NCT05432986

Protocol: 2021-01

Title: Assessment of Flow in Cerebrospinal Fluid Shunts with a Wireless Thermal Anisotropy Measurement Device, Phase B

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Study Purpose and Rationale:

Cerebrospinal fluid (CSF) shunts fail often, but diagnosis is difficult as symptoms are non-specific. Existing non-invasive tests are not able to assess flow directly but rely on secondary measures of shunt function. Conversely, invasive tests can be painful and risk contamination and infection of the shunt system.

This trial will evaluate the performance of FlowSense, a device for non-invasively assessing CSF shunt flow using thermal anisotropy measurements, in a prospective study setting. The objective of this study is to establish the performance of the device in subjects presenting with a possible shunt failure.

Study Design:

This is a prospective, open-label, blinded, multi-center, single-arm observational study of up to 150 (roll-in and main study) subjects at up to 10 trial sites. Patients with an existing CSF shunt and symptoms of a shunt failure will be recruited by the clinical investigators based on the inclusion and exclusion criteria.

Subjects will undergo evaluation with the FlowSense device and standard-of-care testing and will be followed for 7 days to determine if a revision was performed to repair or replace the existing shunt. In subjects undergoing a revision, intraoperative assessment of shunt functionality will establish the presence or absence of a complete shunt obstruction. FlowSense device data will be used to categorize shunt function as “flow confirmed” or “flow not confirmed.” This trial will evaluate the ability of the study device to accurately distinguish between functioning (flowing) and non-functioning (non-flowing) shunts.

Clinical staff will be required to complete training on the protocol and device measurement procedures as well as complete a roll-in study device measurement prior to enrolling main study patients.

Statistical Procedures:

The co-primary endpoints for this study are sensitivity and specificity. Performance measures (sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV)) will be estimated along with 95% two-sided confidence intervals (CI).

To calculate the performance measures, the study device output of either “flow confirmed” or “flow not confirmed” and the standard-of-care clinical treatment will place each patient into one of the following categories:

True Positive (TP):	Device outputs “flow not confirmed” AND a shunt revision surgery with confirmed shunt failure is performed
False Positive (FP):	Device outputs “flow not confirmed” AND either no shunt revision surgery is performed for 7 days or a shunt revision surgery without a confirmed shunt failure is performed
True Negative (TN):	Device outputs “flow confirmed” AND either no shunt revision surgery is performed for 7 days or a shunt revision surgery without a confirmed shunt failure is performed
False Negative (FN):	Device outputs “flow confirmed” AND a shunt revision surgery with confirmed shunt failure is performed

If a patient does not fall within one of these categories (e.g., if shunt patency was not assessed during revision surgery), data for that patient will not be included in the endpoint calculation. Study device sensitivity will be calculated as TP / (TP + FN) and study device specificity will be calculated as TN / (TN + FP).

A minimum of 30 “positive” patients (those who undergo shunt revision surgery with a confirmed shunt failure) will be enrolled.

Secondary subgroup analyses will be performed to report on any variation between pediatric and adult patients. Additional subgroup analyses will be performed to identify any patient characteristics that may impact device performance.

Enrollment Criteria:

Inclusion criteria

1. Existing ventriculoperitoneal CSF shunt on which the patient is dependent

2. At least one symptom of shunt malfunction as determined by the investigator, such as but not limited to seizure, fever, headache, vision problems, dizziness, disorientation, confusion, vomiting, lethargy, irritability, difficulty waking or staying awake, swelling along shunt tract, enlargement of head, loss of balance, gait disturbance, and loss of sensory or motor function

3. Suspicion of shunt obstruction warrants the performance of a test for this condition in the investigator's judgement

4. Region of intact skin overlying an unambiguously identifiable chronically indwelling ventricular shunt which crosses the clavicle and is appropriate in size for application of the study device

5. Available for follow-up for up to seven days

6. Signed informed consent by patient or a parent, legal guardian, health care agent, or surrogate decision maker (according to local statutes, and collectively referred to as "surrogates" in this protocol)

Exclusion criteria

1. Presence of multiple shunts, or presence of more than one distal shunt catheter (regardless of function) crossing the clavicle ipsilateral to the shunt with suspected obstruction

