

**CADTH RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL**

Portable Stroke Diagnosis Devices for Adults with Stroke Symptoms: A Review of Diagnostic Accuracy and Cost-Effectiveness

Service Line: Rapid Response Service
Version: 1.0
Publication Date: July 2, 2019
Report Length: 16 Pages

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Cite As: Portable stroke diagnosis devices for adults with stroke symptoms: a review of diagnostic accuracy and cost-effectiveness. Ottawa: CADTH; 2019 Jul. (CADTH rapid response report: summary with critical appraisal).

ISSN: 1922-8147 (online)

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Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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Abbreviations

3ISS	3 item Stroke Scale
AUC	area under the curve
CinPSS	Cincinnati Pre-hospital Stroke Severity Scale
CRD	Centre for Reviews and Dissemination
CT	computed tomography
MeSH	Medical Subject Headings
MRI	magnetic resonance imaging
N	number of patients
NICE	National Institute for Health and Care Excellence
NIHSS	National Institutes of Health Stroke Scale
NPV	negative predictive value
PASS	Pre-hospital Acute Stroke Severity Scale
PPV	positive predictive value
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QUADAS-2	Quality Assessment of Diagnostic Accuracy Studies 2
VIPS	volumetric impedance phase-shift spectroscopy

Context and Policy Issues

A stroke is the sudden loss of brain function due to cell death resulting from poor or interrupted blood flow within the brain. Strokes are classified as either ischemic, due to lack of blood flow, or hemorrhagic, which are caused by uncontrolled bleeding in the brain.¹ Symptoms of stroke include sudden weakness, inability to move or feel on one side of the body (i.e., paralysis), problems understanding or speaking, dizziness, loss of vision, severe headache, and loss of consciousness.²

Stroke is the second leading cause of death globally,³ accounting for nearly six percent of all deaths in Canada.⁴ There are an estimated 62,000 cases of stroke that occur each year in Canada, and although risk for stroke increases with age, they affect individuals of all age groups.⁵

Clinical diagnosis of stroke can be made using patient history and physical examination, diagnostic tests (e.g., blood glucose, oxygen saturation, prothrombin time, and electrocardiography), and various neuroimaging techniques such as computed tomography (CT) or magnetic resonance imaging (MRI). Although advanced imaging techniques such as CT and MRI are considered the gold standard for stroke identification,⁶⁻⁸ they may not always be readily available in resource-constrained health care settings. A number of novel stroke diagnostic devices have been developed in order to decrease the amount of time required to establish a stroke diagnosis, which is important given that the early identification and treatment of stroke are critical for improving clinical outcomes and ensuring patients receive necessary medical attention.^{5,9} These portable diagnostic devices utilize various imaging techniques, such as Doppler ultrasound, volumetric impedance phase-shift spectroscopy, or microwave tomography to visualize the blood flow characteristics of the brain, providing information on the likelihood a patient has experienced a stroke.¹⁰⁻¹³

This report expands upon a previously completed CADTH report (list of references).¹⁴ The objective of the current report is to evaluate the evidence regarding the diagnostic accuracy and cost-effectiveness of several portable stroke diagnostic devices for adults with symptoms of stroke.

Research Questions

1. What is the diagnostic accuracy of portable stroke diagnostic devices for adults with stroke symptoms?
2. What is the cost-effectiveness of portable stroke diagnostic devices for adults with stroke symptoms?

Key Findings

One relevant non-randomized study was identified regarding diagnostic accuracy of bioimpedance spectroscopy visors for adults with stroke symptoms. This evidence of limited quality suggested that the device accurately differentiated patients requiring severe stroke triage from those who were healthy or who experienced a minor stroke, with a sensitivity of 93% and specificity of 87%.

No evidence regarding the diagnostic accuracy of the combination device (i.e., combination of transcranial Doppler ultrasound, robotic headset blood flow monitor, and machine learning) or of the microwave tomography system for adults with stroke symptoms was identified. Additionally, no evidence regarding the cost-effectiveness of the portable stroke diagnostic devices of interest was identified.

The limitations of the included study (e.g., its open-label nature, unclear recruitment methods, industry-funded status, and potentially limited generalizability) and of this report should be considered when interpreting the results. Further research on the diagnostic test accuracy and cost-effectiveness of portable stroke diagnostic devices in adults with stroke symptoms could reduce this uncertainty.

