Critical Review Form
Diagnostic Test

Quantitative video-oculography to help diagnose stroke in acute vertigo and dizziness: toward an ECG for the eyes. Stroke. 2013 Apr;44(4):1158-61.

Objectives: **"to determine whether the [noninvasive video-oculography] device could be used to help discriminate central from peripheral causes in ED patients with AVS [acute vestibular syndrome]." (p. 1159)**

Methods: **This prospective, proof-on-concept study was conducted at 2 tertiary-care hospital emergency departments. Adult patients with vertigo or dizziness lasting ≥ 1 hour and < 7 days, who were still symptomatic, were enrolled. Patients were include if they had nystagmus and one or more of the following: 1) nausea or vomiting, 2) head motion intolerance, or 3) gait or balance disturbance. Patients with a history of previous vestibular or oculomotor disease, drug or alcohol intoxication, or head trauma were excluded. A noninvasive, quantitative video-oculography device was used to record head and eye velocity measurements during head impulse testing. Examiners then assessed the directionality of nystagmus and the presence or absence of skew deviation.**

Two neuro-otologists, blinded to all clinical information and imaging results, were given the results of video-oculography testing and asked to initially categorized patients as having central or peripheral vertigo based on head impulse test results alone. They were then given the remainder of the physical exam findings and were asked to reassign a diagnosis. Two neuroradiologists, blinded to all clinical information, interpreted CT and MRI scans and assigned a diagnosis of stroke or no stroke.

A total of 14 subjects were screened, of whom 12 were enrolled. The median age of enrolled subjects was 62 years, and 10 subjects were men. All subjects underwent MRI with diffusion-weighted imaging (DWI) between hours and 5 days after symptom onset. There was excellent agreement between the neuroradiologists for the diagnosis of stroke ($\kappa = 0.83$). After adjudication, 6 patients were diagnosed with stroke - 5 ischemic, 1 hemorrhagic - and 6 without stroke. These results matched the original, non-research radiology reports.

<table>
<tr><th colspan="2">s</th><th>Comments</th></tr>
<tr><td>I.</td><td>Are the results valid?</td><td></td></tr>
<tr><td>A.</td><td>Did clinicians face diagnostic uncertainty?</td><td>Yes. Patients with acute vestibular syndrome (AVS) in whom the diagnosis of central vs. peripheral vertigo was uncertain were included in the analysis. This was, however, a moderate to high-risk group of patients (50% diagnosed with stroke).</td></tr>
<tr><td>B.</td><td>Was there a blind comparison with an independent gold standard applied similarly to the treatment group and to the control group?
(Confirmation Bias)</td><td>Yes. All patients enrolled underwent MRI with DWI between 10 hours and 5 days from time of symptom onset. MRIs were interpreted by blinded neuroradiologists, and results were compared to the original non-research study results. One could argue, given previous study results demonstrating that MRI has poor sensitivity for stroke when performed early (Kattah 2009), that this is not truly a "Gold Standard," particularly when performed < 48 hours from symptom onset.</td></tr>
<tr><td>C.</td><td>Did the results of the test being evaluated influence the decision to perform the gold standard?
(Ascertainment Bias)</td><td>No. All patients underwent MRI with DWI. However, the study population selected was at high-risk for stroke. Only patients with "pathological nystagmus" were included, and 50% of the cohort was diagnosed with stroke.</td></tr>
<tr><td>II.</td><td>What are the results?</td><td></td></tr>
<tr><td>A.</td><td>What likelihood ratios were associated with the range of possible test results?</td><td>

Quantitative head impulse testing alone correctly diagnosed all 6 patients with peripheral vertigo, but misdiagnosed 2 patients with stroke as having a peripheral cause (Table 1).
Expert interpretation of the horizontal head impulse test matched a purely quantitative analysis of video-oculography results in all 12 cases.

Table 1. Test characteristics of the head impulse test for the diagnosis of central vertigo (95% CI)
<table>
<tr><td>Sensitivity %</td><td>66.7 (22.7-94.7)</td></tr>
<tr><td>Specificity %</td><td>100.0 (54.1-100.0)</td></tr>
<tr><td>PPV %</td><td>100.0 (40.2-100.0)</td></tr>
<tr><td>NPV %</td><td>75.0 (35.1-96.1))</td></tr>
<tr><td>Positive LR</td><td>∞</td></tr>
<tr><td>Negative LR</td><td>0.33 (0.11-1.03)</td></tr>
<tr><td colspan="2">Calculated online using</td></tr>
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<tr><td></td><td></td><td>http://www.medcalc.org/calc/diagnostic_test.php

• For the combined HINTS exam, there was complete agreement between neuro-otologists (κ = 1.0) and all 12 diagnoses correlated with the adjudicated imaging results (see Table).

