PROTOCOL TITLE: Wearable Sensor Platform to Monitor Stroke Recovery: A Clinical Exploratory Trial

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1 OBJECTIVES:

Aim 1: Assess the feasibility of continuous long-term monitoring of inpatients with stroke using wearable sensors.

We will obtain quantitative health data from research-grade, wireless, wearable sensors (including MC10 BioStampRC) on individuals with subacute and chronic stroke in the inpatient setting, as well as healthy controls.

We will specifically check for variability in device data, as well as consistency and periodicity of sensor readings across the clinical study period. We will analyze test-retest reliability and inter-rater reliability of using the wearable sensor technology for clinical and monitoring applications. Furthermore, we will determine whether the sensors can distinguish biometric and activity characteristics between healthy controls and individuals with stroke.

Aim 2: Quantify upper and lower extremity movement impairments, mobility-related activities, speech and swallowing activities, and clinical parameters during stroke recovery.

We will obtain continuous biometric and movement-based sensor data for clinical symptoms (e.g., muscle activation, heart rate variability, talk time, and gait quality) during the performance of validated clinical tests and during general inpatient activities (e.g., therapy, eating, and sleeping).

We will compare device data with clinically validated measures of movement and language function, such as the Modified Ashworth Scale or Western Aphasia Battery. We will describe variation of device data in subgroups of subjects defined by clinician assessed clinically validated measures (10-Meter Walk Test, Mini-Mental Status Exam, etc.). We will also assess the ability of the sensors to capture response to treatment, such as movement therapy, speech therapy, medication, and Botox by comparing sensor data before and after treatment. We will provide evidence about the degree to which the measured variables are

intercorrelated. Lastly, we will evaluate and compare the state of recovery between patients at time of discharge using sensor-based outcomes.

2 BACKGROUND:

Stroke affects more than 795,000 people per year in the United States. Stroke is a leading cause of long-term disability, reducing mobility and communication skills in more than half of survivors over age 65. Movement deficits are a hallmark of stroke, resulting from weakness or paralysis on one side of the body. Common outcomes of stroke are difficulty walking and reduced walking speed, difficulty using the affected upper arm, rigidity of the limbs, impaired balance, and impaired speech, language, and cognition. Improvements in these deficits are seen during acute recovery after stroke. Early clinical treatments, including physical rehabilitation and medication, aim to build on these improvements and return stroke patients to a certain level of function before hospital discharge. The length of stay in a hospital varies with severity of the stroke and the patient's ability to function in the community. However, determining whether a patient has recovered sufficiently for discharge depends on measures that are subjective and imperfect.

Currently, the monitoring, treatment, and evaluation of stroke patients rely on infrequent clinical assessments, performance-based rehabilitation measures, and patient self-reports. Performance-based rehabilitation measures are limited by lack of sensitivity, reliability, and validity in identifying changes or clinical efficacy of treatment or recovery progression. The quality of patient-reported recovery is limited by recall and rater bias. Thus, there exists a strong need for objective, reliable, and continuous monitoring of stroke patients to assist clinicians and therapists make informed decisions about stroke treatment and recovery.

Body-worn sensor technologies can continuously monitor stroke inpatients and allow clinicians and therapists to offer more customized interventions during inpatient procedures. Specifically, a wireless sensing system enables quantitative measures of body function and activity, tracking biometric data and communication or mobility-related activities.

This project proposes continuous monitoring, quantification, and interpretation of recovery during inpatient treatment of stroke using non-invasive, portable, real-time body-worn sensors. Clinicians and therapists would have customized access to a patient history of sensor-based biometric and activity data, allowing them to more fully measure recovery and assign treatment after stroke.

Recently, body-worn sensors (heart rate, galvanic skin response, IMUs, accelerometers, gyroscopes) have been used to monitor the function and activity or stroke survivors in a non-systematic manner, either inside or outside a clinical setting. In the section below, we summarize the specific aspects of stroke already monitored in a limited population and present suggestions for other characteristics that can be monitored using continuous and advanced body sensors.

3 INCLUSION AND EXCLUSION CRITERIA:

3.1 Inclusion Criteria

<u>Inpatient group</u>

- Individuals diagnosed with stroke admitted to the Shirley Ryan AbilityLab (inpatient), or individuals without any known significant health problem (healthy controls)
- Age 18 or older
- Able and willing to give written consent and comply with study procedures

Healthy control group

- Age 18 or older
- Able and willing to give written consent and comply with study procedures

3.2 Exclusion Criteria

Inpatient group

- Neurological degenerative pathologies as co-morbidities (such as multiple sclerosis, Alzheimer's disease, Parkinson's disease, etc.)
- Pregnant or nursing
- Skin allergies or irritation; open wounds
- Utilizing a powered, implanted cardiac device for monitoring or supporting heart function (i.e. pacemaker, defibrillator, or LVAD)

Healthy control group

- No known history of cerebrovascular accidents or neurological degenerative pathologies (such as multiple sclerosis, Alzheimer's disease, Parkinson's disease, etc.)
- Pregnant or nursing
- Skin allergies or irritation; open wounds
- Utilizing a powered, implanted cardiac device for monitoring or supporting heart function (i.e. pacemaker, defibrillator, or LVAD)

4 STUDY-WIDE NUMBER OF PARTICIPANTS:

The exploratory phase of the study will enroll up to 55 subjects as healthy controls, assuming 10% attrition. The study will enroll up to 100 subjects with subacute and chronic stroke for the inpatient monitoring at the Shirley Ryan AbilityLab (SRALab), assuming 50% attrition.