Methods

Literature Search Methods

This report makes use of a literature search developed for a previous CADTH report.¹⁴ A limited literature search was conducted by an information specialist on key resources including MEDLINE All (1946–) via Ovid, Embase (1974–) via Ovid, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were Cerebrotech, Lucid, Strokefinder, transcranial Doppler ultrasonography, electric impedance, microwave tomography, portable devices, portable diagnosis, and stroke. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 01, 2014 and June 12, 2019.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adults with stroke symptoms
Intervention	Portable diagnostic devices: <ol style="list-style-type: none"> 1. Combination of transcranial Doppler ultrasound, robotic headset blood flow monitor, and machine learning 2. Bioimpedance spectroscopy visor; uses volumetric impedance phase-shift spectroscopy (VIPS) 3. Microwave tomography system
Comparator	Any comparator (e.g., Computed Tomography Angiography; Las Angeles Motor Scale)
Outcomes	Q1: Diagnostic accuracy (e.g., specificity, sensitivity, area under the curve, positive or negative predictive values, accurate triage decision) Q2: Cost-effectiveness
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, and economic evaluations

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2014. Systematic reviews that had broader inclusion criteria than the present review were examined in detail to ascertain whether data could be extracted from a relevant sub-set of included studies, rather than excluding the systematic reviews entirely. If it was not possible to identify relevant primary studies upon detailed investigation the systematic review was excluded.

Critical Appraisal of Individual Studies

One reviewer critically appraised the non-randomized, diagnostic test accuracy study using the QUADAS-2 checklist.¹⁵ Summary scores were not calculated for the included study; rather, a review of the strengths and limitations of the study were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 332 citations were identified in the literature search. Following screening of titles and abstracts, 312 citations were excluded and 20 potentially relevant reports from the electronic search were retrieved for full-text review. In addition, eight potentially relevant publications were retrieved from the grey literature search for full-text review. Of these 28 potentially relevant articles, 27 publications were excluded for various reasons, while one publication, a non-randomized study,¹⁶ met the inclusion criteria and was included in this report. Appendix 1 presents the PRISMA¹⁷ flowchart of the study selection. Additional references of potential interest are provided in Appendix 5.

Summary of Study Characteristics

One non-randomized, diagnostic test accuracy study¹⁶ was identified and included in this review. No relevant health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, or economic evaluations were identified. Detailed characteristics are available in Appendix 2, Table 2.

Study Design

One non-randomized study¹⁶ was identified regarding the diagnostic accuracy of bioimpedance spectroscopy visors for adults with symptoms of stroke. This study was a multi-centre, prospective, diagnostic test accuracy cohort study. Dates of patient recruitment were not reported.

Country of Origin

The included study was conducted in the United States.¹⁶

Patient Population

The non-randomized study¹⁶ pooled data from patient populations recruited into three different cohorts. These cohorts were of variable size and applied different inclusion criteria, as explained below.

- (1) Pilot cohort: a cohort of patients who presented at a comprehensive stroke centre or who were transferred from a satellite hospital with symptoms consistent with acute ischemic stroke (N = 41).
- (2) Healthy cohort: healthy volunteers who had no history of stroke, brain tumour, brain surgery, or significant head trauma. These individuals were included as stroke-free participants (N = 79).
- (3) VITAL cohort: a diverse cohort of patients who presented to one of five comprehensive stroke centres and were undergoing neuroimaging for any brain pathology or neurological presentation (N = 128).

All patients (regardless of cohort) who were found to have implanted medical devices or metal in the head or neck were excluded from the study due to interference with the volumetric impedance phase-shift spectroscopy (VIPS) device recording. The total number of participants included in the study was 252. The mean age of participants was 62 years and the proportion of male participants was 46%.

Interventions and Comparators

The non-randomized study¹⁶ compared the use of mean bioimpedance asymmetry scores, as measured with the VIPS device (index text), to several pre-hospital emergent large vessel occlusion triage scales (i.e., 3 item Stroke Scale [3ISS], Cincinnati Pre-hospital Stroke Severity Scale [CinPSS], National Institutes of Health Stroke Scale [NIHSS], Pre-hospital Acute Stroke Severity Scale [PASS]) and to various neuroimaging techniques (i.e., CT, MRI, angiography – used as the reference standard), for the differentiation of patients with severe stroke from patients with minor stroke or with no stroke.

