Clinical INS Assessment to Determine Maximally Effective Therapy: 
What can the Physician Apply from the Bench to the Bedside? 

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Introduction
This is a tutorial intended for ophthalmologists who see and treat patients with nystagmus; it divides infantile nystagmus syndrome (INS) patients into three groups based on whether they have high, low, or mid-range measured peak visual acuity. The tutorial’s aims are to: 1) apply the results of the past 50 years of ocular motor research in the office/clinic; 2) enable more accurate diagnoses; 3) determine the most effective, patient-specific therapies to improve the visual function of their patients; and 4) identify which patients need eye-movement recordings to accomplish the above. A Key to Abbreviations used in this tutorial appears at its end; these self-explanatory terms allow concise listings of INS characteristics, therapies, and outcome measures. Finally, to enhance its pedagogical impact, the text is devoid of the hundreds of references that anchor much of the content, which is derived from published research from the laboratories of R. Abadi, H. Bedell, as well as the Daroff-Dell’Osso Ocular Motility Laboratory, accessible at http://www.omlab.org/Personnel/lfd/Jrnl_Arts/lfd3.html. These complementary bodies of work are the “ABD’s” of modern nystagmus research; their study and understanding is a prerequisite for the beginning nystagmus researcher. The significant research of others is also referenced in those papers and chapters. For a “single source” containing the above research, therapies, and literature citations, see Hertle, R. W. & Dell’Osso, L. F. (2012) Nystagmus in Infancy and Childhood. Current Concepts in Mechanisms, Diagnoses, and Management. Oxford University Press: Oxford. Pages 1-324.

Ocular motor (OM) research has demonstrated that clinical observation alone cannot reliably accomplish the difficult tasks of accurate and repeatable diagnosis of INS and its differentiation from other types of nystagmus (e.g., fusion maldevelopment nystagmus syndrome, FMNS; nystagmus blockage syndrome, NBS; spasmus nutans syndrome, SNS; acquired nystagmus, AN;
etc.). The complex waveforms of INS exhibit idiopathic variation with gaze angle, convergence, fixating eye, and time; significant changes in specific waveforms or changes to other waveforms cannot be dependably identified clinically by even the most experienced observer, this author included. Thus, post-therapeutic improvements in visual function are often invisible to both the physician (BCVA may be unchanged) and family members (the nystagmus “looks the same”), leaving them unable to understand or explain either patients’ reports that they “see” better or improvements in patients’ visually guided behavior that accompany their improved visual function. The latter is often most evident in infants and children whose parents report dramatic post-therapy behavioral improvements; these can neither be simply dismissed as “placebo” effects nor their therapeutic importance be diminished just because the single, and inadequate, measurement of best-corrected visual acuity (BCVA) may not have improved significantly.

At present, reliable and repeatable measurements of important INS characteristics are only possible from analysis of OM data obtained from carefully controlled and accurately calibrated eye-movement measurement systems using small (≤0.5°), easy to see, non-anxiety-producing targets (e.g., a small laser spot). In addition to eye-movement recording and the associated calculation of OM functions (e.g., eXpanded Nystagmus Acuity Function, NAFX and Longest Foveation Domain, LFD), all INS patients should have their distance BCVA measured at different gaze angles (see below) and at near while in primary position. Visual acuity measurements should be made with both eyes open, even if only one is fixating due to strabismus. From these measurements, the key clinical measures required to assess INS patients are: 1) peak visual acuity (VApk), 2) high-acuity, gaze-angle range (HAgar), and 3) the presence or absence of strabismus. All acuities discussed in this tutorial are BCVA.

Note: The actual visual acuity within the HAgar is idiosyncratic and, in some patients, their “peak” acuity may be quite low.

Research, using eye-movement data, has documented significant improvements in several of the factors contributing to overall visual function (e.g., peak visual acuity, breadth of the high-acuity gaze-angle range, and speed of target acquisition) in most INS patients. This applies to patients with or without associated afferent visual deficits (e.g., ocular albinism, OA) and whether or not such deficits are severe (i.e., moderate or severe foveal dysplasia or aplasia). Thus, contrary to common presumption, foveal dysplasia or other visual deficits are not contraindications for INS therapy aimed at improving visual function. In summary, percentage improvements in the NAFX may be high, moderate, or low for initial NAFX values that are low, mid range, or high, respectively. Similarly, for the LFD, percentage improvements may be high, moderate, or low for initial LFD values that are low, mid range, or high, respectively. The presence, severity, or absence of sensory deficits affects only the absolute value of the NAFX outcome, not the percentage improvements of either; the latter depend solely on the resulting waveform improvements. Thus, for a given pre-therapy foveation quality in INS waveform, the post-therapy improvement percentages (e.g., in NAFX or LFD) will be equal for patients with no, little, or severe associated afferent visual sensory deficits.

What can a physician do to provide the best clinically based evaluation of an INS patient in the absence of eye-movement recordings (as is often the case)? Specifically, is there a way to use clinical data alone to estimate efficacy of various therapies, even while recognizing that such
estimations may not be as accurate as those based on the NAFX and LFD? This tutorial attempts to answer those questions by providing a clinical roadmap to the evaluation of INS patients. It should be used as a supplement to the normal ocular, retinal, and physiological examinations of INS patients, which are not discussed herein. Similarly, the issue of strabismus is discussed only as it affects the potential surgical therapies of INS; the point should be made however, that both the INS and strabismus surgeries should be combined into a single procedure for cost-effectiveness and minimization to anesthesia exposure or other surgical problems. Finally, the details of specific surgical procedures are discussed in the book referenced above.

**Research Foundations and Methods**

Because many therapies for different types of nystagmus are specific for that type, the first, and most important, step is establishing a definitive diagnosis from the differential diagnoses of INS, FMNS, and mixtures of INS and FMNS. In addition, the NBS and SNS must be identified if present. All of these are easily distinguished using eye-movement data. However, in some cases, their clinical characteristics may suggest which is most likely. Distinguishing INS from FMNS using clinical signs alone may be done easily in some cases, with difficulty in others, and may be impossible in some (see also “Time-Varying Nystagmus”).

