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Reliability and comparison of gain values with occurrence of saccades in the EyeSeeCam video head impulse test (vHIT)

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All procedures performed in this study were in accordance with the ethical standards of The Regional Committees on Health Research Ethics for Southern Denmark.
Informed consent was obtained from all individual participants included in the study.
Introduction: The video head impulse test (vHIT) is a new diagnostic tool to assess the function of the three semicircular canals in the vestibular organ, and subsequently the superior and inferior branches of the vestibular nerve [1] [2]. It is based on the vestibulo-ocular reflex (VOR). The VOR ensures that the eyes can maintain visual fixation on a steady target despite head movements.

When the head is moved, the endolymph in the vestibular organ will move as well. This affects the vestibular hair cells. Primary afferent neurons are sent through the vestibular nerve to the nuclei vestibularis in the ponto-medullary region. From here, excitatory signals are transferred to the oculomotor nuclei stimulating the contralateral lateral rectus and the ipsilateral medial rectus muscles and inhibitory projections to the antagonist oculomotor neurons. This results in a horizontal eye movement toward the opposite ear. [3].

If VOR is insufficient, the eyes will not be able to fixate on a target during head movements. Instead, a compensatory quick eye movement will occur, a saccade, towards the target. If this quick eye movement occurs after head rotation has stopped, it is called overt saccades. The quick compensatory eye movements can also occur during head movements and then they are called covert saccades [4].

Overt saccades are detectable for the clinician when performing a bedside head impulse (bHIT). Covert saccades cannot be detected with a bHIT [4] [5].

The EyeSeeCam vHIT contains a high-speed camera that records the eyes’ movement and a gyroscope measuring the speed of head turns during head impulse testing. The recording of the VOR is displayed in a diagram. In the diagram the head impulse and corresponding eye velocities are plotted over time. Right-sided and left-sided impulses are displayed in each diagram.

From the diagram the clinician can detect how well the eye movements correlates the head movement. In case of insufficient VOR both covert and overt saccades will easily be detected in the diagram.

Simultaneously the vHIT calculates a gain value for the head impulse test. The gain value is the relationship between the rotational speed of the head and the movement of the eye in the opposite direction. The calculation is made 40, 60 and 80 ms after the head movement has started [6]. Other device manufactures have applied other gain calculation methods [17].

Normative data for VOR gain values on healthy subject have been obtained by several authors [2] [8] [9] [10] [11]. Blöwdow et al. results showed a normal horizontal VOR gain (hVOR) on 0.96 (SD 0.08), with a lower limit at 0.79 for 20 healthy subjects tested with EyeSeeCam [8]. Mossman et al. found mean hVOR gain on 16 healthy subjects on 0.94 (SD 0.10) tested with the ICS impulse device. No gain fell below 0.65 [11]. Blöwdow also tested subjects with peripheral vestibular disorders and found an average gain value of 0.44 (SD 0.20). But does low gain values necessarily indicate vestibular dysfunction? And are low gain values always accompanied by saccades?

The manufacturer of the EyeSeeCam suggests 0.70 as a cut off value for pathological hVOR gain [12]. MacDougall used 0.68 as cut off value [2]. The question is whether an exact gain value can be used to separate normal from pathologic vHIT results.

The objective of this study was to study the reliability of the vHIT by comparing gain values obtained by two examiners on the same subjects as in the clinical setting. We studied to what extent the gain values were associated with the occurrence of saccades.
**Population:** 25 subjects (33 to 82 years) who had undergone CI surgery were tested 1 month to 1 year after their surgery. The patients had different aetiologies regarding their hearing loss prior to CI surgery. Some of these aetiologies could be accompanied by vestibular abnormalities (see table 1).

Two of four experienced examiners tested the subjects.

**Experimental design:** All tests were performed using the EyeSeeCam vHIT from Interacoustics.

Subjects were seated 1.5 m from a wall. The video goggle was tightened around their head and the camera was adjusted according to the manual of the manufacturer (Interacoustics).

While standing behind the patient, the examiner held the subject’s head in a horizontal plane. The examiners used different hand placements: examiner 1, 3 and 4 held the patients at the jaw and examiner 2 at the top of head. All examiners were careful not to move the goggle during the head movement.

Calibration of the goggles was performed according to the manual of the manufacturer. The calibration was accepted, if the four outer positions of the eye movements were clearly marked and demonstrated a right angled cross without artefacts. Each examiner performed calibration before each examination. Order of examiners was random.