5 STUDY TIMELINES:

Inpatients with stroke will undergo **four types of assessment** (clinical, swallowing/speech, exercise, and sleep/rest) during inpatient stay, from the time of consent until discharge from the hospital or dropout from the study. We anticipate a 12-month period to enroll all inpatient participants. **All assessments will be completed a minimum of three times**, including: (1) upon consent (surrounding admission to hospital), (2) at treatment midpoint (approximated with input from physician), (3) at discharge. Assessments will be completed at additional times as schedules allow.

Healthy controls will undergo **three types of assessment** (clinical, swallowing/speech, and exercise) **during a single laboratory visit** (expected 2-3 hours). We anticipate a 6-month period to enroll all healthy participants.

The assessments and their frequency for each cohort are as follows:

Assessment	# times (inpatient)	# times (healthy)	Time required for each assessment
Clinical	3-5	1	1-2 hours
Swallowing/Speech	3-10	1	≤ 1 hour
Exercise	3-10	1	1 hour
Sleep and Rest	3-10	0	≤ 1 hours per day for rest, overnight for sleep (until wake)

Procedures for each assessment are described in Section 6.2 (inpatients with stroke) and 6.3 (healthy controls).

6 PROCEDURES INVOLVED:

6.1 Overview and Scope

The following sensor data will be collected from healthy controls and inpatients with stroke:

- Biometric data, including electrocardiography (EKG), electromyography (EMG), and sweat.
- Movement data from the limbs, including signals from triaxial accelerometers (ACC) and gyroscopes (GYR).
- Acoustomechanic laryngeal data to detect speech and swallowing events.

The sensors to be used will include those available from the BioStampRC Discovery Kit (MC10, Inc.) as well as custom sensors designed by our collaborators, the John Rogers research group at Northwestern University. The BioStampRC devices measure EKG, EMG, ACC, and GYR, while the custom sensors measure acoustomechanic laryngeal data and sweat.

Most of the BioStamp sensor modalities have been previously validated against gold standard measures for healthy controls and individuals with stroke (Table 1). Thus, feasibility of inpatient monitoring (**Aim 1**) will focus on validating these sensors during common clinical tests and mobility-related activities for healthy controls and subjects with stroke. Quantification of stroke recovery (**Aim 2**) will involve the development of algorithms to analyze sensor data for healthy and stroke cohorts.

Table 1. Validation of sensor modalities (BioStamp and custom sensors)

Sensor	Gold standard	Validation	Methods
EMG (250 Hz and 1000 Hz)	Delsys (2000 Hz)	SRALab: Pilot study – similar SNR during plantarflexion MVC for 1 healthy subject at gastrocnemius (GA). Qualitatively similar signal profile during 10MWT for 1 healthy subject at tibialis anterior (TA). Temporal displacement of spikes possibly due to BioStamp's non-uniform sampling interval SRALab: In progress (data collected) – 9 healthy subjects and 8 with stroke	MVC, sensor at GA 10MWT, sensor at TA
ACC (50 Hz)	Delsys (148.14 Hz)	SRALab: Pilot study – at GA, good correlation with Delsys norms during 10MWT for 2 subjects with stroke. SRALab: In progress (data collected) – 9 healthy subjects and 8 with stroke	10MWT, sensor at GA.
GYR (100 Hz)	ActiLink GT3X (100 Hz)	SRALab: In progress (data collected) – 9 healthy subjects No data for stroke (expected unnecessary: healthy subjects should be sufficient to validate angular velocity at same sampling frequency as GT3X)	N/A
EKG (250 Hz and 1000 Hz)	Polar H7 heart rate monitor & V800 watch (1000 Hz)	SRALab: Pilot study – good agreement of pNN50 and RMSSD for 3 healthy subjects. SRALab: In progress (data collected) – 9 healthy subjects and 8 with stroke	6MWT on treadmill (speed normalized for Fr=~0.16)
Acoustomechanic laryngeal sensors	Videofluoroscopic measurement	SRALab: In progress (data collected on 5 healthy controls and 10 persons with aphasia)	N/A

6.2 Procedures for inpatients with stroke

A. Enrollment, consent, test for exclusion criteria

Individuals with stroke admitted as inpatients to the Shirley Ryan AbilityLab will be asked to potentially enroll in the study. The study coordinator will assess eligibility based on inclusion criteria, obtain informed consent, and answer any questions from the participant.

Participants will complete a demographics and health intake form, by interview. This information will include: age, gender, race, and medical history.

Prior to discharge, information will also be collected about the participant's living and care in the community – for example, whether they will return to independent or assisted living, and whether they will have a full- or part-time caretaker. Because the anticipated support system for patients may affect readiness for discharge (e.g. someone with full time care would not need as much functional independence as someone living alone, and thus might be discharged earlier), we will be prepared to examine amount of recovery at discharge for subsets of the inpatient population related to community living and care.

B. Sensor instrumentation

Participating inpatients with stroke will wear different sensors for each assessment, including clinical, swallowing/speech, exercise, and sleep/rest. The sensor locations for each set are presented in the following sections.

For each sensor location, the skin will be prepped and cleaned using alcohol wipes. Sensors are placed on the skin using adhesive stickers that minimize irritation. Medical dressing (Tegaderm, 3M) may also be used to ensure adhesion and proper contact with the skin. Sensors will be cleaned with soap and water before and after use.

Please note that each BioStampRC Discovery Kit contains 15 sensors. Some assessments will require more than 15 sensors, but never at the same time for a single activity. Sensors will be removed, cleaned, and relocated as needed for different activities in a given assessment.

The battery life of each sensor will depend on which signal modalities are activated for that sensor (e.g. ACC only: 8-35 hours, ACC+GYR: 2-4 hours, ACC+EMG: 11 hours). We will maintain an approximate sensor charging schedule for each participant to facilitate assessment. Research staff and clinical staff will be recruited to assist with sensor charging as needed.