Patients with the NBS have INS with a variable strabismus such that INS is present when the eyes are aligned on a distant target but when the patient performs a *purposive esotropia*, the INS either damps or is converted to a low-amplitude FMNS. This esotropia is not true convergence since the vision in the non-fixating eye is suppressed to prevent diplopia. For either damped INS or FMNS, the nystagmus is usually minimal when the fixating eye is in adduction, resulting in a head turn toward the fixating eye.

Patients with SNS have nystagmus with variable conjugacy that may not be clinically detectable. The oscillations of the two eyes may vary within seconds to minutes from perfect conjugacy to 180° disconjugacy and the relative amplitudes of the eye oscillations may vary from equality to uniocular nystagmus. In addition, some SNS patients exhibit a purposive head shaking to simultaneously damp the nystagmus and use their intact VOR to maintain fixation and improve their acuity. To the observer, the eyes remain fixed on the target during the head oscillation (i.e., there is no nystagmus). This purposive head shaking is *not* the same as the involuntary head tremor sometimes seen in INS. The latter is due to the nystagmus signal itself driving the neck muscles and, to the observer, the eyes continue to have nystagmus. The involuntary head tremor of INS has no beneficial effect on either the nystagmus or visual acuity (i.e., it is not “compensatory”), again due to an intact VOR.

It is important to understand that when an INS patient’s BCVA is measured, the resulting value is dependent on *two components*: the presence (and amount) of a visual sensory deficit and the foveation quality of the INS waveform. Here I am presuming that any optical deficits are correctable after proper refraction. One cannot determine the relative contributions of these two components from measuring BCVA alone. However, measurement of *both* the foveation quality (see discussion of the NAFX below) and the BCVA allows quantification of the sensory deficit. Most INS therapies are aimed at improving foveation quality and do not affect any associated sensory deficit that may be present. Although eye-movement data provide quantitative measures of foveation quality from which therapeutic improvement may be estimated, there are instances
where one can infer foveation quality from BCVA and use the latter to make estimates of therapeutic improvement with varying probabilities. For instance, INS patients with high BCVA may be reliably presumed to have little or no afferent sensory deficits and also good foveation quality in their nystagmus waveform. In these cases, the BCVA value (decimal Snellen) is equal to the NAFX and can be used to estimate therapeutic improvement in BCVA with high probability. Application of these considerations follows in the analyses of Cases 1 and 2 below.

The major deficit in most INS patients is the dramatic loss of VA as the eyes are directed laterally from the angle at which VApk occurs. Thus, the significant clinical deficit is not the less-than-normal peak visual acuity. Although VApk is determined by both afferent sensory visual deficits plus the INS waveform’s foveation characteristics, the dramatic fall-off in BCVA at gaze angles lateral to VApk is due solely to the poorer foveation across the nystagmus field; i.e., it is a dynamic motor deficit added to the static sensory deficit. Therefore, the key to a comprehensive clinical evaluation of INS patients is to document this important but clinically neglected deficit by making multiple visual acuity measurements at different gaze angles. To do this properly, the head should be stabilized by a head mount and chin cup fixed to the chair in which the patient is seated. The patient should be instructed to try to keep their head steady in the straight-ahead position and to use only their eyes to look at the eye chart. If necessary (especially for children), the head may be realigned to the straight-ahead position (vis-à-vis, the body) before each acuity measurement to ensure gaze-angle accuracy. Presentation of acuity targets at different gaze angles can be accomplished in two ways: 1) rotate the chair (and, therefore, the patient’s body and head) to known, accurately marked angles from the acuity display, which remains fixed on the wall in the original primary position or 2) project the targets to known, accurately calibrated angles while the chair and head remain stationary in primary position. Given the space limitations of most clinical offices and the ease of accomplishment, the first is the preferred method. One needs to simply have permanent marks on the floor in front of the chair at 0° (primary position), and ±10°, ±20°, and ±30°. This allows for seven acuity measurements across the 60° central range of gaze angles; for those with a sharp peak in their VA vs. Gaze Angle curve, pre-therapy VA measurements in far lateral gaze (relative to their VApk angle) may not always be possible. A primary-position acuity reading with a free head should also be taken and head angle noted to ensure that VApk is also included; the latter value may then also be plotted on the VA vs. Gaze Angle curve.

Note: A simple and effective way to obtain this curve is to use the Excel spreadsheet to plot the Snellen decimal acuity vs. gaze-angle points and fit the data with a 2nd order polynomial trend line. This can be accomplished automatically by merely entering the measured acuities for each gaze angle into a skeleton spreadsheet set up to plot those values and trend line.

From those clinical measurements, the gaze angle (i.e., opposite to head angle) at which VApk actually occurs (see note below on head turns), and HAgar may be determined. Plots of the measured visual acuities vs. gaze angle will parallel those made from the NAFX analysis of eye-movement data (see Appendix, Figure A3) and can be used in a similar, albeit not as accurate, manner to estimate therapeutic improvements. By design, the NAFXpk ⇐ potential VApk ≥ measured VApk; i.e., for those patients with no afferent deficits, potential acuity = measured acuity, making the latter directly equivalent to the NAFX. The HAgar can be calculated in a manner equivalent to the LFD calculation (i.e., the range of gaze angles where VA ≥ 0.9VApk).
The decrease of visual acuity at gaze angles to either side of the peak acuity is duesolely to the reduction of INS-waveform foveation quality and is independent of any associated sensory visual deficit. Thus, unlike the motor + sensory relationship between NAFXpk and VApk, the purely motor-determined LFD will equal the HAgar regardless of the presence or severity of afferent deficits. Based on the estimations of therapeutic improvements that have been demonstrated from NAFX and LFD data, the clinical measures of VApk and HAgar may help determine whether or not any OM therapy may be expected to improve visual function and the amount of that improvement. If both HAgar is \( \leq 25^\circ \) and VApk is \( \leq 0.6 \) (20/35), INS therapy will probably improve visual function by improving both (i.e., broader HAgar and higher VApk). If HAgar is \( \leq 25^\circ \), INS therapy will probably improve visual function (broader HAgar) regardless of VApk. If HAgar is \( > 25^\circ \) and VApk is \( \leq 0.6 \) (20/35), INS therapy will probably improve visual function (higher VApk). The amounts of improvement in these measures may be estimated using the graphs in Figure A3. Only if both HAgar is \( > 25^\circ \) and VApk is \( > 0.6 \) (20/35), is no INS therapy likely to improve visual function (see Table 1, Group 1, top section where 9 of 12 patient types should receive no OM therapy; the remaining three in that section may benefit from the strong therapeutic effects of BMR). Therapies for corrective shifting of VApk from lateral gaze angles (especially if resulting in head turns) are indicated in those cases where present.

