MindRhythm Incorporated

Large Vessel Occlusion Validation Study

EPISODE_LVO_MR1

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NCT: Not yet assigned

HeadPulse Large Vessel Occlusion Validation Study
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I. Reason For Study

Acute ischemic stroke (AIS) is a treatable disease if patients can be transported and treated at stroke centers. MindRhythm, Inc (sponsor) has developed an investigational medical device that is designed for prehospital field use to differentiate the two major forms of AIS, namely Large Vessel Occlusion (LVO) stroke and non-LVO stroke. The intended use is for paramedics to decide which destination hospital is best for the patient based on the device result. LVO stroke patients should be brought directly to comprehensive stroke centers which can perform thrombectomy, and non-LVO stroke should be brought to primary stroke centers. Use of the device will save time getting the patient to thrombectomy and all others to intravenous thrombolytics improves outcomes for all patients.

The Harmony 5000 device manufactured by MindRhythm has been tested in the pre-hospital environment, but because LVO stroke is less common than non-LVO stroke, the sponsor wants to obtain additional recordings from patients with LVO to better refine their algorithms. The investigator will perform acute recordings on patients who arrive at our medical center who have CTA studies showing LVO stroke, and on patients transferred to our angiography suite for thrombectomy. Recordings are performed in parallel to standard workflow of LVO patients so will not delay treatments.

II. Inclusion Criteria

- Adult patient
- Known LVO (transferred or arrived at the Emergency Department)
    - Internal carotid thrombosis, Middle cerebral artery first segment, Middle cerebral artery second segment or Basilar Artery
- Recording can be made just prior to thrombectomy, or within 2 hours of computed tomography angiography and no thrombectomy performed
- Authorized representative

III. Exclusion Criteria

- Prisoner
- Open scalp wound

IV. Procedure

Subjects who are expected to be enrolled in this study are critically ill individuals who have experienced a significant neurological injury: a large vessel occlusion stroke which

is an acute ischemic injury confirmed by CT angiography. These individuals may have arrived at the emergency department by way of ambulance or by a third private party. A symptom of a large vessel occlusion stroke is a cognitive disruption which may be mild or severe. An individual may also be unconscious as a result of the LVO stroke. This varied cognitive impact may be short or long term which is dependent on many factors.

- Individual arrives to the hospital through the Emergency Department
- Patient is transferred to the radiology suite for emergency thrombectomy to remove the clot usually within a period of 5 minutes after arrival to the hospital
- Patient is qualified as subject based on inclusion criteria for study
- Subject can be officially enrolled in the study for non invasive, non significant risk data collection of HeadPulse (cranial waveform data) with the Harmony headset as follows:
    1. Place ECG leads (3) on chest or arms
    2. Turn on headset and confirm ECG connection on dongle
    3. Place headset on head
    4. Start 90 second recording
    5. Minimize head movements as much as possible (dongle will provide feedback)
    6. Headset can remain on during thrombectomy if the endovascular surgeon judges there to be not significant imaging artifact
- At end of recording, device is removed and Clinical Research Coordinator offloads data to secure folder (box preferred)
- Clinical research form completed, in electronic data center containing deidentified clinical data
- Before Subject is discharged, on site Clinical Coordinator will meet with Subject to consent to use data collected during the recording as well as other deidentified information. Clinical Coordinator will determine if Subject is in a functioning cognitive state for Subject consent or if an Authorized Representative is required to execute the consent form.

V. Number of subjects

- Up to 50

VI. Device Description

The device (Harmony 5000, Figure 1) is a self-contained headset designed to fit on a patient's head in the vertical (coronal) orientation. This device contains a circuit board, battery, and a highly sensitive accelerometer. The circuit board contains a microprocessor and digitizing hardware to convert accelerometry data to digital information which is stored on a removable memory card.

The Harmony Headset is designed to be used in the clinical setting when a medical professional suspects their patient is experiencing stroke. Designed for prehospital use, an Emergency Medical Technologist/Paramedic (EMT/P) places the headset on the person along with the ECG

leads while completing their standard clinical assessment (obtaining a medical history, measuring blood pressure, etc.)