The head impulses were performed by rotating the subject’s head 10-20° in a horizontal plane with a peak velocity of more than 150 °/ms and duration of 150-200 ms. At least 10 impulses were performed to each side.

Instantaneous gain values were calculated by the computer software at 40, 60 and 80 ms after head movement had started. Gain values at 60 ms were obtained and used in the further analysis.

Interpretation of the diagram was carried out by presenting a total of 100 diagrams (one by each examiner from each of the 25 patients) separately to two additional experienced (vHIT) judges, who were without knowledge of the 25 patients. The diagrams included normal as well as pathologic vHIT examinations containing saccades (covert and overt).

Saccades were defined by a change in velocity of the eye movement relative to the head rotation with a peak velocity over 100 °/ms. The saccades were all with similar duration and amplitude, and they appeared in every vHIT tracking curve measured of the eye movements if head rotation exceeded 150 °/ms. Peak velocities under 100 °/ms were considered as artefacts.

The judges categorized the diagrams as normal (rating 1) or pathologic (rating 0).

**Statistical analysis:** All statistical analyses were performed using Stata SE version 14.0 (Stata Corp., Boca Raton, TX).

Interclass coefficient was calculated from the gain values. A power transformation were applied gain values using gain^2. Data now had a normal distribution suitable for further statistic analysis. A quantile-quantile plot was constructed (command qnorm in STATA) to check normal distribution for the new transformation. All models were analyzed without the transformation. Transformation did not affect the overall conclusions of the models.

To study the effects of side on the transformed gain, a linear mixed model was applied (command xtmixed in STATA). Patients were included as random effect parameters in this analysis.

Wald chi-square test was used to verify the overall significance of the different linear mixed models.

Standardized residuals were analyzed against all linear mixed model predictions and evaluated in a residual plot. With the 100 vHIT tests in the study (from the left and right ears in 25 patients tested by two examiners) we would expect one of the observations to fall outside three standard deviations. We have tested the influence of that outlier on the
analyses and it did not affect the overall conclusion. Therefore, the outlier was kept in the analyses.

Kappa’s coefficient was calculated on the interpretation of the diagrams (command \textit{kap observer1 observer2} in Stata).

\section*{Results:}

\subsection*{Differences in gain values between examiners:} Absolute differences in gain values were calculated by subtracting the lowest value from the highest (see table 3). It was done from each ear separately. The difference in the gain value on the right side varied from 0.02 till 0.58 with an average difference at 0.14 (95\% CI 0.12-0.16). Differences in gain on the left side ranged from 0.03 to 0.57 with an average on 0.17 (95\% CI 0.15-0.19).

The average differences in gain values between the examiners were 0.155, which corresponds to 13.8\% difference in gain values between examiners.

\subsection*{Interclass correlation coefficient:} ICC calculated from the gain values by examiner 1 and examiner 2,3,4 ranged from 0.62 to 0.70. Analysis for differences according to side was conducted (see table 2). The right ear was used as reference. A difference of 0.05 in gain values was seen between right and left ear, but the difference was not statistically significant (P=0.315). This indicates that no significant difference in gain value between a patient’s left and right ear occurs.

Analysis for differences amongst examiners was also conducted (see table 2). Examiner 1 had a higher average on gain value compared to both examiner 2, 3 and 4. Only between examiner 1 and examiner 4 the difference was statistically significant (P=0.003).

Analysis for difference in hand placement technique was conducted. Examiner 1 used jaw technique and examiner 2 used top of head technique. Gain values amongst those two in nine subjects were compared. We did not find a statistically significant difference in gain values depending on hand placement technique (-0.10 P=0.302).

When performing the quantile-quantile plot it was clear that one observation was a clear outlier. Gain value for this observation was 1.69. Such high gain value probably occurs due to a technical mistake e.g. loose band strap.

Calculation of ICC without this observation did not affect the overall conclusion.

\subsection*{Diagrams:} 100 diagrams were presented to two judges, who divided them into normal (rating 1) or pathologic (rating 0).

The judgement of diagrams made by the two judges on the same patients was identical regarding occurrence of saccades or not in 93\% of all cases.

Kappa’s coefficient was 0.83 (SE 0.09), which shows a good agreement between the two judges.