Outcomes

The outcomes examined in the non-randomized study were various diagnostic characteristics, including sensitivity, specificity, area under the curve (AUC), positive likelihood ratio, negative likelihood ratio, positive predictive value (PPV), and negative predictive value (NPV).

Summary of Critical Appraisal

Additional details regarding the strengths and limitations of the included publication are provided in Appendix 3, Table 3.

The included non-randomized study¹⁶ had clearly described objectives, interventions, controls, patient inclusion and exclusion criteria, main outcomes, and source of data. Some details on baseline patient characteristics were included (e.g., age, sex, NIHSS scores, pathology); however, the study populations came from three different cohorts that applied varying selection criteria and patient characteristics were not tested for statistically significant differences between cohorts, increasing the risk of confounding. Additionally, it was unclear if index test results and reference standards were conducted independently from each other, if assessors were blinded to the results of the other test, and the methods for patient recruitment (e.g., random, consecutively, at the study authors discretion) were not described. As a result, there was a risk for bias in either direction depending on the perceptions and expectations of clinicians and outcome assessors. Although the main findings of the study were presented in tabular form and generally clearly described, the data regarding the diagnostic characteristics of the VIPS device versus commonly used screening tests did not include confidence intervals; therefore, the magnitude and precision of benefit to using the VIPS device over these screening tests is unclear.

Study participants, care providers, and health care settings appear to be representative of the “real-world” and inappropriate exclusion criteria were avoided, increasing the generalizability of the findings. A final limitation to consider is that study was funded by Cerebrotech Medical Systems, the developer of the VIPS device examined in the study. Additionally, one of the authors acknowledged financial interest in Cerebrotech Medical Systems.

Summary of Findings

The overall findings of the included study are summarized below. A detailed summary of the main findings is available in Appendix 4, Table 4.

Diagnostic Accuracy of Portable Stroke Diagnostic Devices

Evidence regarding the diagnostic accuracy of bioimpedance spectroscopy visors for adults with stroke symptoms was available from one non-randomized study.¹⁶

The accuracy of the VIPS device in identifying patients who had experienced a severe stroke was tested in two populations. The first included both patients who had suffered a severe stroke or a small stroke. In this group, the VIPS device had a sensitivity of 93% (95% CI, 83 to 98), specificity of 92% (95% CI, 75 to 99), and an AUC of 0.93 (95% CI, 0.85 to 0.97). The positive and negative predictive values were 96% (95% C, 88 to 99) and 86% (95% CI, 70 to 94), respectively. Data also demonstrated that the VIPS device had increased accuracy in differentiating severe stroke from small strokes compared with other commonly used screening tests (i.e., NIHSS, PASS, 3ISS, CinPSS) in this study population. In the second scenario, the accuracy of the VIPS device in identifying individuals who experienced a severe stroke from the sample of all subjects included in the study (patients with severe stroke, small stroke, or individuals who did not experience any stroke) was evaluated. The device performed with a sensitivity of 93% (95% CI, 83 to 98), specificity of 87% (95% CI, 81 to 92), and an AUC of 0.93 (95% CI, 0.89 to 0.96). The PPV was 70% (95% CI, 61 to 77) while the NPV was 98% (95% CI, 94 to 99). The findings of

this study indicated that the VIPS device may yield high sensitivity and specificity for detection of severe stroke.

Cost-Effectiveness of Portable Stroke Diagnostic Devices

No relevant evidence regarding the cost-effectiveness of portable stroke diagnostic devices for adults with stroke symptoms was identified; therefore, no summary can be provided.

Limitations

A number of limitations were identified in the critical appraisal (Appendix 4, Table 4), however, additional limitations exist.

The quantity of identified relevant literature was low. Evidence on the diagnostic accuracy of the VIPS device was drawn from a single, open-label, non-randomized study¹⁶ that had significant limitations. This study was at risk for selection bias due to unclear patient recruitment methodology, and clinician perceptions and expectations may have played a role in patient recruitment. Additionally, this study was designed and conducted as a calibration study (i.e., to determine appropriate thresholds to maximize the diagnostic ability of the device to differentiate severe stroke from other patients), and the authors stated that additional validation studies are necessary to confirm their findings in other patient populations and settings.

No evidence regarding the diagnostic accuracy or cost-effectiveness of the combination device (i.e., combination of transcranial Doppler ultrasound, robotic headset blood flow monitor, and machine learning) or of the microwave tomography system for adults with symptoms of stroke was identified.