Note: The presence of a preferred head position indicates two things: 1) there is a gaze angle at which acuity is maximal and, more importantly, 2) acuity drops off sharply at gaze angles lateral to the peak (i.e., the LFD is low). A preferred head position includes primary position; acuities lateral to 0° will fall off sharply. All preferred head positions are indications that INS therapy will improve visual function.

At best, head turns are inaccurate and inconsistent indicators under the control of the patient and therefore, subject to patient bias (e.g., the child, in an effort to please both his parents and doctor, refuses to adopt a head turn immediately after surgery whose goal was “to straighten his head;” even an adult patient may initially maintain a straight-ahead head position). The net result is a time-limited, “false-positive” result. Such a patient initially sacrifices better vision to show the “success” of the surgery in straightening the head. However, as time goes on, the patient will naturally adopt the post-surgical head turn (less than pre-surgically if the surgery was inadequate) that maximizes visual acuity. That scenario gave rise to the myth of the “returning null.” Longitudinal measurements of the actual INS “nulls” in many patients have demonstrated that the post-surgical positions are immediate, stationary over time, and remain in primary position if the surgery was adequate. Inadequate surgeries (such as those resulting from the “one-size-fits-all” approach inherent in strabismus-derived formulae for muscle recessions and resections) may be corrected by a second procedure to move the peak acuity to primary position, negating the need for any head turn.

A patient’s head turn need not be measured nor should attempts to measure it be used to determine the amount of surgery that might be necessary; head turns/tilts do, however, serve as an indication that VApk is at some gaze (or tilt) angle other than primary position. Nystagmus surgery should be aimed at, and direct therapeutic outcomes measured by, centering and improving the INS best waveforms over the greatest range of gaze angles, not correcting a head turn, which is a problematic, patient-controlled, secondary effect of the INS characteristics. When the former is achieved, the latter will automatically follow; i.e., since it is no longer
beneficial, the head turn will disappear when VApk is moved from its pre-therapy lateral gaze angle to primary position.

Once it is determined whether therapy would benefit an INS patient, the more difficult determination of which therapy should provide the greatest improvements to visual function must be made. This tutorial contains summaries and discussions of illustrative types of INS patients with subtle differences in their clinical profiles along with the inferences that may (or, in certain cases, may not) be drawn in the absence of eye-movement data; when possible, estimated therapeutic outcomes are included. For simplicity and to best illustrate this approach to INS therapy, only the more common horizontal variations are presented. These may be extended to cover more complex cases with both horizontal and vertical variations of horizontal INS or even multiplanar INS. The six illustrative cases begin with the simplest (INS alone, Cases 1 and 2) and progress to the more complex INS plus associated afferent visual deficits (Cases 3 - 6). In each case, the clinical characteristics are first outlined, motor and sensory inferences listed, INS therapies with their expected improvements listed, and lastly, possible therapies are discussed. To ensure internal completeness, each case presentation includes all of the above elements despite the resulting redundancy. Thus, once the clinician identifies the case that fits a particular patient, everything needed for accurate diagnosis, therapy determination, estimation of therapeutic effectiveness, and measurements of the latter is available in one place.

Illustrative Cases
The cases in this tutorial illustrate the considerations producing the therapeutic choices listed in the Tables; Cases 1 and 2 when VApk is high (>0.6, Table 1), Cases 3 and 4, when it is low (<0.25, Table 2), and Cases 5 and 6, when it is mid range (≥0.25 to ≤0.6, Table 3). These Cases appear highlighted and superscripted in their respective Tables. In cases of either high or low VApk, the physician can make some high-probability inferences about the patient’s NAFX and LFD and use them to identify the best INS therapy; mid-range VApk values are more problematic. Pre-therapeutic, clinically based estimations of therapeutic efficacy are necessarily imprecise since, without the NAFX and LFD values specific for the INS motor contributions to visual function, accurate or repeatable estimations based on clinical data alone are not possible at this time. The purpose of the information presented herein is to provide guidelines to the many clinicians who have no access to eye-movement data and help in determining: the cases where INS therapy would be beneficial; the best therapy; and the amount of surgery required on each EOM to provide the greatest improvements in visual function. This tutorial is not meant to infer that clinical analysis alone is the best standard of care in INS. Eye-movement data and their analyses remain the only bases for accurate and repeatable diagnoses, reliable pre-therapy estimations of therapeutic efficacy, and accurate post-therapy measurements of the improvements in INS that are the direct outcomes of both surgical and non-surgical INS therapies. Therefore, specific cases in which clinical assessments alone are insufficient to make the above judgments should be referred to centers where eye-movement recordings and analyses can be performed and therapeutic suggestions offered, before proceeding to treatment.

Each INS characteristic and sensory deficit impacts on whether or not a specific therapy is indicated and to what extent that therapy might improve the patient’s visual function. Their many combinations determine which, if any, INS therapies might improve visual function and the magnitude of their effectiveness. Both VApk and HAgar may be high, low, or mid range,
resulting in 9 combinations of these two variables alone. Then, VA at far could be ≥ near (although it is not likely to exceed near VA) or < near, raising the total to 18 combinations. For each of these, VApk may occur in either primary position, < ±10°, or ≥ ±10°; that yields 54 combinations. Finally, the patient may or may not have strabismus, making the final number, 108. Because, in many of these cases, the presence or absence of strabismus does not alter the nystagmus portion of the surgery, this number is effectively reduced to 81. Of all these different combinations of INS characteristics, few are unlikely to benefit from OM therapy of any kind (surgical or non-surgical). As described above, these few lie in the categories with both high VApk (in primary position) and high HAgar (see Table 1). Thus, for most INS patients, therapies exist that will improve their visual function in one or more ways whether or not they also have an associated afferent visual deficit.

Illustrative Cases (High Acuity, Table 1)
The cases below illustrate the considerations producing the therapeutic choices listed in Table 1, Cases 1 and 2; the Cases appear highlighted and superscripted in Table 1. Patients with high VApk (>0.6) either have “unassociated” (or “isolated”) INS or some minimal associated afferent deficit and allow for high-probability inferences about their NAFX and LFD that can be used to identify the best INS therapy.