Table 2. Test characteristics of the HINTS exam for the diagnosis of central vertigo (95% CI)<table><tr><td>Sensitivity %</td><td>100.0 (54.1-100.0)</td></tr><tr><td>Specificity %</td><td>100.0 (54.1-100.0)</td></tr><tr><td>PPV %</td><td>100.0 (54.1-100.0)</td></tr><tr><td>NPV %</td><td>100.0 (54.1-100.0)</td></tr><tr><td>Positive LR</td><td>∞</td></tr><tr><td>Negative LR</td><td>0</td></tr></table></td></tr>
<tr><td>III.</td><td>How can I apply the results to patient care?</td><td></td></tr>
<tr><td>A.</td><td>Will the reproducibility of the test result and its interpretation be satisfactory in my clinical setting?</td><td>Uncertain. For the combined HINTS exam, there was complete agreement between neuro-otologists (κ = 1.0). However, the HINTS exam is a difficult test, and its accuracy and reproducibility may be different in the hands of the emergency physician. The amount of training necessary for emergency physicians to become proficient with testing has not been evaluated. Additionally, this was a very small proof-of-concept study, and its results will need to be verified in a larger study to be comfortable with the results.</td></tr>
<tr><td>B.</td><td>Are the results applicable to the patients in my practice?</td><td>Yes. Patients with vertigo frequently present to the ED. Distinguishing central from peripheral causes of vertigo is clinically difficult, and patients in whom there is clinical concern often undergo neurologic consultation, admission, and advanced neuroimaging (MRI). The ability to differentiate between these two entities by clinical exam would reduce unnecessary testing and admission and reduce the risk of missing potentially dangerous central pathology.</td></tr>
<tr><td>C.</td><td>Will the results change my management strategy?</td><td>No. This was a small "proof-of-concept" study and its results with need to be verified with a larger</td></tr>
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		cohort of patients. Additionally, in the current study the HINTS exam was performed by neuro-otologists, who would likely be familiar and comfortable with the components of the oculomotor exam. Further studies will need to address the accuracy and reliability of the HINTS exam in the hands of the emergency physician, will need to assess the extent of training necessary for proficiency with the exam, and should examine the impact of the exam on patient-centered outcomes, such as decreasing unnecessary testing and reducing cases of missed stroke.
D.	**Will patients be better off as a result of the test?**	Uncertain. The diagnostic test characteristics of the HINTS exam are promising, and it seems likely that its use could result in a decrease in the incidence of missed posterior circulation stroke. This is especially true in light of the risk of missed posterior circulation stroke on MRI (Oppenheim 2000, Morita 2011). Further research will need to assess the impact of the test on clinical decision-making and on patient-centered outcomes.

Limitations:

1. **Potential for false-negative tests in patients with initially normal MRI whose symptoms did not progress, potentially representing TIAs.**

2. **This is a high-risk study population 50% of whom were diagnosed with posterior fossa stroke. While the prevalence of disease should not affect sensitivity or specificity, there is the possibility of spectrum bias.**

3. **This study included a small sample size, and hence the results are imprecise (i.e. there are wide confidence intervals around the estimates of the diagnostic test characteristics).**

4. **The exam was performed by neuro-otologists in this study. The accuracy and reliability of the exam in the hands of emergency physicians still needs to be assessed.**

5. **The accuracy and reliability of the HINTS exam, when aided by a video-oculography device, was not compared to the unaided HINTS exam. If the device does not improve the accuracy or reliability of HINTS, then it would not warrant the added cost.**

Bottom Line

The 3-part oculomotor HINTS exam, aided by a video-oculography device, demonstrated excellent diagnostic test characteristics (sensitivity and specificity 100%, LR+ of ∞, and LR- of 0). Unfortunately, this was a very small study, including only 12 patients, and hence the precision of the results is poor. The study also involved a moderate risk population with a stroke prevalence of 50%, and involved oculomotor examinations performed by neuro-otologists. The external validity of these results to patients in the emergency department with testing performed by emergency physicians is uncertain. Further research will need to assess the accuracy and reliability of the exam in these conditions, the impact of the test on clinical decision-making and on patient-centered outcomes, and the exam's impact on lower-risk patient populations. Additionally, further research will need to show increased accuracy of the HINTS exam when aided by the video-oculography device in order to justify its cost.