\subsection*{Discussion:} The objective was to investigate the reliability of gain values in the EyeSeeCam vHIT between examiners in the same subjects, and to see how differences were related to the occurrence of saccades. This is important in the question of whether an exact gain value can be used to determine vHIT results as normal or pathologic.

We found modest differences in gain value between examiners. Variance in gain values occurs for several reasons. Patterson et al. found that placing the hands on the top of the head resulted in significantly higher mean gain values than placing them on the chin [16]. In our study hand placement did
not lead to significant differences in gain value (table 2). The analysis was however only made on nine subjects, which
may not be enough to detect a significant difference. To investigate how hand placement affects gain values a new
study with more restricted criteria on population, examiners and technique with hand placement as the only variable
factor, must be carried out.

Velocity of the head movement will also affect gain values. Clearly different velocities between two examiners will
lead to gain differences [10]. The EyeSeeCam vHIT does not provide information about the average velocities of head
impulses. We were therefore not able to determine which impact different head velocities among examiners had on gain
values.

There were no significant difference in gain values between the left and the right ear. This is, however, a difficult
comparison since the measurements were made after CI-surgery on one of the ears. CI-surgery was usually done on the
poorer hearing ear and the balance may have been more affected on the operated ear compared to the ear with better
hearing. However, no significant difference in gain was seen and this indicated that the operated ear was not worse
compared to the non-operated ear, but it is not possible to identify, if the gain has changed due to the CI-surgery.

Different distance from the patient to the wall will be equalized during calibration and do not affect gain value.

How tightly the headband is placed around the patient’s head, is an important factor for gain calculation. Is the goggle
too loose, this may lead to too high gain values (>1.12). This may explain the finding in one of our subjects, who had a
gain value of 1.69. In the case of such high values, the test must be repeated. In some situations, this might not be
possible due to the condition of the patients. Instead, looking at the occurrence of saccades or not is a reliable predictor
of the patient’s vestibular function.

The manufacturer suggests 0.70 as a cut off value for separating normal from abnormal vHIT results [12].

Three subjects out of 25 with gain values below 0.70 when tested by examiner 2, had gain values above 0.70 when
tested by examiner 1. This means the subjects were classified as normal by the first examiner and abnormal by the
second examiner using 0.70 as a cut off value. However, the first and second examiner classified the diagrams of the
VOR in all three cases equally. This suggests that the occurrence of saccades may be a more reliable predictor of
vestibulopathy compared to an exact gain value.

ICC was calculated between gain values found by examiner 1 and examiner 2, 3, 4. ICC ranged from 0.62 to 0.70. This
means that 62-70% of the variances found between gain values are due to variances within patients, while 30-38% are
due to variances among examiners.

The ICC of this study is lower than ICC found in previous studies [13] [15].

Kidd et al. found an ICC between 0.61 and 0.85 between gain values found by two different examiners both testing 44
healthy subjects [15]. We tested subjects with vestibular dysfunctions as a part of the daily clinical work, where the
above-mentioned variations occur, which might explain the lower ICC in this study. Kidd used the ICS Impulse device,
which uses a different calculation method for determination of gain than the EyeSeeCam. Different way of calculating
gain might also affect the variation in gain values.

Ulmer et al. found a mean percentage deficit on the horizontal canal approximately 8 % on fifty-three healthy subjects
using the Synapsis vHIT [14]. Mabrey et al. found mean canal deficits on the horizontal canals on 7.5 to 8.9%
investigated on 30 healthy subjects with the Synapsis vHIT [13]. In our study we found a mean percentage deficit on
13%. Ulmer et al. and Mabrey et al. tested only healthy subjects, whereas we tested subjects with various vestibular
disorders, which may explain our higher deficits in gain value.
EyeSeeCam software calculates gain values as instantaneous gain at 40, 60 and 80 ms [6]. MacDougall assumes, that this method of calculating gain might be more sensitive to artefacts, such as bump artefacts and goggle slippage, which can appear around 60-80 ms [7].

To avoid artefacts interrupting gain calculation MacDougall (2013) suggests a de-saccaded position gain over the entire head movement [7]. They found that instantaneous gain calculation could lead to 50% error between vHIT and scleral search coil. However, it is remarkable that they did not find this error using instantaneous gain calculation in their study from 2009 [2]. Instead they concluded that there is a closely correlation between search coil and vHIT.

