A Multicenter Study of Noninvasive Wireless Assessment of Cerebrospinal Fluid Shunt Function in Hydrocephalus Patients

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Presented in part, as a digital poster at the 2023 Annual Meeting of the AANS/CNS Section on Pediatric Neurological Surgery in Oklahoma City, OK from November 29 to December 2, 2023.

Presented in part at the International Society for Pediatric Neurosurgery in Toronto, Canada from October 13-17, 2024.

Presented in part at the 2024 Annual Meeting of the AANS/CNS Section on Pediatric Neurological Surgery in New York City, NY from December 12-15, 2024.

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Received, January 02, 2025; **Accepted,** March 06, 2025; **Published Online,** June 16, 2025.

Neurosurgery 00:1–9, 2025 https://doi.org/10.1227/neu.0000000000003569

BACKGROUND AND OBJECTIVES: Diagnosis of cerebrospinal fluid (CSF) shunt failure is complex, relying on a combination of patient symptoms, history, and indirect tests, in part due to the inability to easily access information about shunt function. The objective of this study was to evaluate the performance of a novel noninvasive wearable wireless device in assessing the presence of shunt flow in patients presenting with possible shunt failure.

METHODS: This was a prospective validation study including patients with an existing implanted CSF shunt system and symptoms of possible shunt failure. Subjects underwent evaluation with the study device in addition to standard-of-care evaluation. Device measurement data were evaluated with 2 algorithms and classified as "flow confirmed" or "flow not confirmed." Subjects were followed for 7 days and, in patients undergoing shunt surgery, intraoperative assessment of shunt functionality established the presence or absence of complete shunt failure. Additional subjects were enrolled for user training and algorithm development.

RESULTS: In total, the study device was used on 182 subjects for user training, algorithm development, and validation. The final algorithm validation data set included 112 subjects. The random forest algorithm outperformed the binary threshold algorithm. The sensitivity of the random forest algorithm (correct identification of complete shunt failure) was 88.9%, and the specificity (correct identification of an absence of complete shunt failure) was 49.2% with a negative predictive value of 96.8%.

CONCLUSION: This study established the performance of a first-generation wearable thermal anisotropy sensor in the identification of CSF shunt flow in symptomatic patients. The high negative predictive value suggests potential application to identify flowing shunts. Additional device performance and clinical outcome studies are underway.

KEY WORDS: Hydrocephalus, Shunt failure, Diagnostic performance, CSF shunt

ABBREVIATIONS: NPV, negative predictive value; **PPV,** positive predictive value.

BACKGROUND

The mainstay treatment for hydrocephalus and other cerebrospinal fluid (CSF) disorders is placement of a permanent ventricular CSF shunt. Although shunts can be lifesaving, they have high failure rates with up to 85% of shunts failing within 10 years in children.[1-3] This problem is compounded by difficulty in diagnosing shunt failure as presenting symptoms are often nonspecific,[4-8] and existing tests can perform poorly and carry risks associated with radiation, sedation, and infection.[9-18]

Imaging tests including X-ray shunt series, CT, and MRI are currently used as front-line tests. However, X-ray shunt series have low sensitivity (4%-27%)[10,19-29] whereas CT and MRI have sensitivities in the 50% to 80% range[10,19,21,22,24-38] when used to identify patients requiring shunt surgery. Radionucleotide shunt studies report sensitivities >85%, but specificity is quite variable between studies (43%-96%).[14,15,39-43] In addition, radionucleotide shunt studies are often used only after a negative CT or MRI, are invasive, and can have long protocols.[13-15,40]

Objectives

Thermally mediated flow sensing techniques have shown potential utility in the assessment of CSF flow through shunt tubing.[44-47] This study evaluated the performance of a wearable device for noninvasively assessing CSF shunt flow using thermal anisotropy measurements in a prospective study setting.

METHODS

Study Design

This was a prospective, blinded, multicenter observational study.

Setting

The study was conducted between August 2021 and November 2023 at 9 hospitals. The research protocol was approved by a central Institutional Review Board and by the Institutional Review Board at each participating site. Informed consent was obtained before study device use. Pediatric and adult subjects were enrolled for device user training and the creation of algorithm development and validation data sets.

Participants

Before enrolling subjects for the algorithm development or validation data sets, clinical staff were required to complete protocol and device user training, including a roll-in study device measurement on a shunted patient.