Case 1. A high VApk in or near (< ±5°) primary position with a low HAgar; near acuity same as or greater than distance; ± strabismus (Table 1, Group 1, Types hlfp, hlfpS, hlnp, and hlnpS)

A. far acuity ≥ near; ± strabismus (Table 1, Group 1, Types hlfp, hlfpS)

**Inferences:**

OM ➔

- a high NAFXpk in or near primary position at distance (unchanged with convergence)
- a low LFD

Sensory ➔

- little or no afferent sensory deficit (e.g., OA with little foveal dysplasia)

**INS Therapies:**

T&R ➔

- little or no improvement in VApk (little-changed NAFXpk)
- large broadening of the HAgar (increased LFD)

SCL ➔

- little or no improvement in VApk (little-changed NAFXpk)
- possibly large broadening of the HAgar (increased LFD)
Table 1: INS Characteristics and Preferred Therapies for High Visual Acuity Patients

<table>
<thead>
<tr>
<th>INS Characteristics</th>
<th>Group 1</th>
<th>Group 2</th>
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<tbody>
<tr>
<td>VApk = peak visual acuity; HAgar = high-acute gaze-angle range</td>
<td></td>
<td></td>
</tr>
<tr>
<td>m = mid range (10° &lt; mid ≤ 25°); f = far; n = near; p = primary position; s = small lateral angle (&lt;10°);</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L = large lateral angle (≥10°); S = strabismus surgery; K = Kestenbaum; BMR = bimedial recession;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BOPr = base-out prisms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SS = no; Y = yes; SCL = soft contact lenses; T&amp;R = tenotomy and reattachment</td>
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<td></td>
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<tr>
<td>Based on the probability of highest percentage improvements</td>
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</table>

Group identification letters simply reflect the "Y" responses in each column.
B. near acuity > far; ± strabismus* (Table 1, Group 1, Types hlnp, hlnpS)

Inferences:
- OM → a high NAFXpk in or near primary position at distance (improved with convergence)
  a low LFD
- Sensory → little or no afferent sensory deficit (e.g., OA with little foveal dysplasia)

INS Therapies:
- BMR* → improvement in VApk (increased NAFXpk)
  large broadening of the HAgar (increased LFD)
- BOPr** → improvement in VApk (increased NAFXpk)
  large broadening of the HAgar (increased LFD)
  * if strabismus, BMR is not an option and BOPr is usually not an option
  ** with -1.00 S added OU to refraction for pre-presbyopic patients and removed when the patient becomes presbyopic
- T&R → little or no improvement in VApk (little-changed NAFXpk)
  large broadening of the HAgar (increased LFD)
- SCL → little or no improvement in VApk (little-changed NAFXpk)
  possibly large broadening of the HAgar (increased LFD)

Discussion:
Case 1 patients have isolated, unassociated INS with no significant afferent deficits; there may or may not be strabismus and measured acuity may or may not improve at near. The high peak acuity that falls off quickly in lateral gaze means that eye-movement data would show a high NAFXpk in or near primary position and a low LFD. Because of a good afferent visual system, the INS alone limits visual acuity and improvements in the foveation quality of INS waveforms will be translated directly into improvements in visual function.

Two types of INS therapy are possible for Case 1A.
1. Surgically, the 4-muscle T&R procedure may be expected to broaden the high-acuity, gaze-angle region (HAgar=LFD) with little or no improvement in peak acuity (VApk=NAFXpk) since acuity is already high and further improvement in foveation quality has a diminishing effect. If strabismus is present, it should be corrected at the same time as the T&R procedure by suitable recessions and/or resections.
2. Soft contact lenses may have the same positive effects on visual function. In this, and all cases, soft contact lenses may also be used in addition to other therapies.

Note: A good way to identify those INS patients in whom contact lenses would have a beneficial effect is to gently rub or scratch the forehead above one eye and observe the nystagmus. If this afferent stimulation of the ophthalmic division of the trigeminal nerve damps the nystagmus, contact lenses should also.

Four types of INS therapy are possible for Case 1B (if strabismus is present, this is reduced to two, “3” and “4”).
1. Surgically, the BMR procedure may be expected to broaden the high-acuity, gaze-angle region (HAgar=LFD) and provide improvement in peak acuity (VApk=NAFXpk).
2. Non-surgically, base-out prisms (7 PD) in both eyes with -1.00 S added OU to the patient’s refractive correction (if pre-presbyopic) would have similar effects.

3. Surgically, the 4-muscle T&R procedure may be expected to broaden the high-acuity, gaze-angle region (HAgar=LFD) but not to improve peak acuity (VApk=NAFXpk).

4. Soft contact lenses may have some positive effects on visual function.

Note: Initially, based on the 4-muscle data from the Kestenbaum procedure, we recommended that the 2-muscle BMR be accompanied by a 2-muscle T&R of the lateral rectus muscles. However, subsequent data from studies of the effects of convergence and prisms on INS demonstrated that convergence alone maximally damps INS; therefore, the addition of the T&R of the lateral rectus muscles is neither required nor recommended. Thus, the BMR is the only 2-muscle procedure recommended to damp INS.

Figure 1 illustrates the expected improvements in VApk and HAgar resulting from either the T&R (for patients without convergence damping or with strabismus) or BMR (or BOPr) (for binocular patients) therapies. Because VApk is high, VA measurements are equal to NAFX values. The initial low VAgar value (≤10°) may be expected to increase post-therapy to approximately 30° for the T&R and >40° for the BMR. For those patients without strabismus whose INS damps with convergence, BMR or BOPr may be expected to improve VApk and HAgar to a greater extent than the T&R. This patient should improve from someone who is effectively blind when looking laterally to VApk to one who substantially has their highest VApk across a wider range of gaze angles.

**INS Therapy is indicated** because broadening of the range of gaze angles where the patient has the highest acuity is the single most important improvement to better visual function in most daily activities and especially in sports, where reduced target acquisition time will also improve visual function and allow both participation in, and enjoyment of, many sports (see Summary, Observations, and Conclusions).
Figure 1. Measured VA vs. Gaze Angle plots for Case-1 patients with high VApk = NAFXpk in or near primary position and low HAgar = LFD including: VAf = VAn, ± strabismus [Case 1A] and VAf < VAn, no strabismus [Case 1B]. In Figure legends 1 – 6, f = far, and n = near. Solid = pre-therapy curve, and dashed and dot-dashed = post-therapy T&R [Case 1A] and BMR/BOPr [Case 1B] curves respectively. Because they include different possible combinations of INS characteristics, Figures 2 – 6 are more complex than the simple plot from an individual patient, which, like Figure 1, would only contain that patient’s personal pre- and post-therapy acuities.