The applicability of the evidence to Canadian settings is unclear as the non-randomized study¹⁶ was conducted in the United States. Any differences in care pathway for adults with symptoms of stroke or in diagnostic scales used in Canadian practice may affect the generalizability of the findings.

Conclusions and Implications for Decision or Policy Making

This review was comprised of one non-randomized study¹⁶ regarding the diagnostic accuracy of bioimpedance spectroscopy visors for adults with stroke symptoms. No evidence was identified for the diagnostic accuracy of the combination device (i.e., combination of transcranial Doppler ultrasound, robotic headset blood flow monitor, and machine learning) or for the microwave tomography system. Additionally, no evidence regarding the cost-effectiveness of the portable stroke diagnostic devices of interest was identified.

Evidence from the non-randomized study¹⁶ suggested that the VIPS device may have the ability to differentiate patients who have experienced severe stroke from those with small stroke or no stroke. The device yielded a sensitivity of 93% and specificity of 87% within the study population. The volume of clinical evidence found in this report regarding bioimpedance spectroscopy visors is consistent with a briefing from the National Institute for Health and Care Excellence (NICE), published in December of 2018.¹⁸

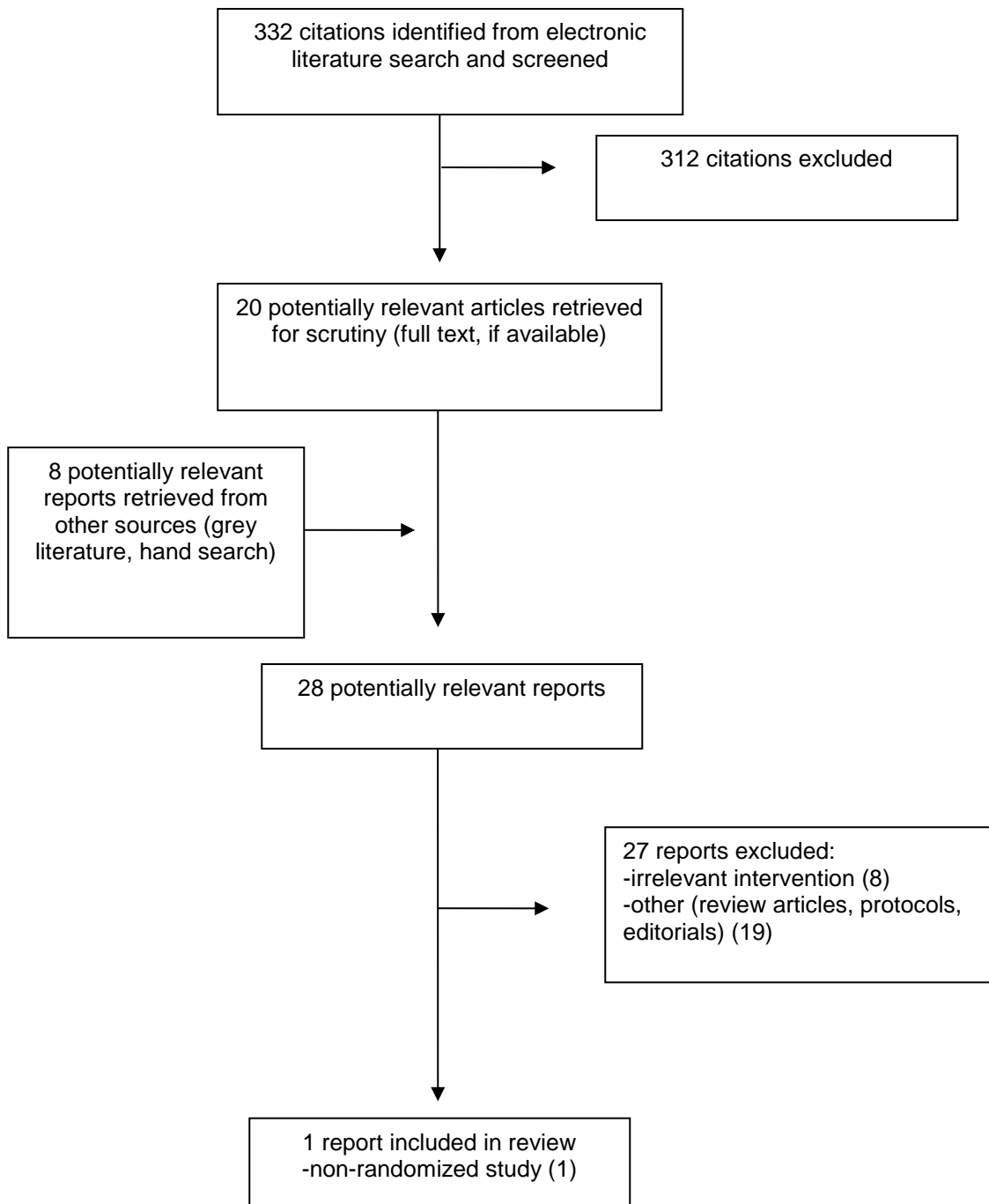
The limitations of the included studies and of this report should be considered when interpreting the results. The findings highlighted in this review come with a high degree of uncertainty due to the limited quantity of available evidence. Further research investigating