For the algorithm development and validation data sets, patients with an existing implanted ventriculoperitoneal shunt who were experiencing symptoms of potential shunt failure were recruited. Patients were included if the shunt crossed the clavicle and there was a region of skin appropriate in size for the study device.[48] Patients were excluded if they had more than 1 distal shunt catheter crossing the clavicle ipsilateral to the shunt being measured, an interfering open wound or edema over any portion of the shunt, a patient-reported history of adverse skin reactions to adhesives, if participation in the study would interfere with, or be detrimental to, administration of optimal health care to the subject, or if the investigator determined the patient would likely be lost to follow-up. No hydrocephalus etiologies were excluded.

Variables and Data Sources

The study device was used to assess shunt CSF flow. Subjects and the medical staff were blinded to the results. Standard-of-care assessments of shunt function were performed, and surgical intervention occurred solely based on the judgment of the treating neurosurgeon. Subjects were followed for 7 days to determine if shunt surgery occurred.

Study Device

Flow Evaluation

The study device is designed to provide noninvasive wireless assessment of flow in implanted CSF shunts by thermal anisotropy measurements. The study devices are investigational devices and are not cleared/approved for use by the Food and Drug Administration. The single-use device includes a low-power (44 mW) heating element, a set of 5 temperature sensors, a Bluetooth low-energy wireless chip, and a coin cell battery enclosed in a flexible housing (Figure 1; the patient consented to the publication of his/her images). It is similar in size to a conventional adhesive bandage and communicates with an iPad application to perform measurements and report results in <10 minutes. During the validation study, a binary threshold algorithm was preloaded on the iPad and provided real-time results to indicate if the measurement was completed successfully or not. All raw measurement data were collected to support offline analysis with a random forest algorithm.

Flow Identification Algorithms

Using the algorithm development data set, benchtop data, and other clinical and nonclinical data, 2 algorithms were developed: a binary threshold algorithm and a random forest algorithm. The binary threshold algorithm is based on a 2-layer decision tree, with a threshold at each layer based on the statistical distribution of a calculated thermal flow value in the algorithm development data set. The random forest algorithm was developed using a machine learning process to construct a more granular

FIGURE 1. *Study device.*

decision tree using thermal flow features extracted from multiple time points throughout the measurement and was further coupled with additional feature analysis for vascular flow in the superior (cranial) direction. Both algorithms were locked before the unblinding of the validation data set. There was no significant overlap between the subjects in the algorithm development and validation data sets, with only 1 subject enrolled in both studies.

Instructions for Study Device Use

Users oriented subjects as close to an upright sitting position as possible. The shunt tubing near the clavicle was palpated, and the location for device placement was marked. The device was adhered to the skin, and the measurement was initiated through the iPad application. Successfully completed measurement results ("flow confirmed" or "flow not confirmed") displayed on the iPad as an encoded alphanumeric string. If data triggered an invalid measurement using the binary threshold algorithm, the application displayed troubleshooting steps to guide a new measurement. If a successful measurement was not obtained, the subject's measurement data were recorded as incomplete, and the subject was considered a screening failure. Photograph(s) were taken for device placement evaluation.

Ease-of-Use

For each patient, device users completed a survey covering 6 areas: removing the device from the packaging, pairing the device and mobile application, identifying and marking the catheter location, aligning the sensor with the shunt catheter, using the mobile application and obtaining a device reading, and removing the device from the patient. The device user indicated how strongly they agreed or disagreed with the statement, "I was able to easily…" for each area. A composite score including all 6 areas was computed.

Adverse Events

Patients were monitored for adverse events during the use of the study device and up to 20 minutes afterward. For the purposes of this study, patients were only monitored for newly diagnosed skin conditions at the device application site.

Clinical Data

Ground Truth Determination

Shunt revision surgery was defined as any surgical intervention to repair or replace an existing ventriculoperitoneal CSF shunt in whole or in part, not including shunt taps, radionucleotide injections, or reprogramming of existing shunt valves. Intraoperative assessment of shunt functionality established the presence or absence of a complete shunt failure. A revision surgery with a complete shunt failure meant a shunt revision surgery in which the surgeon visually confirmed shunt obstruction through a:

1. disconnected shunt,
2. complete lack of observable flow, or
3. complete distal obstruction when checked with a manometer.