C. Clinical assessments

Clinical assessment will monitor patients during various clinical tests. Sensors will measure vital signs as well as movement and muscle activation in the upper and lower limbs. Sensor placement for this assessment is depicted in Figure 1:

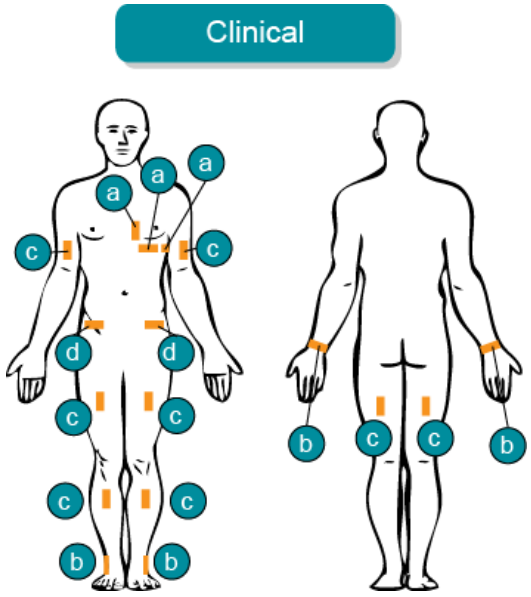

Figure 1: BioStampRC placement for inpatient clinical assessment

Sensor Type	Location	Modalities	Purpose	Clinical test
a	Left parasternal and mid-clavicular line, Left parasternal line, Left mid-axillary line	EKG	Heart rate during/after test	All
b	Wrists, Ankles (bilateral)	ACC+GYR	Movement detection, activity recognition	10MWT, 6MWT, TUG, gait analysis, FIM
c	Tibialis anterior, Hamstring, Rectus femoris (bilateral)	EMG+ACC	Muscle activation (spasticity detection)	MAS
			Joint angles of knee during walking, postural sway during standing	10MWT, 6MWT, TUG, gait analysis, BBS, FIM
	Biceps brachii (bilateral)	EMG+ACC	Muscle activation	MMT, ARAT, FIM
d	Hip (bilateral)	ACC (Hip)	Joint angles of hip during walking	10MWT, 6MWT, TUG, gait analysis, FIM

Participants will perform a series of common clinical tests that are used to evaluate functional performance after stroke. Clinical tests will include:

1. Modified Ashworth Scale (MAS)
2. 10-Meter Walk Test (10MWT)
3. 6-Minute Walk Test with or without VO2 analysis (6MWT)
4. Berg Balance Scale (BBS)
5. Functional Independence Measure (FIM)
6. Timed Up and Go (TUG)
7. Manual Muscle Test (MMT)
8. Action Research Arm Test (ARAT)
9. Fugl-Meyer Assessment (FMA)

All tests will be performed by a licensed physical therapist or occupational therapist. Therapist-reported outcomes for each test will be recorded separately. The participant will be given rest breaks as needed between tests to minimize fatigue. Therapist assistance and body-weight support will be provided as needed.

Research staff will be responsible for all sensor recording practices, such as instrumenting the sensors and marking therapy activities on a computer tablet using the BioStampRC software. Research staff will also keep a written log of activities as they are undertaken during the assessments, including notable events, amount and type of assistance, or use of external devices. Logs will be consulted during analysis to compare with the timestamped sensor data.

D. Swallowing/Speech assessment

Swallowing/Speech assessment will monitor patients' swallow behavior during mealtimes, swallow behavior during bedside/videofluoroscopic swallow assessment, and speech behavior during speech and language therapy. All tests will be performed by a licensed speech-language pathologist, with assistance from research staff. Two custom acoustomechanic sensors (Rogers research group) will be placed as shown in Figure 2. The acoustomechanic sensor will be paired to an Android phone to record all data from the sensor.

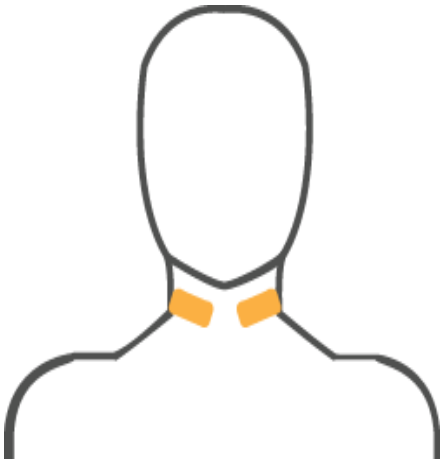

Figure 2: Acoustomechanic sensor placement (bilateral to the hyolaryngeal complex) for swallowing assessment

To measure swallowing during eating, the sensor will be placed at least 15 minutes before scheduled mealtime. The participant will then be asked to eat their meal. During the meal, research staff will observe behavior and time stamp the swallowing events associated with eating. Additional observations will be made of coughs, wheezes, or gurgling noises. After the meal, research staff will observe the participant for at least 15 minutes afterward.

To measure swallowing during bedside or videofluoroscopic analysis, the sensor will be placed immediately prior to the measurement. The videofluoroscopic swallow assessment will be performed only on those stroke patients for whom it is standard of care. Videofluoroscopic analysis is a radiologic examination of swallowing function that uses a special movie-type x-ray called fluoroscopy. The patient is observed swallowing various consistencies of barium-coated liquids and solid foods, in order to evaluate the ability to swallow safely and effectively. (Because this exam is part of the standard of care, a Radiation Dosimetry Form is not needed). Research staff will observe behavior and time stamp the swallowing events, coughs, wheezes, or gurgling noises for the acoustomechanic sensor throughout analysis.