2. Use of the study device would interfere with standard patient care, or emergency surgery that cannot be delayed

3. Presence of an interfering open wound or edema over any portion of the shunt

4. Patient-reported history of adverse skin reactions to adhesives

5. Investigator judges that the subject is likely to be lost to follow-up due to unavailability or clinical outcome being unobtainable

6. Participation in the study will interfere with, or be detrimental to, administration of optimal health-care to the subject

7. Prior enrollment in this study (multiple main study enrollments of the same patient are disallowed)

8. Participation in any other investigational procedural, pharmaceutical, and/or device study that may influence the collection of valid data under this study

Study Procedures:

Pediatric and adult shunt-dependent hydrocephalus patients with an existing CSF shunt and shunt failure symptoms will be screened and enrolled based on the inclusion and

exclusion criteria. Written informed consent will be obtained from all subjects or their legal representative before enrollment into the trial.

To use the study device, the patient will be oriented in an upright, seated position. The location of the CSF catheter near the clavicle will be marked and the device will be adhered to the skin. The study staff will press down on the device to ensure good contact, and the device measurement will be initiated through a mobile application that has been preloaded onto an iPad. The measurement result will be displayed on the iPad as an encoded alphanumeric string.

The temperature data and device photos will be stored directly onto the iPad. Radiology, medical oncology, surgery, and pathology records may also be collected.

Study Device:

Device name: FlowSense®

Device description: FlowSense (Rhaeos, Inc.; Model Number FS01), the study device, is designed to provide non-invasive wireless measurement of flow in implanted CSF shunts via thermal anisotropy measurements. The single-use device, which includes a low-power heating element, a set of temperature sensors, a Bluetooth low energy (BLE) wireless chip, and a coin cell battery enclosed in a flexible housing, is similar in size to a conventional adhesive bandage and communicates with an iPad application to perform measurements and report the results.

Research Questions(s)/Hypothesis(es):

Primary objectives: The primary objectives of this study are to determine the sensitivity and specificity of the study device for identifying the presence or absence of complete shunt failure in symptomatic hydrocephalus patients with CSF shunts.

Secondary objectives: The secondary objectives of this study are to determine the accuracy, positive predictive value (PPV), and negative predictive value (NPV) of the study device in this population. Additional objectives include collecting and describing clinical, demographic, and hydrocephalus (e.g., etiology, shunt system type, shunt system brand, shunt valve settings) characteristics of the study population, device user feedback, and shunt testing data (e.g., imaging studies). Additional study device diagnostic and performance data (e.g., temperature data and error codes) will be collected for adjudication and review purposes. The diagnostic performance of an additional flow

assessment algorithm will also be assessed using the data acquired in this study by the study device.

Scientific Abstract:

Diagnosing cerebrospinal fluid (CSF) shunt failure can be difficult and currently relies on a combination of indirect and/or invasive methods. This study will evaluate the performance of the non-invasive FlowSense wireless device to rapidly assess shunt flow.

The objective of this study is to establish performance of the study device in subjects presenting with symptoms of a possible shunt failure.

This is a prospective, blinded, observational multi-center study. Patients will undergo evaluation with the FlowSense device and standard-of-care imaging and will be followed for 7 days to determine if a revision was performed to repair or replace the existing shunt. In patients undergoing a revision, intraoperative assessment of shunt functionality established the presence or absence of a complete obstruction. FlowSense device data will be used to categorize shunt function as “flow confirmed” or “flow not confirmed.”

Lay Abstract:

Cerebrospinal fluid (CSF) shunts often fail. However, it can be difficult to know when the device has failed because the symptoms patients experience are common (such as headache, nausea, and tiredness) and can have many causes that are unrelated to the CSF shunt. In addition, the current tests used to determine if a CSF shunt has failed are not always correct. When a CSF shunt does fail, patients typically have a shunt revision surgery. During the surgery, the entire shunt or some of its components are repaired or replaced.

This trial will determine if the study device can accurately distinguish between functioning (flowing) and non-functioning (non-flowing) shunts. The study will enroll patients who have a CSF shunt and are experiencing symptoms of possible shunt failure. The patients and clinical staff will not see the study device results, and the patients will receive their normal care. The patients will be followed for 7 days to see if they have a shunt revision surgery. In patients who do have surgery, the doctors will check the shunt to see if fluid can flow through it. The study device results of “flow confirmed” or “flow not confirmed” will then be compared to the patient outcome (no revision surgery/revision surgery with a flowing shunt or revision surgery with a non-flowing shunt).