Case 2. A high VApk in lateral gaze with a low HAgar

A. far acuity ≥ near; ± strabismus (Table 1, Group 1, Types hlfS, hlfLS)

i) VApk @ < ±10° lateral gaze (Table 1, Group 1, Types hlfS, hlfLS)

Inferences:
OM→ a high NAFXpk in lateral gaze angle at distance (unchanged with convergence)
a low LFD
Sensory→ little or no afferent sensory deficit (e.g., OA with little foveal dysplasia)

INS Therapies:
A+T&R→ VApk shifted to primary position (also NAFXpk)
little or no improvement in VApk (little-changed NAFXpk)
large broadening of the HAgar (increased LFD)
SCL→ no shifting of, and little or no improvement in, VApk (little-changed NAFXpk) possibly large broadening of the HAgar (increased LFD)

\( ii) \) VApk @ ±10° lateral gaze (Table 1, Group 1, Types hlL, hlLs)

**Inferences:**
- OM→ a high NAFXpk in lateral gaze angle at distance (unchanged with convergence) a low LFD
- Sensory→ little or no afferent sensory deficit (e.g., OA with little foveal dysplasia)

**INS Therapies:**
- K→ VApk shifted to primary position (also NAFXpk) little or no improvement in VApk (little-changed NAFXpk) large broadening of the HAgar (increased LFD)
- SCL→ no shifting of, and little or no improvement in, VApk (little-changed NAFXpk) possibly large broadening of the HAgar (increased LFD)

**B. near acuity > far; ± strabismus* (Table 1, Group 1, Types hlns, hlnSS*, hlnL, hlnLS*)**

\( i) \) VApk @ < ±10° lateral gaze (Table 1, Group 1, Types hlns, hlnSS*)

**Inferences:**
- OM→ a high NAFXpk in small lateral gaze at distance and higher with convergence a low LFD
- Sensory→ little or no afferent sensory deficit (e.g., OA with little foveal dysplasia)

**INS Therapies:**
- BMR*+→ VApk shifted to primary position (also NAFXpk) improvement in VApk (increased NAFXpk) large broadening of the HAgar (increased LFD)
- A+T&R→ improvement in VApk (increased NAFXpk) large broadening of the HAgar (increased LFD)
- BMR*→ improvement in VApk (increased NAFXpk) large broadening of the HAgar (increased LFD)
- BOPr**→ improvement in VApk (increased NAFXpk) large broadening of the HAgar (increased LFD)

* if strabismus, BMR is not an option and BOPr is usually not an option

** with -1.00 S added OU to refraction for pre-presbyopic patients and removed when the patient becomes presbyopic

- SCL→ little or no improvement in VApk (little-changed NAFXpk) possibly large broadening of the HAgar (increased LFD)

\( ii) \) VApk @ ±10° lateral gaze (Table 1, Group 1, Types hlnL, hlnLS*)

- BMR*+K→ VApk shifted to primary position (also NAFXpk) improvement in VApk (increased NAFXpk) large broadening of the HAgar (increased LFD)
- BOPr**→ improvement in VApk (increased NAFXpk) large broadening of the HAgar (increased LFD)

* if strabismus, BMR is not an option and BOPr is usually not an option
** with -1.00 S added OU to refraction for pre-presbyopic patients and removed when the patient becomes presbyopic

SCL \( \rightarrow \) no shifting of, and little or no improvement in, VApk (little-changed NAFXpk)

possibly large broadening of the HAgar (increased LFD)

**Discussion:**
Case 2A is similar to Case 1, with isolated, unassociated INS and no significant afferent deficits; there may or may not be strabismus and measured acuity does not improve at near. The high peak acuity that falls off quickly in gaze to either side of the lateral peak means that eye-movement data would show a high NAFXpk at a specific lateral gaze position (i.e., the INS “null”) and a low LFD. Because of a good afferent visual system, the INS alone limits visual acuity and improvements in the foveation quality of INS waveforms will translate directly into improvements in measured visual acuity.

Note: Although INS patients with afferent deficits will have lower pre- and post-therapy measured visual acuities than indicated by their NAFX values, the percent improvements in foveation quality still translate directly into percent improvements in visual function.

Two types of INS therapy are possible for Case 2A i).

1. Surgically, a 2-muscle Anderson recession procedure combined with a T&R of the remaining 2 horizontal muscles will achieve similar improvements to the 4-muscle Kestenbaum procedure. That is, it may be expected to broaden the high-acuity and gaze-angle region (HAgar=LFD) with little or no improvement in peak acuity (VApk=NAFXpk) since it is already high and further improvement in foveation quality has a diminishing effect on acuity. However, peak acuity would be shifted from the prior lateral gaze angle to primary position. If strabismus is present, it should be corrected at the same time as the surgical procedure by suitable recessions and/or resections.

Note: There are no NAFX analyses demonstrating that a 2-muscle Anderson procedure by itself (i.e., without the additional T&R) would have equivalent beneficial effects on visual function (e.g., HAgar broadening). Therefore, an Anderson procedure, by itself, is not currently recommended for INS.

2. Soft contact lenses may have the same positive effects on visual function but will not shift the peak-acuity gaze angle to primary position.

Two types of INS therapy are possible for Case 2A ii).

1. Surgically, the 4-muscle Kestenbaum procedure may be expected to broaden the high-acuity, gaze-angle region (HAgar=LFD) with little or no improvement in peak acuity (VApk=NAFXpk) since it is already high and further improvement in foveation quality has a diminishing effect on acuity. However, peak acuity would be shifted from the prior lateral gaze angle to primary position. If the peak-acuity gaze angle is large, the 4-muscle Kestenbaum procedure is the surgery of choice. If strabismus is present, it should be corrected at the same time as the surgical procedure by suitable recessions and/or resections.
2. Soft contact lenses may have the same positive effects on visual function but will not shift the peak-acuity gaze angle to primary position.