To measure speech, the sensor will be placed immediately prior to the patient's scheduled speech and language (SL) therapy. The sensor will monitor laryngeal activity during common SL exercises and during testing with the Western Aphasia Battery-Revised (WAB-R). The Aphasia Quotient (AQ) of the WAB-R provides an overall quantitative metric of aphasia severity that is based on auditory comprehension and oral expression skills. Tasks of the AQ include naming pictures, repeating words and sentences, reading words and sentences aloud, describing pictures, and having a conversation.

E. Exercise assessment

Exercise assessment will monitor patients during various types of scheduled therapy, including occupational therapy (OT), gait therapy (i.e. treadmill training and overground walking), and other prevalent exercises undertaken during therapy. Sensors will measure vital signs as well as movement and muscle activity in the upper and lower limbs. Sensor placement for this assessment, depending on the therapy type, is depicted in Figure 3.

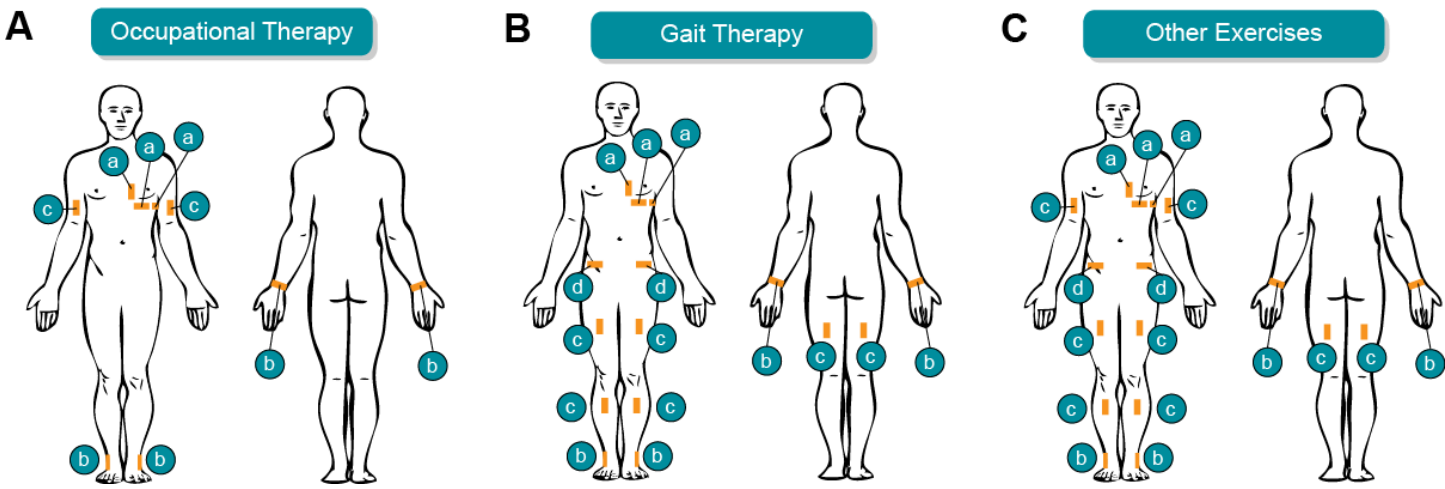

Figure 3: BioStampRC placement for inpatient exercise assessment

Sensor Type	Location	Modalities	Purpose	Therapy Type
a	Left parasternal and mid-clavicular line, Left parasternal line, Left mid-axillary line	EKG	Heart rate during/after exercise, % time in target HR range during therapy (from Tanaka formula)	All
b	Wrists, Ankles (bilateral)	ACC+GYR	Movement detection, activity recognition	All
c	Tibialis anterior, Hamstring, Rectus femoris (bilateral)	EMG+ACC	Muscle activation (spasticity detection)	Gait Therapy, Other
			Joint angles of knee during walking, postural sway during standing	Gait Therapy, Other
	Biceps brachii (bilateral)	EMG+ACC	Muscle activation	Occupational Therapy, Other
d	Hip (bilateral)	ACC (Hip)	Joint angles of hip during walking	Gait Therapy, Other
Sweat	Forehead (bilateral)	Sweat microfluidics	Sweat rate, pH, concentrations of chloride, glucose, lactate	Gait Therapy

All exercises will be supervised by a clinician or therapist and will be recorded as they occur during a regular therapy session. Types of exercises recorded during each type of therapy may include, but are not limited to:

- *Occupational Therapy:* Box and Blocks, 9-Hole Peg Test
- *Gait Therapy:* Treadmill Training and overground walking. Patients' Ratings of Perceived Exertion will be recorded immediately after each exercise.
- *Other Exercises:* such as stair climbing or upper/lower limb cycling. Relevant sensors will be used from Fig. 3C.

We will also record 10 minutes of quiet rest before exercise and 10 minutes of rest after exercise, as permitted by the structure of the therapy session. Pilot testing with the BioStamp sensors has shown that 10 minutes is sufficient to capture recovery (i.e. return to resting heart rate) following exercise for individuals with stroke.

Research staff will be responsible for all sensor recording practices, such as instrumenting the sensors and marking therapy activities on a computer tablet using the BioStampRC software. Research staff will also keep a written log of activities as they are undertaken during the assessments, including notable events, amount and type of assistance, or use of external devices. Logs will be consulted during analysis to compare with the timestamped sensor data.

F. Sleep and Rest assessment

Sleep and rest assessment will monitor patients during overnight sleep and during wakeful rest in their rooms. Sensors will measure vital signs and movement in the upper and lower limbs. Sensor placement for this assessment is depicted in Figure 4.