All other shunt revision surgeries were categorized as being without a complete shunt failure. The 7-day follow-up period began at the time of study device use.

Subjects were classified as ground truth positive if they had a shunt revision surgery with a complete shunt failure within the follow-up period. Subjects were classified as ground truth negative if they had either no shunt revision surgery performed or a shunt revision surgery without a complete shunt failure within the follow-up period (Figure 2).

Additional Clinical Data

Additional clinical data included demographic data, hydrocephalus characteristics, clinical setting, other shunt testing data (eg, imaging), and symptomology as part of this study.

Bias

Bias was minimized through blinding of the device results.

Study Size

Enrollment in the validation study continued until the enrollment target of 30 ground truth positive subjects was met.

Statistical Methods

The diagnostic performance of the 2 algorithms was assessed based on measurement categorization as true positive, false positive, true negative, or false negative (Figure 2). If a patient did not fall within one of these categories (eg, due to an incomplete device measurement) or if the device was incorrectly placed per the instructions for use, data for that subject were not included in the performance calculations.

The performance measures sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) were estimated along with 95% 2-sided CI. Diagnostic performance measures were also calculated post hoc using an alternative workflow that combined the random forest algorithm results with CT or MRI results (Figure 3).

Data Handling

This clinical trial was conducted in compliance with the protocol, good clinical practice, and regulatory requirements. The study is registered on clinicaltrials.gov (NCT05015751, NCT05432986).

RESULTS

Participants and Descriptive Data

Algorithm Development Data Set

Thirty-two patients were screened, 31 were enrolled, and 27 data sets, assessed to have high ground truth confidence, from 26 patients were used for algorithm development. An additional 10

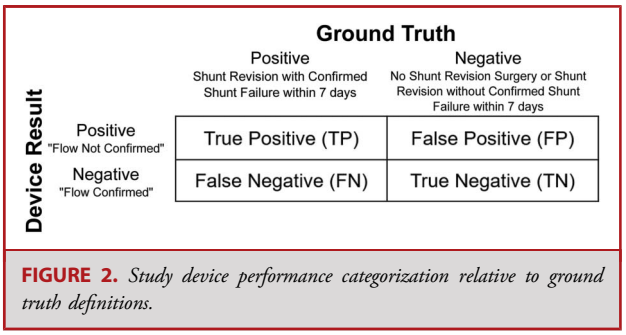

FIGURE 2. *Study device performance categorization relative to ground truth definitions.*

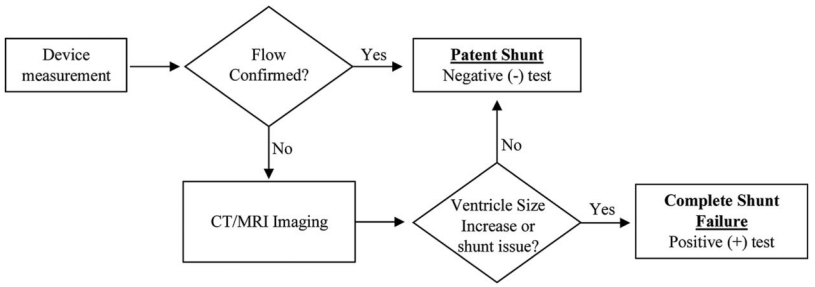

FIGURE 3. *Combined random forest algorithm and CT/MRI workflow. CT, computed tomography.*

TABLE 1. Demographic Characteristics

	Training (%)	Validation (%)
Total subjects	36 (100)	128 (100)
Neonate (0-28 d)	0 (0.0)	0 (0.0)
Infant (29 d-1 y)	1 (2.8)	17 (13.3)
Child (2-11 y)	11 (30.55)	48 (37.5)
Adolescent (12-21 y)	11 (30.55)	46 (35.9)
Adult (≥22 y)	13 (36.1)	17 (13.3)
Age (median, y)	15	11
Minimum (y)	0	0
Maximum (y)	75	87
Sex		
Male	13 (36.1)	52 (40.6)
Female	23 (63.9)	76 (59.4)
Ethnicity		
Hispanic or Latino	9 (25.0)	18 (14.1)
Not Hispanic or Latino	26 (72.2)	107 (83.6)
Not available	1 (2.8)	3 (2.3)
Race		
American Indian or Alaska Native	0	1 (0.8)
Asian	3 (8.3)	3 (2.3)
Black of African American	2 (5.6)	17 (13.3)
Native Hawaiian or other Pacific Islander	0	0 (0.0)
White	21 (58.3)	95 (74.2)
Other	8 (22.2)	2 (1.6)
Not available	2 (5.6)	10 (7.8)

Validation data set including subjects with incomplete measurements. Observed values are given as median, minimum, maximum, or number of subjects (%).