Note: For the Kestenbaum and Anderson procedures, the actual amounts of recessions and resections should be determined from the graph in Figure 7 of Dell’Osso and Flynn, Arch Ophthalmol 97:462-469, 1979 by using the gaze angle at which peak acuity was measured, and not from the various strabismus formulae which are neither applicable to nystagmus surgery nor patient-specific to their exact gaze angle for peak acuity. Using equal of amounts of recessions and resections maintains homeostasis by equalizing the surgical repositioning. [A usable worksheet from this Figure may be found in Figure D.4 of Hertle, R. W. & Dell’Osso, L. F. (2012) Nystagmus in Infancy and Childhood. Current Concepts in Mechanisms, Diagnoses, and Management. Oxford University Press: Oxford and is downloadable as Figure F.3.1 from http://www.oup.com/us/nystagmus.]

Figure 2 illustrates the expected improvements in VApk and HAgar resulting from either the A+T&R or K (for patients without convergence damping or with strabismus) or BMR+A+T&R (or BOPr) or BMR+K (for binocular patients) therapies. Because VApk is high, VA measurements are equal to NAFX values. The initial low VAgar values (≤10°) may be expected to increase post-therapy to approximately 30° for the A+T&R or K and >40° for the BMR+A+T&R or BMR+K. For those patients without strabismus whose INS damps with convergence, BMR or BOPr may be expected to improve VApk and HAgar to a greater extent then the T&R. They should improve from being effectively blind when looking lateral to VApk to patients who substantially have their highest VApk across a wider range of gaze angles. Note that the expected results are the same regardless of the lateral extent of VApk and are equal to those in Figure 1, for a primary-position VApk.

**INS Therapy is indicated** in Case 2A i) and ii) because of the broadening of the range of gaze angles where the patient has the highest acuity. The shifting of the gaze angle with the highest acuity to primary position has both visual function and orthopedic benefits, making the two surgical therapies preferable.

Again, Case 2B i) is similar to Case 1, with unassociated INS and no significant afferent deficits; however, there is no strabismus and measured acuity does improve at near. The high peak acuity that falls off quickly in gaze to either side of the small lateral peak means that eye-movement data would show a high NAFXpk at a specific lateral gaze position (i.e., the INS “null”) and a low LFD; convergence would increase both the NAFXpk and LFD values. Because of a good afferent visual system, the INS alone limits visual acuity and improvements in the foveation quality of INS waveforms will translate directly into improvements in visual acuity.

Four types of INS therapy are possible for Case 2B i).

1. Surgically, a 2-muscle Anderson plus 2-muscle T&R combined with a BMR procedure may be expected to shift and broaden the high-acuity, gaze-angle region (HAgar=LFD) and provide improvement in peak acuity (VApk=NAFXpk). Because of the Anderson portion of the procedure, peak acuity would also be shifted from the prior lateral gaze angle to primary position. If there is strabismus, the BMR is contraindicated leaving a 2-muscle Anderson plus 2-
muscle T&R. Because of the Anderson portion of the procedure, peak acuity would also be shifted from the prior lateral gaze angle to primary position.

**Measured Visual Acuity**

![Graph of measured visual acuity vs. gaze angle](image)

Figure 2. Measured VA vs. Gaze Angle plots for Case-2 patients with high VApk = NAFXpk at a small [i] VApk @ < 10° or large [ii] VApk @ ≥ 10° lateral gaze angle, and low HAgar = LFD including: VAf = VAn, ± strabismus [Case 2A] or VAf < VAn, no strabismus [Case 2B]. Solid = possible pre-therapy curves, and dashed and dot-dashed = post-therapy A+T&R [Case 2A i] or K [Case 2A ii] and BMR* = BMR±(A+T&R)/BOPr [Case 2B i] or BMR* = BMR+K [Case 2B ii] curves respectively. Consistent with the Tables, s = small lateral angle (<10°) and L = large lateral angle (≥10°).

2. The BMR procedure alone may be expected to broaden the high-acuity, gaze-angle region (HAgar=LFD) and provide improvement in peak acuity (VApk=NAFXpk). Also, if a small amount of lateral gaze is required for peak acuity and there is sufficient broadening of the resulting high-acuity, gaze-angle region (HAgar=LFD), peak acuity could shift from the prior lateral gaze angle, closer to primary position. If there is strabismus, the BMR is contraindicated.

3. Non-surgically, base-out prisms (7 PD) in both eyes with -1.00 S added OU to the patient’s refractive correction (if pre-presbyopic) would have similar effects. If there is strabismus, the use of base-out prisms is contraindicated.
4. Soft contact lenses may have the same positive effects on the breadth of the high-acuity, gaze-angle region (HAgar=LFD) but will neither shift the peak-acuity gaze angle to primary position nor raise peak acuity appreciably.

*Note:* The amount of BOPr used therapeutically is based on the convergence necessary to damp the INS for distant targets while still allowing the patient to further converge on near targets; it is not determined by the convergence that produces maximal INS damping. The same applies for the magnitude of the recessions in the BMR procedure.

*Note:* After refracting each eye individually, once you add the BOPr OU, the final refraction (to determine the amount of additional –S required to cancel the vergence-induced accommodation) must be done binocularly. That is, you add small amounts of negative spheres in equal pairs to determine the final spherical correction needed for BCVA at distance. Do not occlude either eye or convergence will cease, INS will increase, and the monocular acuity obtained will be for adduction of the non-occluded eye.

**INS Therapy is indicated** in Case 2B i) because of the broadening of the range of gaze angles where the patient has the highest acuity. The additional improvement in the highest acuity makes the surgical and prismatic therapies preferable, with the above caveats in cases with strabismus.

Case 2B ii) is similar to the Case 2B i), with unassociated INS and no significant afferent deficits; there is no strabismus but measured acuity does improve at near; occasionally acuity improves at near even in the presence of strabismus. The peak acuity occurs at a larger lateral gaze angle. The high peak acuity that falls off quickly in gaze to either side of the lateral peak means that eye-movement data would show a high NAFXpk at a specific lateral gaze position (i.e., the “null”) and a low LFD; convergence would increase both the NAFXpk and LFD values. Because of a good afferent visual system, the INS alone limits visual acuity and improvements in the foveation quality of INS waveforms will translate directly into improvements in visual acuity.