The LCD screen provides a count-down time (starting at 180 seconds), and an indicator of patient motion. If the motion is excessive, the screen display feedback to the user to ask the patient to hold still and not speak, chew, etc. The device performs an ongoing assessment of the data and within 90 seconds displays a result of “LVO”, “non-LVO”. For this proposed study, the investigators will be blinded to the immediate result so as not to interfere with stand of care treatment.

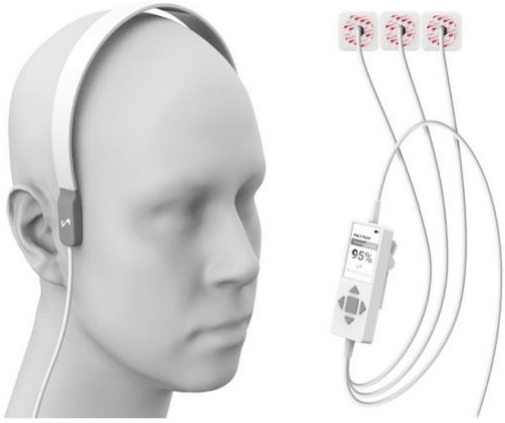

Figure 1- The Harmony 5000 device

The device is experimental but is being manufactured according to ISO standards. The device uses a 1.5 Volt AA battery and is considered a non-significant risk device. Protypes of this design have been used in multiple clinical studies at UCSF where it was certified as non-significant risk. A penultimate protype to the Harmony 5000 is being used in a multicenter clinical trial in Michigan and California.

VII. How the Device Works

The device utilizes an accelerometer placed in contact with the scalp along with transduction of the electrocardiogram.

A three-axis accelerometer is affixed to the headset to collect accelerometry and electrocardiogram outputs. The device then digitizes (at 200 Hz) the accelerometer and electrocardiogram (ECG) outputs resulting in digitized signals, referred to as the "headpulse." The methods regarding acquisition of accelerometry data are explained in the clinical paper, "A Unique Signature of Cardiac-induced Cranial Forces During Acute Large Vessel Stroke" [1]. Software was written in MATLAB to remove noise and sort Harmony headpulse traces synchronized to the ECG. In the original software training, three-minute recordings were performed immediately after CT angiography (CTA) and/or immediately before and after attempted mechanical thrombectomy in patents with suspected stroke. In the original development study, timing of the ECG is determined by simple Schmidt-Trigger rising edge of the signal and each signal was visually inspected to guard against missed or duplicate triggers. The resulting waveforms were inspected by eye and then subjected to supervised machine learning (MATLAB Classification Learner R2018a) to train a model using fivefold cross-validation. False ECG triggering is rejected by limiting triggers to be in the range of physiological heart rates in addition to elimination of patient motion. Motion artifact to the accelerometry traces is removed by excluding any data where acceleration (force) exceeded three standard deviations of the baseline headpulse acceleration, and all included/excluded segments were visually verified. Development of algorithms to fully automate ECG validation, noise, and/or motion artifact rejection is underway and will be used on the Harmony 5000 device.

Each axis of the 3D accelerometer was analyzed for each ECG trigger. Figure 2 (from Figure 3 in reference [1]) show examples of normal (Fig 2A), small vessel stroke (Fig 2B), and stroke mimics (Fig 2C).

Note that each superimposed headpulse waveform closely resembles other ECG- aligned waveforms- a normal condition or "low chaos." In LVO stroke however, the headpulses despite being of similar amplitude no longer are correlated with the cardiac contraction (Fig 2D). This is called "chaos" as the individual traces do not resemble each other when aligned to the ECG. Immediately following thrombectomy (within minutes) the waveforms begin to be more correlated (Fig 2E) and the following day they return to normal (Fig 2F), "low chaos".