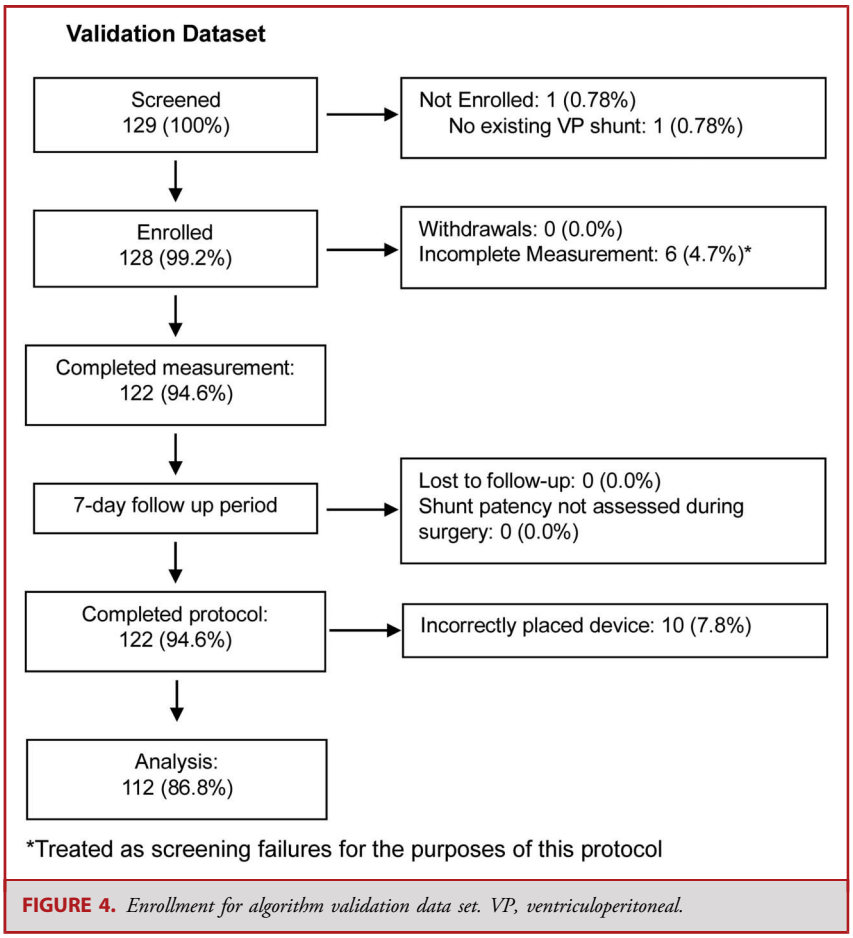

FIGURE 4. *Enrollment for algorithm validation data set. VP, ventriculoperitoneal.*

data sets from 10 roll-in subjects were also used for a total of 37 algorithm development data sets. The median age of this cohort was 15 years (range: 0-75 years). Children (0-21 years of age) accounted for 63.9% of the subjects. Most subjects (63.9%) were female, and 58.3% of subjects identified as White (Table 1).

Validation Data Set

One hundred twenty-nine patients were screened, and 128 were enrolled (Figure 4). The median age of this cohort was 11.0 years (range: 0-87 years). Children accounted for 86.7% of the subjects, 59.4% of subjects were female, and the majority (74.2%) identified as White (Table 1). The most common hydrocephalus etiologies were hemorrhage (31.3%) and spina bifida (24.2%) (Table 2). The most common presenting symptoms were headache (56.3%) and vomiting (51.6%). 81.3% of study device measurements were taken in an emergency department or inpatient setting (Table 2).

There were no withdrawals. Six subjects had incomplete study device measurements using the binary threshold algorithm and were categorized as screening failures. One hundred twenty-two subjects had complete measurements (Figure 4).