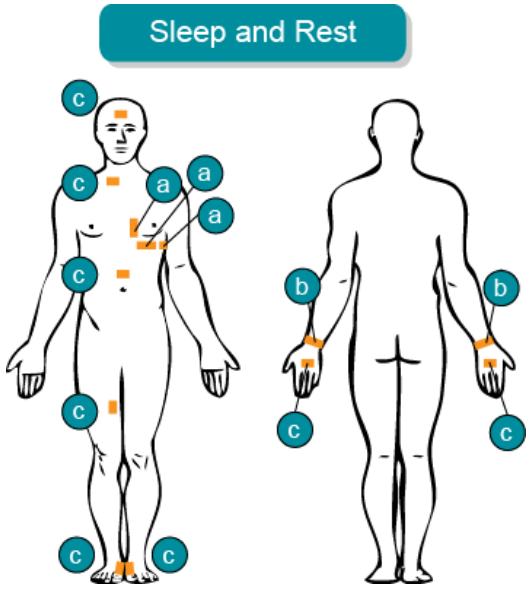

Figure 4: BioStampRC placement for inpatient sleep and rest assessment

Sensor Type	Location	Modalities	Purpose	Assessment
a	Left parasternal and mid-clavicular line, Left parasternal line, Left mid-axillary line	EKG	Heart rate (and variability), abnormalities (i.e. ectopy rate)	Sleep, Rest
b	Wrists (bilateral)	ACC+GYR	Movement detection to evaluate sleep events and quality	Sleep
			Movement detection, activity recognition	Rest
c	Hands, feet (bilateral) Forehead, thigh, intraclavicular region, stomach	Skin temperature	Skin temperature to evaluate sleep events and quality	Sleep

Research staff may record continuous sensor data for various rest-related activities, such as sitting or moving in a wheelchair, for use in activity recognition models.

Clinicians will log sleep and movement events as noticed during their usual patient rounds. After assessment, they will also ask the patient for information about bedtime, wake-up time, total sleep time, sleep latency, wake after sleep onset, naps, any unusual events during the day or night, and rating of overall sleep quality, recording as much information as is communicable by the patient. Logs will be consulted during analysis to compare with the timestamped sensor data.

6.3 Procedures for healthy controls

A. Enrollment, consent, test for exclusion criteria

Potential subjects will visit the Shirley Ryan AbilityLab. The study coordinator will assess eligibility based on inclusion criteria, obtain informed consent, and answer any questions from the subject.

Participants will complete a demographics and health intake form, by interview or self-report. This information will include: age, gender, race, and medical history.

B. Sensor instrumentation

BioStampRC sensors will be used for clinical and exercise assessments. These sensors will be placed after obtaining informed consent, at the locations depicted in Figure 5. Additional sensors will be placed for swallowing assessment, as depicted in Figure 2 and described in 6.2.D.

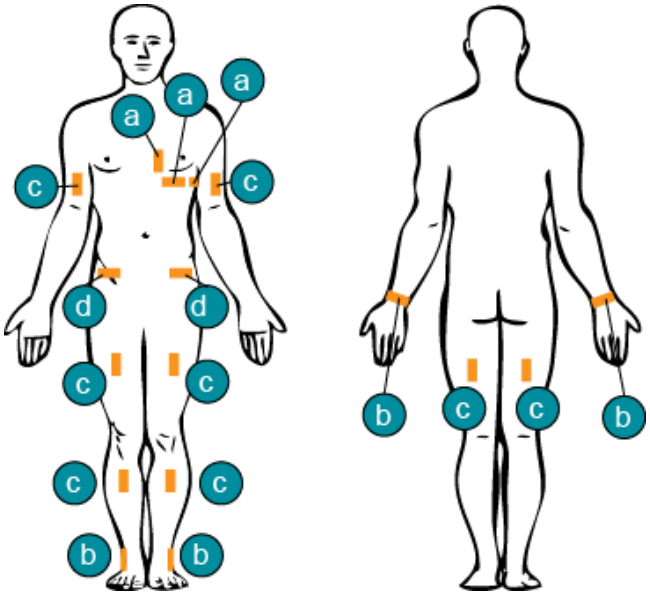

Figure 5: BioStampRC placement for clinical and exercise assessment in healthy controls

Sensor Type	Location	Modalities	Purpose	Assessment
a	Left parasternal and mid-clavicular line, Left parasternal line, Left mid-axillary line	EKG	Heart rate during/after exercise	Exercise
b	Wrists, Ankles (bilateral)	ACC+GYR	Movement detection, activity recognition, stride time, swing time, stance time, cadence, step count	Clinical (10MWT, 6MWT, TUG, gait analysis), Exercise
c	Tibialis anterior, Hamstring, Rectus femoris (bilateral)	EMG+ACC	Muscle activation (spasticity detection)	Clinical (MAS), Exercise, FMA
			Joint angles of knee during walking, postural sway during standing	Clinical (10MWT, 6MWT, TUG, gait analysis, BBS), Exercise, FMA
	Biceps brachii (bilateral)	EMG+ACC	Muscle activation	Clinical (MMT), Exercise, FMA

d	Hip (bilateral)	ACC (Hip)	Joint angles of hip during walking	Clinical (10MWT, 6MWT, TUG, gait analysis), Exercise
Sweat	Forehead (bilateral)	Sweat microfluidics	Sweat rate, pH, concentrations of chloride, glucose, lactate	Exercise

For each location, the skin will be prepped and cleaned using alcohol wipes. Sensors are placed on the skin using adhesive stickers that minimize irritation. Medical dressing (Tegaderm, 3M) may also be used to ensure adhesion and proper contact with the skin. Sensors will be cleaned with soap and water before and after use.

The battery life of each sensor will depend on which signal modalities are activated for that sensor (e.g. ACC only: 8-35 hours, ACC+GYR: 2-4 hours, ACC+EMG: 11 hours). Considering the design of the study for healthy controls and expected duration, we do not anticipate that sensors will require recharging during this laboratory visit. However, we will have charged sensors on backup for each subject and will replace depleted sensors as needed.