Three types of INS therapy are possible for Case 2B ii).
1. Surgically, a 4-muscle Kestenbaum combined with a BMR procedure may be expected to broaden the high-acuity, gaze-angle region (HAgar=LFD) and provide improvement in peak acuity (VApk=NAFXpk). If there is strabismus, the BMR is contraindicated leaving a 4-muscle Kestenbaum procedure. Because of the Kestenbaum procedure, peak acuity would also be shifted from the prior lateral gaze angle to primary position.
2. Non-surgically, base-out prisms (7 PD) in both eyes with -1.00 S added OU to the patient’s refractive correction (if pre-presbyopic) will have similar effects on the high-acuity, gaze-angle region (HAgar=LFD) but a residual shift would remain at the gaze angle at which peak acuity is found. If there is strabismus, the use of base-out prisms is contraindicated.
3. Soft contact lenses may have the same positive effects on the breadth of the high-acuity, gaze-angle region (HAgar=LFD) but will neither shift the peak-acuity gaze angle to primary position nor raise peak acuity appreciably.

**INS Therapy is indicated** in Case 2B ii) because of the broadening of the range of gaze angles where the patient has the highest acuity. The additional improvement of shifting the highest
acuity point to primary position makes the surgical therapy the best and the broadening plus rising of peak acuity makes the prismatic therapy preferable to the soft contact lenses.

**Illustrative Cases (Low Acuity, Table 2)**
The cases below illustrate the considerations producing the therapeutic choices listed in Table 2, Cases 3 and 4; the Cases appear highlighted and superscripted in Table 2. In cases of low VApk (<0.25), we can make some high-probability inferences about the patient’s NAFX and LFD and use them to identify the best INS therapy.
## Table 2. INS Characteristics and Preferred Therapies for Low Visual Acuity Patients

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VApk = peak visual acuity; HAgar = high-acuity gaze-angle range; h = high (>25°); l = low (≤10°); m = mid range (10° < mid ≤ 25°); f = far; n = near; p = primary position; s = small lateral angle (<10°); L = large lateral angle (≥10°); S = strabismus; None = no therapy likely to make significant improvements; N = no; Y = yes; SCL = soft contact lenses; T&R = tenotomy and reattachment; SS = strabismus surgery; A = Anderson; K = Kestenbaum; BMR = bimedial recession; BOPr = base-out prisms

1 Based on the probability of highest percentage improvements
2 Depending on the breadth of HAgar, no peak may be discernable

Group identification letters simply reflect the “Y” responses in each column

Case 1 (see text); Case 2 (see text)
Case 3. A low VApk in or near (< ±5°) primary position with a low HAgar; far acuity ≥ near; ± strabismus (Table 2, Group 2, Types llfp, llfpS)

Inferences:

OM

OM → a) a low NAFXpk in or near primary position at distance (unchanged with convergence) or
b) a mid-range NAFXpk in or near primary position at distance (unchanged with convergence) or
c) a high NAFXpk in or near primary position at distance (unchanged with convergence) and a low LFD

Sensory

d) little or no afferent sensory deficit (e.g., OA + little foveal dysplasia) or
e) moderate afferent sensory deficit (e.g., OA + foveal dysplasia) or
f) significant afferent sensory deficit (e.g., OA + foveal aplasia)

Note: This case illustrates how the same clinical picture may result from patients with very different combinations of OM and sensory abnormalities. The OM and sensory combinations that would produce low acuity are a&d,e,f), b&e,f), or c&f).

INS Therapies:

T&R

T&R → a&d,e,f) large improvement in VApk (large increase in NAFXpk) or
b&e,f) some improvement in VApk (some increase in NAFXpk) or
c&f) no improvement in VApk (no increase in NAFXpk) and large broadening of the HAgar (increased LFD)

SCL

SCL → a&d,e,f) improvement in VApk (increase in NAFXpk) or
b&e,f) some improvement in VApk (some increase in NAFXpk) or
c&f) no improvement in VApk (no increase in NAFXpk) and large broadening of the HAgar (increased LFD)

Discussion:

Unlike Cases 1 and 2, Case 3 represents some of the many patients whose visual acuities are influenced by both afferent visual deficits and INS foveation quality. Without eye-movement data analysis, it is very difficult and sometimes impossible to determine what portion of measured acuity is determined by each of those factors. As is shown above, that has a profound impact on the ability to estimate therapeutic improvements and makes choosing the most effective therapy more problematic. The NAFX was specifically designed to separate out only the INS-waveform contributions to visual acuity, independent of the presence, absence, or severity of afferent visual deficits. That is why, by design, it was fit to potential visual acuity in INS patients with no known visual deficit and not to the general INS population. It is that design characteristic that results in its analytical and predictive power. Other mathematical functions are either approximations of the general INS population or fail to include all of the critical factors that determine acuity; they cannot accurately provide this invaluable separation of the motor from the sensory components of measured visual acuity.

For example, the clinical descriptions in Case 3 may result from either: a low NAFXpk and a small, moderate, or significant sensory deficit (a&d,e,f); a mid-range NAFXpk and a moderate or significant sensory deficit (b&e,f); or a high NAFXpk and a significant sensory deficit (c&f).
Without the ability of the NAFX and LFD to distinguish between these possibilities, it is not possible to determine with assurance what visual function benefits might result from therapeutic intervention aimed at improved INS waveforms (e.g., nystagmus surgery and soft contact lenses) in all patient types included in Case 3.

There are two possible INS therapies with variable outcomes, depending into which possible combination of categories (a-f) the patient falls.

1. If soft contact lenses are tried first and if they have positive therapeutic effects, the results could be used to determine which category is most likely. For instance, if, in addition to broadening the high-acuity, gaze-angle range, there is a significant improvement in peak acuity, the patient would most probably fall into category a&d,e,f), if there is some improvement in peak acuity, into category b&e,f), and if no improvement, into category c&f).

2. Based on the positive results of soft contact lenses, a T&R procedure should be considered for those in categories a&d,e,f) and b&e) and could even be considered in b&f) and c&f), since a broader range of high-acuity gaze angles would result which, by itself, improves visual function. If strabismus is present, it should be corrected at the same time as the T&R procedure by suitable resections and/or resections.