Outcome Data

All validation data set subjects were categorized as ground truth positive or negative. Shunt function was assessed intraoperatively in all 47 subjects who had shunt surgery within 7 days of the device measurement. Of these, 87.2% of shunt surgeries occurred within 3 days and 30 were categorized as ground truth positive.

The device was incorrectly placed on 10 subjects, yielding a validation data set of 112 subjects (Figure 4). Twenty-five subjects in the final validation data set were ground truth positive for a complete shunt failure (25/112, 22.3%). All other subjects (87/112, 77.7%), including 13 who had a shunt revision without a complete shunt failure and 2 who underwent shunt surgery but did not have shunt components removed or replaced, were categorized as ground truth negative.

Main Results

Study Device Performance

The sensitivity of the study device using the random forest algorithm was 88.9%, and the specificity was 49.2%. The accuracy, PPV, and NPV of the device were 54.3%, 20.5%, and 96.8%, respectively. The no result rate was 37.5% (42/112) because of incomplete measurements.

TABLE 2. Hydrocephalus and Presenting Characteristics

	Validation (%)
Total subjects	128 (100)
Hydrocephalus etiology[a]	
Myelodysplasia	2 (1.6)
Spina bifida	31 (24.2)
Encephalocele	0 (0.0)
Aqueductal stenosis	16 (12.5)
Dandy-Walker complex	2 (1.6)
Meningitis	3 (2.3)
Arachnoid cyst	3 (2.3)
Tumor	14 (10.9)
Infection	1 (0.8)
Hemorrhage	40 (31.3)
Traumatic brain injury	1 (0.8)
Other	18 (14.1)
Missing	4 (3.1)
Hydrocephalus type	
Obstructive/noncommunicating	60 (46.9)
Nonobstructive/communicating	47 (36.7)
Missing	21 (16.4)
Presenting symptoms[a]	
Seizure	10 (7.8)
Fever	13 (10.2)
Headache	72 (56.3)
Vision problems	10 (7.8)
Dizziness	5 (3.9)
Disorientation	4 (3.1)
Confusion	6 (4.7)
Vomiting	66 (51.6)
Lethargy	31 (24.2)
Irritability	19 (14.8)
Difficulty waking or staying awake	5 (3.9)
Swelling along shunt tract	6 (4.7)
Enlargement of head	1 (0.8)
Loss of balance	5 (3.9)
Gait disturbance	5 (3.9)
Other symptom(s)	52 (40.6)
Study device measurement setting	
Emergency department	27 (21.1)
Inpatient setting	77 (60.2)
Outpatient setting	24 (18.7)

[a]Observed values will not add up to 100%.
Validation data set including subjects with incomplete measurements.
Observed values are number of subjects (%).

The sensitivity of the study device using the binary threshold algorithm was 28.0%, and the specificity was 59.8%. Lower sensitivity in the binary algorithm was primarily due to the misclassification of interfering vascular flow as CSF flow and the reduced ability to identify shunt signals due to the limited feature set used in the decision tree.

All device performance data including pediatric and adult breakdowns are presented in Table 3. Meaningful comparisons between the pediatric and adult performance data could not be made due to the low counts for the adult cohort.

Other Analyses

Standard-of-Care Diagnostic Test Performance

Performance measures were also calculated for standard-of-care tests used in the determination of complete shunt failure. 76.2% of the subjects had ≥2 tests (range: 0-5) within ±48 hours of the study device measurement. Performance data for the 4 most frequent tests are presented in Table 4. CT (N = 81) had the highest sensitivity (82.4%) and specificity (83.3%) (Table 4).

Random Forest Algorithm With Cranial Imaging

Given the high NPV using the random forest algorithm, the data were analyzed post hoc to assess a possible use case in which study device and CT or MRI results were used together as in Figure 3.

In this use case, the sensitivity was 71.4% and the specificity was 93.3%. The accuracy, PPV, and NPV of the combined diagnostic tests were 91.0%, 55.6%, and 96.6%, respectively (Table 3). 45% of subjects had a study device "flow confirmed" output, whereas 55% had a "flow not confirmed" output.