C. Clinical assessments

Once instrumented, the participant will complete a battery of clinical tests, including:

1. Modified Ashworth Scale (MAS)
2. 10-Meter Walk Test (10MWT)
3. 6-Minute Walk Test with VO2 analysis (6MWT)
4. Berg Balance Scale (BBS)
5. Timed Up and Go (TUG)
6. Manual Muscle Test (MMT)
7. Gait analysis using GaitRite: self-selected and fast walking speeds (3 trials each)

All other procedures for this assessment are the same as that for inpatients, described in section 6.2.C.

D. Swallowing/Speech assessment

Swallowing will also be assessed in this laboratory visit, during a break from physical activities. Participants will be asked to complete oral facial movements and swallow a variety of food consistencies and a beverage. Participants will also be engaged in a brief (5-minute) conversation about an established topic to provide a representative sample of their typical language. Procedures for sensor use during this assessment are the same as that for inpatients, described in section 6.2.D.

E. Exercise assessment

Healthy participants will perform physical exercises during this laboratory visit to measure heart rate during comfortable exercise and during recovery. We will continuously record sensor data for each of the following exercises:

1. Walking on a treadmill (up to 45 minutes)
2. Walking up and down stairs (up to 10 minutes)

3. Cycling (lower limbs, up to 10 minutes

We will also record 10 minutes of quiet rest before the exercise and 10 minutes of rest after the exercise. For each exercise, participants will be asked to move at a comfortable pace. All other procedures for this assessment are the same as that for inpatients, described in section 6.2.E.

6.4 Description of clinical assessments

- **Modified Ashworth Scale (MAS):** The MAS is a 6-point ordinal scale used to grade the amount of hypertonicity in individuals with neurological diagnoses. A score of 0 on the scale indicates no increase in tone while a score of 4 indicates rigidity. Tone is scored by passively moving the individual's limb and assessing the amount of resistance to movement felt by the examiner.

- **10-Meter Walk Test (10MWT):** The 10MWT is a common clinical measure of gait speed. Subjects will be directed to walk at their preferred maximum but safe speed. Subjects will be positioned 1 meter before the start line and instructed to walk the entire 10-meter distance and past the end line approximately 1 meter. The distance before and after the course are meant to minimize the effect of acceleration and deceleration. Time will be recorded using a stopwatch and recorded to the one hundredth of a second (ex: 2.15 sec). The test will be recorded 3 times, with adequate rest in between. The average of the 3 times should be recorded.

- **6-Minute Walk Test with VO2 analysis (6MWT):** The 6MWT measures the distance a subject can walk indoors on a flat, hard surface in a period of 6 minutes, using assistive devices, as necessary. The test is a reliable and valid evaluation of functional exercise capacity and is used as a sub-maximal test of aerobic capacity and endurance. The minimal detectable change in distance for people with sub-acute stroke is 60.98 meters. The test is self-paced and assesses the level of functional capacity. Subjects are allowed to stop and rest during the test, however, the timer does not stop. If the subject is unable to complete the time, the time stopped is noted and reason for stopping prematurely is recorded. This test may be administered while wearing a mask to measure oxygen consumption.

- **Berg Balance Scale (BBS):** The BBS is a 14-item test, scored on a 5-level ordinal scale. It is used to measure functional balance in a clinical setting and includes static and dynamic tasks (such as sitting, standing, transitioning from sitting to standing, standing on one foot, retrieving an object from the floor), during which subjects must maintain their balance.

- **Timed Up and Go (TUG):** The TUG assesses mobility by measuring the time that a person takes to rise from a chair, walk three meters, turn around, walk back to the chair, and sit down. During the test, the subject is expected to wear their regular footwear and use any mobility aids that they would normally require.

- **Functional Independence Measure (FIM):** The FIM is an 18-item test (13 motor tasks, 5 cognitive tasks) for evaluating level of disability, and how much assistance

is needed for a subject to perform certain activities of daily living. Each item is scored on a 7-point ordinal scale, ranging from total assistance to total independence. Items include eating, grooming, bathing, dressing, toileting, bladder/bowel management, transfers, locomotion and stairs, comprehension, expression, social interaction, problem solving, and memory. The minimally clinical important difference for people with acute stroke is 22 points (17 on motor subscale, 3 on cognitive subscale).

- **Manual Muscle Test (MMT):** The MMT is a procedure for evaluating the strength of 16 individual muscles relative to gravity and manual resistance. Instructions are provided to the subject before testing each muscle. A muscle is isolated, and gradual external force is applied at a right angle to the muscle's long axis. Each muscle is scored on a graded scale of "weak" to "strong" based on the subject's ability to resist the external force. The test is first completed for muscles on the unimpaired side to determine normal strength before being repeated on the impaired side. Weaker subjects may be tested while lying prone (gravity eliminated).

- **Action Research Arm Test (ARAT):** The ARAT is a 19-item test, scored on a 4-point ordinal scale. It is used to assess upper limb function and is divided into four subtests: grasp, grip, pinch, and gross movement. The subject picks up various items (wooden block, ball, stone, tube, marble, ball bearing) and is scored on ability to do so.

- **Fugl-Meyer Assessment (FMA):** The FMA is a performance-based impairment index designed to assess motor functioning, balance, sensation and joint functioning in hemiplegia stroke patients. These domains are assessed on a 3-point ordinal scale from 0-2. "0" is equal to "cannot perform", "1" is equal to "performs partially", and "2" is equal to "performs fully." The domains for upper extremity and lower extremity motor function will be used.

- **Gait analysis:** Gait analysis provides a quantitative means of assessing walking function based on spatiotemporal parameters of gait. Subjects walk at a comfortable and fast pace on the GaitRite® system, an electronic walkway with integrated sensors. Data from GaitRite® is considered reliable and valid for evaluating walking characteristics and will provide a gold standard for validating gait parameters obtained from the wearable sensors. For gait analysis, we will focus on 5 parameters: stride time, swing time, stance time, step length, and cadence.