A de-saccaded gain calculation can though be influenced by other ocular motor systems, such as the cervico-ocular reflex and smooth pursuit, which occur after 100 ms. This may interfere with gain calculation. Instantaneous gain calculation at 40, 60 and 80 ms is not affected by ocular reflexes and smooth pursuit. Moreover, using median of head impulses (instantaneous gain) instead of mean of head impulses, protects better against outliers such as eye blink artefacts [6].

The reproducibility of saccades between examiners where highly consistent despite modest variations in gain values amongst examiners. Saccades were reproducible for both examiners in 93% of cases. Just in 7 of the 100 diagrams the judges disagreed on the occurrence of saccades. In these cases, the diagrams were of poor quality and saccades could easily be misinterpreted as technical artefacts. The occurrence of artefacts seems to cause misinterpretation. This demonstrates the importance of performing sufficient number of head impulses (we recommend at least ten impulses to each side) and to repeat the test, if the quality is not good enough.

Another weakness of the head impulse diagram is that it is a subjective interpretation. Experience with vHIT may affect the interpretation. Making official guidelines for the interpretation of saccades could limit this weakness.

Kappa’s coefficient estimated the inter-observer agreement amongst our to judges. Kappa’s coefficient was calculated to 0.83. This demonstrates a good agreement amongst our two judges on occurrence of saccades or not. We can therefore be quite sure that the interpretation of the diagrams was valid and not affected by coincidences.

Only two judges were used to interpret the diagrams, which is a limitation of the study.

We conclude that the occurrence of saccades is more reliable than the gain value in the judgment of vHIT results using the EyeSeeCam device. Gain values vary due to several factors, whereas interpretation of the diagram only seem to be affected by the appearance of artefacts. The impacts of the different factors on the gain values are poorly investigated for the EyeSeeCam device. More investigations on the EyeSeeCam should be carried out.

The strength of this study was that it reflects the EyeSeeCam’s reliability in the clinical life where both healthy, as well as vestibular non-healthy patients, are being examined. It also puts out several questions of EyeSeeCam’s variability calling for further investigations.

**Conclusion:** Differences in gain values amongst examiners did not seem to affect the occurrence of saccades in the same patient. The occurrence of saccades therefore seems to be more reliable than the gain value in the evaluation of the vestibular function. ICC ranged 0.62 to 0.70 between different examiners. The Kappa’s coefficient on the occurrence of saccades was 0.83. This information is important for the clinician performing and analysing vHIT results. Interpretation of vHIT results should therefore primarily depend on the occurrence of saccades and secondly on the gain value.
Compliance with Ethical Standards: The study is sponsored by The Oticon Foundation, MED-EL G.m.b.H and Danaflex a/s. The authors declare no other conflict of interest. All procedures performed in this study were in accordance with the ethical standards of The Regional Committees on Health Research Ethics for Southern Denmark. Informed consent was obtained from all individual participants included in the study.

References:


Table 1. Vestibular history, gender and average age on subjects.

<table>
<thead>
<tr>
<th>Vestibular history</th>
<th>No.</th>
<th>Gender</th>
<th>Average age (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Otosclerosis</td>
<td>1</td>
<td>1F</td>
<td>55</td>
</tr>
<tr>
<td>Malformation of inner ear</td>
<td>3</td>
<td>3M</td>
<td>54 (33-64)</td>
</tr>
<tr>
<td>Bacterial infection</td>
<td>2</td>
<td>1F/1M</td>
<td>58 (57-60)</td>
</tr>
<tr>
<td>Cholesteatoma</td>
<td>2</td>
<td>2F</td>
<td>58 (55-61)</td>
</tr>
<tr>
<td>Meniere’s Disease</td>
<td>3</td>
<td>3F</td>
<td>65 (61-74)</td>
</tr>
<tr>
<td>Other ear surgery</td>
<td>3</td>
<td>2F</td>
<td>55 (55-55)</td>
</tr>
<tr>
<td>No vestibular history</td>
<td>12</td>
<td>6F/6M</td>
<td>64 (48-82)</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>15F/10M</td>
<td>58 (33-82)</td>
</tr>
</tbody>
</table>
Table 2: Side and examiner affecting gain values with standard error (SE) and significant level (P). Examiner 1 is reference for examiner 2, 3, 4. Right ear as baseline for side differences. Interclass correlation coefficient (ICC) between examiner 1 and examiner 2,3,4.