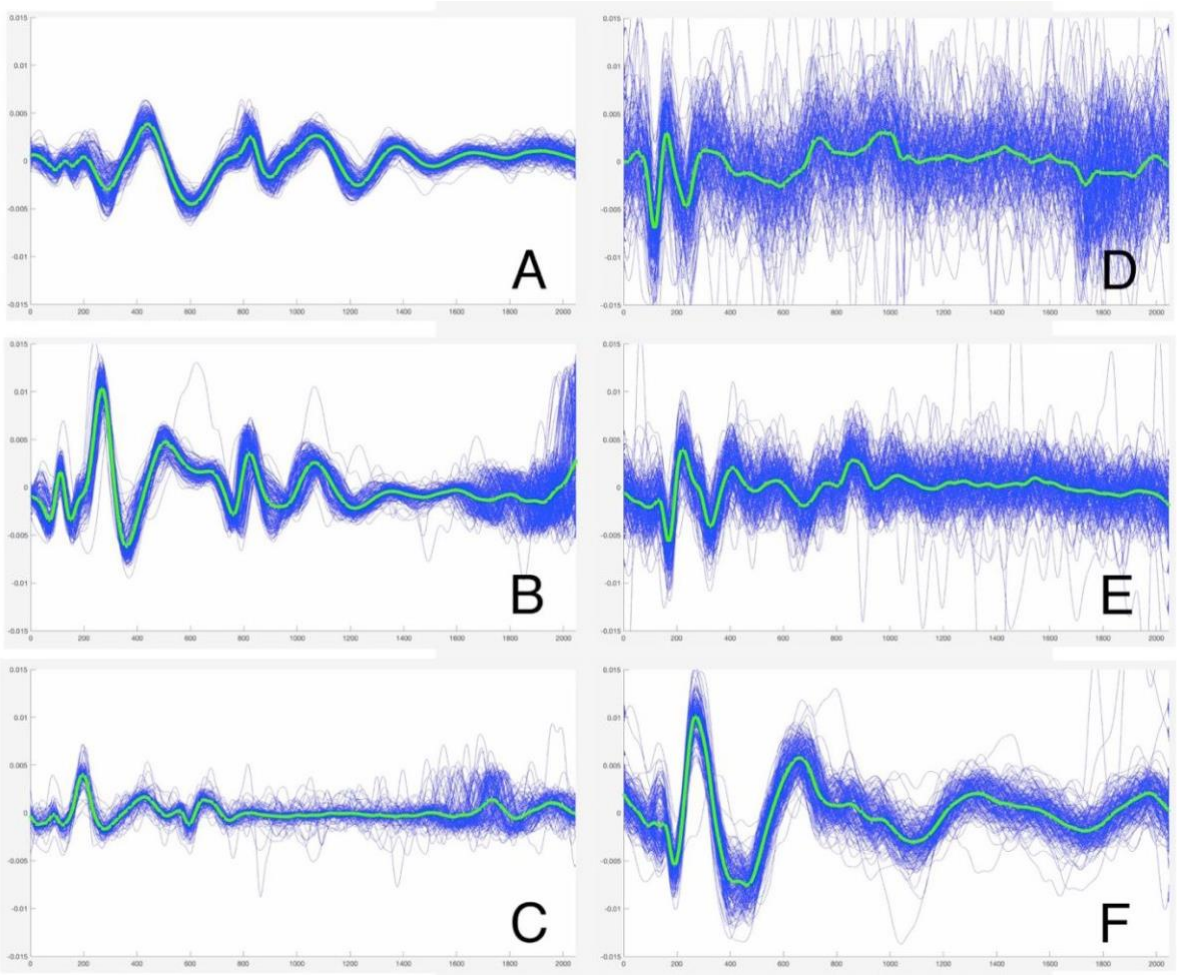

Figure 2. (A) Headpulse recordings from a normal subject. Each sample of the headpulse is superimposed on the prior starting at the ECG R wave onset. The green line is the mean of all traces during the recording. X-axis is time spanning approximately 1 second set by the average of all R-R intervals. (B) Headpulses of a patient with a small vessel stroke. (C) Headpulses from a patient with a migraine (stroke mimic). (D) Headpulses from a patient with a right MCA occlusion just prior to thrombectomy. (E) The same subject as in D within minutes of a successful TICI 2B thrombectomy. (F) The same subject as in D and E but one day later with near full recovery of left-sided strength. Reference for figure [1]