7 DATA COLLECTION AND ANALYSIS

Healthy controls and inpatients with stroke will be instrumented with wireless sensors. Data from healthy controls will be collected to validate sensor signals and clinical outcomes. Data from inpatients will be collected during hospital stay, including clinical, swallowing, exercise, and sleep/rest assessments. For all subjects, biometric information will be derived using sensor-based electrocardiography, electromyography, and accelerometry. Movement of the upper and

lower limbs will be detected as changes in the acceleration and gyroscope values in three axes. Speech and swallowing activities will be detected as changes in the acoustical waveform obtained from the laryngeal sensor. Clinical scores and therapist evaluations will be incorporated to further validate sensor-based outcomes and map these outcomes onto traditional measures of stroke recovery.

The complete medical history of the inpatients, including physical findings, radiological reports such lesion size, location, type, medications and therapist-assessed clinical outcomes may be used to associate with biometric and movement obtained from the wearable sensors.

Subjects' records will be kept completely confidential. Data will be collected and kept confidential and compliant with HIPPAA requirements. Research data will be de-identified and stored in locked cabinets in the lab with access only to research staff. Electronic data will be de-identified and kept on secure, password protected files and password protected computers (see Sec. 7 for details).

We will use kinematic models to estimate gait-based parameters (such as step duration or joint angles) and physiological models to estimate cardiac parameters (such as MET intensities or time in target heart rate zone). We will use machine learning techniques for activity recognition, classifying different mobility-related activities (such as walking or stair use). We will also use traditional multiple correlation and regression analysis to identify associations of clinical outcomes with measures of body structure and function, activity limitations and demographic characteristics. Analysis will be performed in subsets of the stroke cohort and also in comparison with the healthy controls. This will guide us the ability to create clinical predictors for recovery following stroke and measure the state of recovery prior to hospital discharge.

8 DATA STORAGE

Keeping the confidentiality of all data collected through this study is paramount and we will devise numerous procedures to ensure the privacy of the participants.

Data from the BioStampRC sensors will be accessed via a private MC10 Inc. Investigator Portal, a cloud-based system. The BioStampRC system, including the Investigator Portal, complies with security best practices at all system levels. For example, data is transmitted to the cloud using HTTPS protocols, via an encrypted connection. The BioStampRC system does not support data streaming.

Data will be de-identified when using the BioStampRC collection system, so information stored on the private Investigator Portal cannot be linked to subjects. Upon completion of data collection phase of the study, all data will be transferred to internal servers and removed from the Investigator Portal.

Data from additional sensors, such as sweat sensors and acoustomechanical sensors to assess swallowing/speech, will also be de-identified and stored on internal servers only. This data will also be accessible to the John Rogers research group.

Access to data on internal servers is highly restricted by the following measures:

- Firewalls and other digital security measures

- Written protocols and permission systems that require those who can have access to understand how they can use the data, where they can use it, and training in the procedures for handling such data
- Identifiers will be used as keys allowing researchers to link information on an as-needed basis

The database server used for long-term storage will only be visible to the SRALab network.

9 DATA AND SPECIMEN MANAGEMENT:

We will use kinematic models to estimate gait-based parameters (such as step duration or joint angles) and physiological models to estimate cardiac parameters (such as MET intensities or time in target heart rate zone). We will use machine learning techniques for activity recognition, classifying different mobility-related activities (such as walking or stair use) and swallowing/speech events. We will also use traditional multiple correlation and regression analysis to identify associations of clinical outcomes with measures of body structure and function, activity limitations and demographic characteristics. Analysis will be performed in subsets of the stroke cohort and also in comparison with the healthy controls. This will guide us the ability to create clinical predictors for recovery following stroke and measure the state of recovery prior to hospital discharge.

10 WITHDRAWAL OF PARTICIPANTS:

Subjects will be withdrawn from the study in the event of a medical event or complication that may alter the inclusion/exclusion criteria or which limits the patient from safely completing the remainder of the study, or at the discretion of the PI.

Subjects can voluntarily discontinue the study at any time. The participant will then be requested to notify the Principal Investigator, Dr. Arun Jayaraman, in writing or call at 312-238-6875, if assistance is needed in this process. Information collected prior to the study discontinuation by a participant may still be used by the research team.

The researchers reserve the right to discontinue study participation for any individual or for the study as a whole at their discretion.

11 RISKS TO PARTICIPANTS:

All testing and training sessions will be under supervision of a trained researcher. Manual assistance or cueing will be provided as necessary for safety and balance. Vital signs will be monitored before and after physical exertion and during activities, as needed. All subjects will be permitted to stop physical activity or rest at any time during the study.

- There is a risk of muscle soreness due to increased physical activity during testing sessions. All subjects will work with trained therapists and researchers. Adequate rest will be given and subjects will be monitored by the therapist for verbal or visual signs of fatigue or discomfort.

- There is a risk of falling during testing. The risk of falling will be reduced by having each participant supervised during training and testing by a trained researcher proficient in all testing procedures. During testing, the participant will use a gait belt for safety. The risk is similar to that during any clinical inpatient outpatient therapy session.

- There is a risk of irritation to the skin from device wear. This risk will be reduced by minimized by excluding people who have a known allergy and discontinued use if skin irritation occurs.

- Risks associated with swallowing and speech activities are the same as those associated with routine standard of care. Participants may experience difficulties swallowing or choking during mealtimes. There may also be frustration if speech tasks are deemed too difficult. Trained therapists will be present for all swallow/speech tasks, and participants will be given frequent rest breaks as needed.