<table>
<thead>
<tr>
<th>Side</th>
<th>Coefficient</th>
<th>SE</th>
<th>P</th>
<th>ICC</th>
<th>No. of subjects tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>Side</td>
<td>0.05 (-0.05; 0.17)</td>
<td>0.05</td>
<td>0.315</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Examiner 2</td>
<td>-0.10 (-0.29; 0.09)</td>
<td>0.09</td>
<td>0.302</td>
<td>0.67</td>
<td>9</td>
</tr>
<tr>
<td>Examiner 3</td>
<td>-0.23 (-0.43; -0.02)</td>
<td>0.11</td>
<td>0.031</td>
<td>0.79</td>
<td>7</td>
</tr>
<tr>
<td>Examiner 4</td>
<td>-0.27 (-0.44; -0.09)</td>
<td>0.09</td>
<td>0.003</td>
<td>0.62</td>
<td>9</td>
</tr>
</tbody>
</table>
Table 3: Results of vHIT testing.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Right ear</th>
<th>Left ear</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gain (SD)</td>
<td>Difference</td>
</tr>
<tr>
<td>Examiner</td>
<td>Examiner</td>
<td>Examiner</td>
</tr>
<tr>
<td>1</td>
<td>1,00 (0,06)</td>
<td>0,88 (0,21)</td>
</tr>
<tr>
<td>2</td>
<td>1,05 (0,05)</td>
<td>0,77 (0,19)</td>
</tr>
<tr>
<td>3</td>
<td>0,04 (0,13)</td>
<td>-0,30 (0,09)</td>
</tr>
<tr>
<td>4</td>
<td>0,88 (0,15)</td>
<td>0,81 (0,10)</td>
</tr>
<tr>
<td>5</td>
<td>0,93 (0,13)</td>
<td>1,05 (0,08)</td>
</tr>
<tr>
<td>6</td>
<td>1,01 (0,12)</td>
<td>0,86 (0,09)</td>
</tr>
<tr>
<td>7</td>
<td>1,00 (0,08)</td>
<td>0,76 (0,05)</td>
</tr>
<tr>
<td>8</td>
<td>0,95 (0,04)</td>
<td>1,05 (0,08)</td>
</tr>
<tr>
<td>9</td>
<td>0,80 (0,08)</td>
<td>0,84 (0,15)</td>
</tr>
<tr>
<td>10</td>
<td>1,08 (0,04)</td>
<td>0,89 (0,14)</td>
</tr>
<tr>
<td>11</td>
<td>1,15 (0,10)</td>
<td>1,07 (0,05)</td>
</tr>
<tr>
<td>12</td>
<td>0,91 (0,10)</td>
<td>0,81 (0,13)</td>
</tr>
<tr>
<td>13</td>
<td>1,14 (0,16)</td>
<td>1,10 (0,09)</td>
</tr>
<tr>
<td>14</td>
<td>1,02 (0,06)</td>
<td>1,00 (0,06)</td>
</tr>
<tr>
<td>15</td>
<td>1,08 (0,04)</td>
<td>0,90 (0,11)</td>
</tr>
<tr>
<td>16</td>
<td>0,62 (0,05)</td>
<td>0,49 (0,10)</td>
</tr>
<tr>
<td>17</td>
<td>0,88 (0,21)</td>
<td>0,75 (0,06)</td>
</tr>
<tr>
<td>18</td>
<td>0,67 (0,13)</td>
<td>0,60 (0,07)</td>
</tr>
<tr>
<td>19</td>
<td>0,83 (0,13)</td>
<td>0,74 (0,06)</td>
</tr>
<tr>
<td>20</td>
<td>0,45 (0,05)</td>
<td>0,31 (0,09)</td>
</tr>
<tr>
<td>21</td>
<td>1,04 (0,08)</td>
<td>0,95 (0,04)</td>
</tr>
<tr>
<td>22</td>
<td>1,69 (0,21)</td>
<td>1,11 (0,23)</td>
</tr>
<tr>
<td>23</td>
<td>0,66 (0,06)</td>
<td>0,55 (0,07)</td>
</tr>
<tr>
<td>24</td>
<td>0,20 (0,04)</td>
<td>0,22 (0,02)</td>
</tr>
<tr>
<td>25</td>
<td>0,99 (0,10)</td>
<td>0,87 (0,15)</td>
</tr>
</tbody>
</table>

Mean: 0,1396, 0,1292; 0,18, 0,1416