the diagnostic accuracy and cost-effectiveness of portable stroke diagnostic devices in adults with stroke symptoms could reduce this uncertainty.

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Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of the Included Primary Clinical Study

First Author, Publication Year, Country	Study Design, Setting, Objective	Patient Characteristics	Index Test and Reference Standard	Clinical Outcomes
Kellner, 2018 ¹⁶ United States	<p>Study design: Multi-centre, prospective, diagnostic test accuracy cohort study</p> <p>Setting: Participants were recruited into one of three study cohorts: a single centre pilot cohort (from a comprehensive stroke centre), a cohort of healthy normal subjects, and the multicentre VITAL study (from five comprehensive stroke centres)</p> <p>Objective: To evaluate the diagnostic accuracy of a portable, non-invasive, and easy to use device for the detection of stroke (the VIPS device)</p>	<p>Inclusion criteria: The study population consisted of three cohorts: 1) a pilot cohort of patients who presented with symptoms consistent with acute ischemic stroke (N = 41), 2) a healthy cohort of normal volunteers who had no history of stroke, brain tumour, or significant head trauma (N = 79), 3) the VITAL cohort of patients who were undergoing neuroimaging for any brain pathology or neurologic presentation (N = 128)</p> <p>Excluded: Patients who were found to have implanted medical devices or metal in the head or neck due to interference with the VIPS device recording</p> <p>Number of patients: 248 (41 in the pilot cohort; 79 in the healthy cohort; 128 in the VITAL cohort)</p> <p>Mean age, years (SD): 71 (15) in the pilot cohort; 58 (15) in the healthy cohort; 62 (16) in the VITAL cohort; 62 (16) in the entire study population</p> <p>Sex: 54% male in the pilot cohort; 44% male in the healthy cohort; 45% male in the VITAL cohort; 46% male in the entire study population</p>	<p>Index test: The use of mean bioimpedance asymmetry scores, as measured with the VIPS device, to diagnose stroke</p> <p>Reference standard: Neuroimaging performed within 30 minutes of VIPS evaluation</p> <p>Comparators: Assessment using one of the following pre-hospital triage scales: NIHSS, PASS, 3ISS, or CinPSS</p>	<p>Outcomes:</p> <ul style="list-style-type: none"> - Sensitivity - Specificity - AUC - Positive likelihood ratio - Negative likelihood ratio - Positive predictive value - Negative predictive value

3ISS = 3 item Stroke Scale; AUC = area under the curve; CinPSS = Cincinnati Pre-hospital Stroke Severity Scale; N = number of patients; NIHSS = National Institutes of Health Stroke Scale; PASS = Pre-hospital Acute Stroke Severity Scale; VIPS = volumetric impedance phase shift spectroscopy; VITAL = VIPS for the Non-Invasive Detection of Hemispheric Bioimpedance Asymmetry in Severe Brain Pathology.

Appendix 3: Critical Appraisal of Included Publications

Table 3: Strengths and Limitations of Diagnostic Test Accuracy Studies using the QUADAS-2 Checklist¹⁵