12 POTENTIAL BENEFITS TO PARTICIPANTS:

There will likely be no direct benefit by participating in this research study. The participants might get some information on the state of their clinical symptoms over an extended time period. The long-term goal of this research is to improve the ability to quantify symptoms of Stroke and look at the impact of novel therapeutic interventions during the inpatient stay. This benefit could lead to better treatments in the future.

13 SETTING:

Location: The study will occur at the Shirley Ryan AbilityLab, 355 E. Erie Street, Chicago IL 60611 in room 11-1401 or in the Ability Labs on inpatient units.

14 RESOURCES AVAILABLE:

Experienced and trained therapists will be leading all training sessions and providing assistance as needed for safety. Each staff member involved in the study will be trained on the protocol and procedures by the study coordinator.

All staff assisting with training are employees or interns of the Shirley Ryan AbilityLab therefore are familiar with the study site and are experienced with the study population.

The Shirley Ryan AbilityLab is an acute inpatient rehabilitation hospital. The 24th floor is one of the floors within the rehabilitation hospital in which patients with a diagnosis of a stroke are likely to be admitted. This unit has 27 beds. Of those beds, on average approximately 25-40% can meet the inclusion criteria at a given time. The study will occur in the Ability Labs on the floor in which they are staying or in room 11-1402.

There will be medical resources including a resident on call and nursing staff available 24 hours a day if needed in case of an emergency.

15 RECRUITMENT METHODS:

This study will involve recruitment of individuals with CVA from the inpatient units at the Shirley Ryan AbilityLab (SRALab). Clinicians at this location will be informed of the inclusion and exclusion criteria for this study in order to refer appropriate subjects. Information regarding this study will be posted on SRALab's available research studies webpage. Potential research subjects will be referred to, and evaluated by, authorized research personnel. Potential research subjects will be identified based on inclusion and exclusion criteria using the Cerner application. After identification of subject based on inclusion and exclusion criteria, a verbal permission from the patient will be obtained to request medical clearance from their physician.

16 NUMBER OF LOCAL PARTICIPANTS:

The exploratory phase of the study will enroll up to 55 subjects as healthy controls, assuming 10% attrition. The study will enroll up to 100 subjects with subacute and chronic stroke for the inpatient monitoring at the Shirley Ryan AbilityLab, assuming 50% attrition.

17 CONFIDENTIALITY:

All personal information (names, addresses, email or phone numbers, etc.) gathered for this study that can identify participants will be kept secure to protect their privacy and will never be shared at any time with any person or entity. Data collected during the study and shared with others will reference participants only by an alphanumeric code. The "master list" linking personal information to the alphanumeric code will not be shared, and will be kept by the study PI in a secure location. All personal information linking participants to their data will be destroyed after 7 years following the completion of the study.

18 PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF PARTICIPANTS:

Every possible precaution will be taken to protect the privacy interests of subjects. To begin with participation in this is completely voluntary. Trained research personnel will explain the purpose of the study and intended use of subject's personal health information and precautions taken to keep the study information and data confidential.

19 COMPENSATION FOR RESEARCH-RELATED INJURY:

If the subject gets an injury or illness as a result of study, the subject is required to promptly notify the PI of the study about the illness or injury. The hospital [Researchers, Shirley Ryan AbilityLab, Northwestern University and all affiliated clinical sites] will not pay for medical care required because of a bad outcome resulting from participation in this research study. However, this does not keep subject from seeking to be paid back for care required because of a bad outcome.

20 ECONOMIC BURDEN TO PARTICIPANTS:

There is no anticipated economic burden to the subjects since the subjects will be in inpatient and the study will occur in the same building. Subjects will not receive compensation for their participation in this study.

21 CONSENT PROCESS:

Before recruitment and enrollment onto this study, the patient will be given a full explanation of the study and will be given the opportunity to review the consent form. Each consent form must include all the relevant elements as approved by the Northwestern University Institutional Review Board. Once this essential information has been provided to the patient and the investigator is assured that the patient understands the implications of participating in the study, the patient will be asked to give consent to participate in the study by signing an IRB-approved consent form. Subjects will be consented with a new consent form if changes are made to the protocol.

Prior to a patient's participation in the trial, the written informed consent form must be signed and personally dated by the patient and by the person who conducted the informed consent discussion. The consent process will take place at the Shirley Ryan AbilityLab in Room 11-1401or on the inpatient floor.

Non-English Speaking Subjects

Non-English speaking subjects will be permissible for recruitment and enrollment in the study.

If subjects who do not speak English are recruited, all study written and oral communication will be conducted in subjects' native language with the use of an interpreter.

22 PROCESS TO DOCUMENT CONSENT IN WRITING:

Informed consent will take place at Shirley Ryan AbilityLab in 11-1402 or on the inpatient floor with authorized study personnel.

Trained research personnel will guide the subject through consenting process. Subject will be given detailed explanation of the purpose, time line, commitment, procedures, data handling and privacy and confidentiality of information pertaining to the study.

23 DRUGS OR DEVICES:

The purpose of the study is NOT to evaluate the safety and effectiveness of devices or to seek premarket approval of the devices. The devices will be used only as a means of collecting bio-physiological data.

For example, the acoustomechanic laryngeal sensors measure laryngeal movement data during swallowing and speaking, which are converted into an acoustical waveform that can provide an estimate of swallow function or how much a person is talking. Previous versions of this device have been used for bio-physiological data collection in other medical conditions, and have

confirmed that there is minimal risk to participants. Similarly, the sweat sensors collect sweat loss during exercise and detect the pH of sweat, as well as concentrations of chloride, glucose, and lactate. This device has previously been used for bio-physiological data collection during exercise, and confirmed that there is minimal risk to participants.

We are merely collecting these data using non-significant risk devices, without manipulation of any variables. These devices are therefore exempt from any IDE requirements.