Ease-of-Use

Overall, the device users "strongly agreed" or "agreed" with the ease-of-use statements in 97.4% (748/768) of responses. There were only 2 instances in which the study staff "strongly disagreed" with a statement: once for the statement, "I was able to easily remove the device from the packaging" and once for "I was able to

TABLE 3. Performance of the Study Device

Algorithm	Total	TP	FP	TN	FN	No result	Sensitivity	Specificity	Accuracy	PPV	NPV
Random forest											
All	112	8	31	30	1	42	88.9 (68.4, 100.0)	49.2 (36.6, 61.7)	54.3 (42.6, 66.0)	20.5 (7.8, 33.2)	96.8 (90.6, 100.0)
Children (0-21)	99	7	28	25	1	38	87.5 (64.6, 100.0)	47.2 (33.7, 60.6)	52.5 (39.9, 65.0)	20.0 (6.7, 33.3)	96.2 (88.8, 100.0)
Adults (≥22)	13	1	3	5	0	4	100.0 (100.0, 100.0)	62.5 (29.0, 96.0)	66.7 (35.9, 97.5)	25.0 (0.0, 67.4)	100.0 (100.0, 100.0)
Binary threshold											
All	112	7	35	52	18	—	28.0 (10.4, 45.6)	59.8 (49.5, 70.1)	52.7 (43.4, 61.9)	16.7 (5.4, 27.9)	74.3 (64.0, 84.5)
Children	99	6	33	42	18	—	25.0 (7.7, 42.3)	56.0 (44.8, 67.2)	48.5 (38.6, 58.3)	15.4 (4.1, 26.7)	70.0 (58.4, 81.6)
Adults	13	1	2	10	0	—	100.0 (100.0, 100.0)	83.3 (62.2, 100.0)	84.6 (65.0, 100.0)	33.3 (0.0, 86.7)	100.0 (100.0, 100.0)
Random forest with CT/MRI											
All	112	5	4	56	2	45	71.4 (38.0, 100.0)	93.3 (87.0, 99.6)	91.0 (84.2, 97.9)	55.6 (23.1, 88.0)	96.6 (91.9, 100.0)

CT, computed tomography; FN, false negative; FP, false positive; NPV, negative predictive value; PPV, positive predictive value; TN, true negative; TP, true positive.
Values are given as number of subjects or percent (95% CI).

easily use the mobile app and obtain a device reading." There were 10 instances in which the study staff "disagreed" with a statement. Half of these instances were for the statement, "I was able to easily use the mobile app and obtain a device reading."

Adverse Events

There were 7 adverse events in 7 subjects of the 182 subjects in which a study device measurement was attempted (inclusive of subjects enrolled for device user training, algorithm development, and algorithm validation). The adverse events were all skin observations of "redness" after device removal and resolved quickly. There were no serious adverse events.

DISCUSSION

Key Results

The goal of this study was to establish the performance of a noninvasive CSF shunt flow assessment device in a symptomatic patient population. Using a random forest algorithm, the device had a high sensitivity and NPV, similar to other flow detection devices but with the benefits of being wireless and not requiring an icepack.[46,49] This performance stands in contrast to the moderate sensitivity and high specificity demonstrated by standard-of-care tools, such as CT and MRI.[50] It is important to note that the calculated sensitivity of CT and MRI in this study is higher than those reported in the literature likely due to differences in the ground truth definitions. The study data suggest that the study device and random forest algorithm may support shunt failure risk stratification in a symptomatic population, especially when combined with cranial imaging.

Limitations

Participants in this study were enrolled as a convenience sample which may have over-represented pediatric cases. However, the subjects represented a wide age range with many different hydrocephalus etiologies. In addition, the shunt surgery rate (36.7%; 47/128) is within the range published by others using larger sample sizes.[20,21,25,30,51]

TABLE 4. Performance of Additional Tests

	Total	TP	FP	TN	FN	Sensitivity	Specificity	Accuracy	PPV	NPV
CT	83	14	11	55	3	82.4 (64.2, 100.0)	83.3 (74.3, 92.3)	83.1 (75.1, 91.2)	56.0 (36.5, 75.5)	94.8 (89.1, 100.0)
MRI	39	9	7	20	3	75.0 (50.5, 99.5)	74.1 (57.5, 90.6)	74.4 (60.7, 88.1)	56.3 (31.9, 80.6)	87.0 (73.2, 100.0)
Shunt series	93	7	0	69	17	29.2 (11.0, 47.4)	100.0 (100.0, 100.0)	81.7 (73.9, 89.6)	100.0 (100.0, 100.0)	80.2 (71.8, 88.6)
Shunt tap	15	1	4	7	3	25.0 (0.0, 67.4)	63.6 (35.2, 92.1)	53.3 (28.1, 78.6)	20.0 (0.0, 55.1)	70.0 (41.6, 98.4)

CT, computed tomography; FN, false negative; FP, false positive; NPV, negative predictive value; PPV, positive predictive value; TN, true negative; TP, true positive.
Values are given as number of subjects or percent (95% CI).