Strengths	Limitations
Kellner, 2018 ¹⁶	
<ul style="list-style-type: none"> • The objectives, interventions, controls, and main outcomes were clearly described • The data source for the study was provided • A case-control study design was avoided • Patient inclusion and exclusion criteria were included • Inappropriate exclusion criteria were avoided • Population characteristics (e.g., age, sex, NIHSS scores, pathology) were clearly described • The reference standard was likely to correctly classify the target condition (i.e., stroke) • There was an appropriate time interval between VIPS testing and reference standard (i.e., 30 minutes) • Estimates of random variability (95% confidence intervals) were reported for most outcomes • The main findings of the study were presented in tabular form and clearly described • Study participants, care providers, and setting appear to be representative of the population and care setting of interest 	<ul style="list-style-type: none"> • Baseline patient characteristics were not tested for statistically significant differences • It is unclear if patients were sampled consecutively, randomly, or using another method • Study populations came from three different cohorts (the pilot, healthy, and VITAL cohorts) that applied different selection criteria; therefore, a number of uncontrolled factors may have contributed to the findings of the study • 13 subjects were removed from the VITAL cohort due to the presence of cranial metallic hardware or a history of craniotomy • It is unclear if index test results and reference standards were conducted independently and if assessors were blinded to the results of the other test • Due to the design of this study, an MBA score threshold was not pre-specified; data from this study were used to derive cut-off values • Confidence intervals for the diagnostic characteristics of the VIPS device versus commonly used screening tests were not reported; therefore, the magnitude of benefit to using the VIPS device over these screening tests is unclear • Sources of funding were disclosed and may have influenced the findings of the study (the study was funded by Cerebrotech Medical Systems, the developer of the VIPS device) • One author acknowledged financial interest in Cerebrotech Medical Systems • This study was conducted in comprehensive stroke centres in the United States; the generalizability to the Canadian setting is unclear

MBA = mean bioimpedance asymmetry; NIHSS = National Institutes of Health Stroke Scale; VIPS = volumetric impedance phase shift spectroscopy; VITAL = VIPS for the Non-Invasive Detection of Hemispheric Bioimpedance Asymmetry in Severe Brain Pathology.

Appendix 4: Main Study Findings and Authors' Conclusions

Table 4: Summary of Findings of the Included Primary Clinical Study

Main Study Findings	Authors' Conclusion
Kellner, 2018 ¹⁶	
<p>A prospective, non-randomized cohort study that examined the diagnostic accuracy of the VIPS device for the differentiation of major stroke, small stroke, and subjects without stroke (N = 248).</p> <p><u>Summary of relevant findings:</u></p> <ul style="list-style-type: none"> - Diagnostic characteristics for the VIPS device's ability to differentiate patients with severe stroke from patients with small stroke <ul style="list-style-type: none"> o Sensitivity <ul style="list-style-type: none"> ▪ 93% (95% CI, 83 to 98) o Specificity <ul style="list-style-type: none"> ▪ 92% (95% CI, 75 to 99) o AUC <ul style="list-style-type: none"> ▪ 0.93 (95% CI, 0.85 to 0.97) o Positive likelihood ratio <ul style="list-style-type: none"> ▪ 12.09 (95% CI, 3.2 to 45.9) o Negative likelihood ratio <ul style="list-style-type: none"> ▪ 0.076 (95% CI, 0.03 to 0.2) o PPV <ul style="list-style-type: none"> ▪ 96% (95% CI, 88 to 99) o NPV <ul style="list-style-type: none"> ▪ 86% (95% CI, 70 to 94) - Diagnostic characteristics for the VIPS device's ability to differentiate patients with severe stroke from all evaluated patients (including healthy subjects) <ul style="list-style-type: none"> o Sensitivity <ul style="list-style-type: none"> ▪ 93% (95% CI, 83 to 98) o Specificity <ul style="list-style-type: none"> ▪ 87% (95% CI, 81 to 92) o AUC <ul style="list-style-type: none"> ▪ 0.93 (95% CI, 0.89 to 0.96) o Positive likelihood ratio <ul style="list-style-type: none"> ▪ 7.20 (95% CI, 4.9 to 10.6) o Negative likelihood ratio <ul style="list-style-type: none"> ▪ 0.081 (95% CI, 0.03 to 0.2) o PPV <ul style="list-style-type: none"> ▪ 70% (95% CI, 61 to 77) o NPV <ul style="list-style-type: none"> ▪ 98% (95% CI, 94 to 99) - Additional diagnostic characteristics on the ability to differentiate patients with severe stroke from patients with small stroke were calculated for the VIPS device as well as several pre-hospital triage scales (i.e., NIHSS, PASS, 3ISS, and CinPSS) <ul style="list-style-type: none"> o <u>VIPS</u> <ul style="list-style-type: none"> ▪ False negative rate <ul style="list-style-type: none"> • 7% (95% CI, NR) ▪ False positive rate <ul style="list-style-type: none"> • 8% (95% CI, NR) o <u>NIHSS</u> <ul style="list-style-type: none"> ▪ False negative rate <ul style="list-style-type: none"> • 21% (95% CI, NR) ▪ Sensitivity <ul style="list-style-type: none"> • 79% (95% CI, NR) 	<p>"Evaluation in a multicenter clinical derivation study has demonstrated that the VIPS device appears to accurately diagnose patients requiring severe stroke triage, including patients suffering from ELVO. The VIPS device is a portable, non-invasive, and easy to use tool that may aid in the detection of severe stroke, including ELVO, with a sensitivity of 93% and specificity of 92% in this derivation study. Additional validation studies are necessary to confirm these findings in specific patient populations and medical settings."¹⁶ (p. 6)</p>

