigators are licensed physical therapists and most study staff and students have training in CPR and first aid. All of the aforementioned risks will also be mitigated through the following: • Potential Study Participants will be provided with the consent form and be provided ample time to read it and ask questions. The research team will address any concerns. Study Participants will be told that participation in the study is completely voluntary and they have the right to withdraw from the study at any time. • Adequate rest periods and water will be encouraged to optimize comfort and reduce fatigue. • Total walking time per therapy session will be limited to one half hour. • Trained investigators may monitor vital signs and check for symptoms of distress during the initial therapy session with the MR-Stride Plus. Any findings out of the ordinary will be reported to the participant's primary healthcare provider or emergency services should they require medical attention. All participants are free to end testing or procedures that cause anxiety or discomfort at any time, this will not affect any remuneration or transportation they are entitled to.
Data Analysis	UMass Memorial Health Care will be responsible for data analysis. Intent to treat: All Study Participants that enrolled in the study, regardless of withdrawal or incomplete data (if analysis can be made)

Confidentiality	The Principal Investigator and designees, employees, and agents involved with this study will comply with relevant state and federal laws relating to the confidentiality, privacy and security of Participant's health information. They will only create, maintain, use or disclose any data that is generated by this study or other information disclosed to the Principal Investigator or their employees or agents during the course of the study to MedRhythms, Institutional Review Board, Regulatory Authority or other authorized recipients as appropriate for the execution, analysis, review and reporting of this study. Such information shall not be used for any other purposes and will remain confidential. Study Participants will be informed that all data collected for study purposes will be held in strict confidence and used for research purposes only. Records may be paper or electronic. Privacy of participants will be protected by conducting all in-person interactions in a semi-private or private space within the rehabilitation laboratories. No personally identifiable information will be discussed in common areas. *Paper Documents* Will be stored in a locked file cabinet that only the study staff has access to. Study Participant files may also be scanned and stored on a secure, password-protected server authorized to store restricted data, with access provided only to the PI and key study staff. *Codified Study Participant Identification Number* Data collected during this research will be labeled using a codified participant identification number. *Research Data* Data collected specifically for the study will be labeled with the applicable Study Participant ID and stored on a secure, password-protected server. Data may be transferred as a local copy to password-protected study staff computers for processing or to prepare media material for publications, presentations or training purposes. *System Data* The MR-Stride Plus device will collect and store data related to the platform's performance on a secured cloud-based drive owned by MedRhythm's. Personally identifiable information will not be collected by the platform or stored by the company. Only the PI and designated study staff will have access to the data collected under this protocol. The PI and all study staff will have access to all coded data housed on a password-protected secured network drive.
Compliance	Changes or amendments to the protocol will be submitted to the institutional review board (IRB), as required. Subsequently, Study Participants will be notified of protocol changes that may affect their participation in the study. Further participation may be contingent upon re-signing an Informed Consent form. Protocol deviations will be collected and described in the final report. Occurrences of adverse events will be described and recorded and any medical attention sought will be documented. If a deviation in data collection/usage, adverse or unanticipated event involving risks to participants or others, or a breach in confidentiality is suspected or found, the study will be halted until a resolution is determined in accordance with the Institutional Review Board.