The ground truth negative definition included a 7-day follow-up period without a shunt revision surgery. Although this is not equivalent to confirmation of shunt function, it is a well-established criterion in the literature.[9,15,16,19-22,24-29,31-37,42,43,46,49,52-54] The ground truth positive definition included visual intraoperative assessment. Although this definition is consistent with the study device determination of "flow confirmed" or "flow not confirmed," in practice, CSF underdrainage without a complete absence of flow may warrant surgery and underscores the need for multiple tools to aid surgical decision making.

Finally, because the random forest algorithm was not used during data acquisition, an incomplete measurement, such as due to determination of interfering vascular flow, could not be remedied through sensor repositioning. This, along with incorrect device placement, decreased the counts for data analysis. Additional studies using the random forest algorithm and user interface improvements are currently underway to assess performance in representative patient populations and additional care settings.

CONCLUSION

Interpretation

The study device is a wireless, noninvasive, easy-to-use sensor that does not require capital equipment. Although not appropriate for use as a stand-alone tool, the device's high sensitivity and NPV demonstrate its substantial utility in the landscape of existing methods. Finally, use of the device has minimal risk, with a low rate of mild adverse events and no associated serious adverse events, and the device does not require radiation or sedation as with other tools currently in use.

Generalizability

This multicenter study tested the clinical performance of a flow detection device in symptomatic patients. The results are expected to be broadly generalizable in this population; however, caution must be used given the limitations discussed above.

Funding

This research was supported by the National Instutites of Health U44NS121555 and Rhaeos Inc.

Disclosures

Clinical sites received study equipment and funding from Rhaeos Inc. Chase F. Correia, Alex Burton, Jenna E. Koschnitzky, R. Chad Webb, and Adam M. Zysk are employees of Rhaeos, Inc. David D. Limbrick serves as Chief Medical Officer for Rhaeos, Inc. Jesse Skoch contributed to study on behalf of his institution through funding received from Rhaeos. The other authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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Acknowledgments

The authors thank the study participants, their families, and the hospital study staff for their contribution to advancing hydrocephalus research and Musculoskeletal Clinical Regulatory Advisers (MCRA) for statistical analysis support. Author Contribution: David D. Limbrick, Jesse Skoch, Kurtis Auguste, Gerald A. Grant, Sandi K. Lam, Matthew C. Tate, David J. Langer, Jarod L. Roland, Tord D. Alden, Fady T. Charbel, and Robert M. Lober contributed to the study design, data collection, data interpretation, and manuscript revision. Chase F. Correia, Alex Burton, R. Chad Webb, and Adam M. Zysk the study design, data analysis, data interpretation, and manuscript composition and revision. Keith Patten, Elaine Kennedy, Caroline Farless, Samantha Himsworth, Rachel Fasbender, Linda Lovell-Ewen, and Diego M. Morales contributed to data collection and manuscript revision. Jenna E. Koschnitzky contributed to the data analysis, data interpretation, and manuscript composition and revision.

COMMENTS

The authors report the results of a multicenter trial assessing a noninvasive method to confirm shunt function based on thermal anisotropy with a small self-contained device and tablet-based, wireless interface. Under the reported configuration, results are defined as 'flow confirmed' or 'flow not confirmed'. The device addresses a common clinical conundrum—is the shunt working? As simple as this question appears, it is often not simply answered. In absence of change in ventricular caliber on axial imaging, accompanied by subtle clinical signs or subjective symptoms, the decision to operate often relies on ancillary testing (shunt tap, nuclear medicine flow study and others). Ideally, the technology will advance and ultimately allow for determination functional vs nonfunctional shunt—until then, it may provide an additional data point to sort out which patients can safely avoid potentially unwarranted surgical intervention.

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