Main Study Findings	Authors' Conclusion
<ul style="list-style-type: none"> <ul style="list-style-type: none"> ▪ Specificity <ul style="list-style-type: none"> • 71% (95% CI, NR) ○ <u>PASS</u> <ul style="list-style-type: none"> ▪ False negative rate <ul style="list-style-type: none"> • 21% (95% CI, NR) ▪ Sensitivity <ul style="list-style-type: none"> • 79% (95% CI, NR) ▪ Specificity <ul style="list-style-type: none"> • 75% (95% CI, NR) ○ <u>3ISS</u> <ul style="list-style-type: none"> ▪ False negative rate <ul style="list-style-type: none"> • 25% (95% CI, NR) ▪ Sensitivity <ul style="list-style-type: none"> • 75% (95% CI, NR) ▪ Specificity <ul style="list-style-type: none"> • 63% (95% CI, NR) ○ <u>CinPSS</u> <ul style="list-style-type: none"> ▪ False negative rate <ul style="list-style-type: none"> • 25% (95% CI, NR) ▪ Sensitivity <ul style="list-style-type: none"> • 75% (95% CI, NR) ▪ Specificity <ul style="list-style-type: none"> • 71% (95% CI, NR) 	

3ISS = 3 item Stroke Scale; AUC = area under the curve; CI = confidence interval; CinPSS = Cincinnati Pre-hospital Stroke Severity Scale; ELVO = emergent large vessel occlusion; N = number of patients; NIHSS = National Institutes of Health Stroke Scale; NPV = negative predictive value; NR = not reported; PASS = Pre-hospital Acute Stroke Severity Scale; PPV = positive predictive value; VIPS = volumetric impedance phase shift spectroscopy.

Appendix 5: Additional References of Potential Interest

Previous CADTH Reports

Mobile stroke units for prehospital care of ischemic stroke. (*CADTH issues in emerging health technologies no. 154*). Ottawa (ON): CADTH; 2017:

https://www.cadth.ca/sites/default/files/pdf/eh0047_mobile_stroke_units_for_prehospital_care_of_ischemic_stroke.pdf. Accessed 2019 Jun 14.

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<https://www.cadth.ca/sites/default/files/pdf/htis/2016/RC0827%20CTA%20for%20Stroke%20Final.pdf>. Accessed 2019 Jun 14.

Systematic Reviews and Meta-analyses – Alternative Interventions

Burton KR, Perlis N, Aviv RI, et al. Systematic review, critical appraisal, and analysis of the quality of economic evaluations in stroke imaging. *Stroke*. 2014;45(3):807-814.

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Ongoing Clinical Trials

Kellner C, Sauvageau E, Snyder K, et al. Vital phase II: volumetric impedance phase-shift spectroscopy for the noninvasive detection of hemispheric bioimpedance asymmetry in a cohort of patients presenting with acute ischemic stroke. *Eur Stroke J*. 2018 May;3(1 Suppl 1):250.

Granhed H. NCT02728908: Detecting traumatic intracranial hemorrhage with microwave technology. *ClinicalTrials.gov*. Bethesda (MD): U.S. National Library of Medicine; 2016: <https://clinicaltrials.gov/ct2/show/NCT02728908>. Accessed 2019 Jun 14.

Cerebrotech Medical Systems Inc. NCT03148340: Volumetric integral phase-shift spectroscopy for noninvasive detection of hemispheric bioimpedance asymmetry in acute brain pathology (VITAL). *ClinicalTrials.gov*. Bethesda (MD): U.S. National Library of Medicine; 2018: <https://clinicaltrials.gov/ct2/show/NCT03148340>. Accessed 2019 Jun 26.