Figure 3 illustrates the expected improvements in VApk and HAgar resulting from the T&R therapy. Because VApk is low, VA measurements are usually less than NAFX values; possible curves for high and mid-range NAFXpk are shown in grey. The initial low VAgar values (≤10°) may be expected to increase post-therapy to approximately 30°. These patients should improve from being effectively blind when looking lateral to VApk to patients who substantially have their highest VApk across a wider range of gaze angles. Note that the expected HAgar results are the same regardless of the NAFXpk values although the latter do effect the amount of expected improvement in VApk.

**INS Therapy is indicated** to a variable degree in patients with the clinical picture of Case 3 because of the broadening of the range of gaze angles where the patient has the highest acuity. The probability of a higher peak visual acuity in a&d,e,f) and b&e) makes the T&R procedure preferable to the soft contact lenses.
Figure 3. Measured VA vs. Gaze Angle plots for Case-3 patients with low VApk ≤ NAFXpk in or near primary position, low HAgar = LFD, and VAf = VAn ± strabismus including the following possibilities: a) low NAFXpk at near and far; b) mid-range NAFXpk at near and far; or c) high NAFXpk at near and far. For clarity in the more complex cases of Figures 3 – 6, individual VA measurements were deemphasized in favor of the 2nd-order trend lines for some of the possible conditions. Pre-therapy NAFX curves of equal LFD values and post-therapy VA curves for conditions b) and c) are shown in grey. Solid = pre-therapy VA and possible NAFX curves and dashed = post-therapy T&R [Case 3 a-c] curves. Consistent with the Tables, h = high NAFXpk (>0.6), m = mid-range NAFXpk (0.25 ≤ NAFXpk ≤ 0.6), and l = low NAFXpk (<0.25).

Case 4. A low VApk in lateral gaze with a mid-range HAgar (Table 2, Group 2, Types lmnS, lmnSS, lmfL, lmfLS, lmnL, lmnLS)

A. far acuity ≥ near; ± strabismus (Table 2, Group 2, Types lmfs, lmfsS, lmfL, lmfLS)

Inferences:
OM⇒
  a) a low NAFXpk @ lateral gaze angle at distance (unchanged with convergence) or
  b) a mid-range NAFXpk @ lateral gaze angle at distance (unchanged with convergence) or
c) a high NAFXpk @ lateral gaze angle at distance (unchanged with convergence) and a mid-range LFD

Sensory→

d) little/no afferent sensory deficit (e.g., OA + little foveal dysplasia) or
e) moderate afferent sensory deficit (e.g., OA + foveal dysplasia) or
f) significant afferent sensory deficit (e.g., OA + foveal aplasia)

**INS Therapies:**

i) \( \text{VApk} @ < \pm 10^\circ \text{ lateral gaze} \) (Table 2, Group 2, Types lmfs, lmfsS)

A+T&R→ VApk shifted to primary position (also NAFXpk)

ii) \( \text{VApk} @ \geq \pm 10^\circ \text{ lateral gaze} \) (Table 2, Group 2, Types lmfl, lmflS)

K→ VApk shifted to primary position (also NAFXpk)

a\&d,e,f) large improvement in VApk (large increase in NAFXpk) or
b\&e,f) some improvement in VApk (some increase in NAFXpk) or
c\&f) little improvement in VApk (little increase in NAFXpk) and some broadening of the HAgar (increased LFD)

SCL→

a\&d,e,f) improvement in VApk (increase in NAFXpk) or
b\&e,f) some improvement in VApk (some increase in NAFXpk) or
c\&f) little improvement in VApk (little increase in NAFXpk) and some broadening of the HAgar (increased LFD)

**B. near acuity > far; ± strabismus (Table 2, Group 2, Type lmns, lmnsS, lmnL, lmnLS)**

**Inferences:**

OM→

a) a low NAFXpk @ lateral gaze angle at distance (higher with convergence) or
b) a mid-range NAFXpk @ lateral gaze angle at distance (higher with convergence) or
c) a high NAFXpk @ lateral gaze angle at distance (higher with convergence) and a mid-range LFD

Sensory→

d) little or no afferent sensory deficit (e.g., OA + little foveal dysplasia) or
e) moderate afferent sensory deficit (e.g., OA + foveal dysplasia) or
f) significant afferent sensory deficit (e.g., OA + foveal aplasia)

**INS Therapies:**

i) \( \text{VApk} @ < \pm 10^\circ \text{ lateral gaze} \) (Table 2, Group 2, Types lmns, lmnsS*)

BMR*+ → VApk shifted to primary position (also NAFXpk)

A+T&R

ii) \( \text{VApk} @ \geq \pm 10^\circ \text{ lateral gaze} \) (Table 2, Group 2, Types lmnL, lmnLS*)

BMR*+K→ VApk shifted to primary position (also NAFXpk)

a\&d,e,f) large improvement in VApk (large increase in NAFXpk) or
b\&e,f) some improvement in VApk (some increase in NAFXpk) or
c\&f) little improvement in VApk (little increase in NAFXpk) and
some broadening of the HAgar (increased LFD)

**BMR**⇒ a&d,e,f) large improvement in VApk (large increase in NAFXpk) or
b&e,f) some improvement in VApk (some increase in NAFXpk) or
c&f) little improvement in VApk (little increase in NAFXpk) and
some broadening of the HAgar (increased LFD)

**BOPr**⇒ a&d,e,f) large improvement in VApk (large increase in NAFXpk) or
b&e,f) some improvement in VApk (some increase in NAFXpk) or
c&f) little improvement in VApk (little increase in NAFXpk) and
some broadening of the HAgar (increased LFD)

* if strabismus, BMR is not an option and BOPr is usually not an option
** with -1.00 S added OU to refraction for pre-presbyopic patients and removed when the patient becomes presbyopic

**SCL**⇒ a&d,e,f) improvement in VApk (increase in NAFXpk) or
b&e,f) some improvement in VApk (some increase in NAFXpk) or
c&f) little improvement in VApk (little increase in NAFXpk) and
some broadening of the HAgar (increased LFD)

**Discussion:**

Similar to Case 3, Case 4 is complex, requiring the consideration of different possible combinations of OM and afferent visual characteristics. In addition, one must consider: the relationship between near and far acuity (A or B) and whether VApk ≤ NAFXpk is near (i) or far (ii) from primary position. These patients have low peak acuities in lateral gaze that only decreases moderately to either side of the peak and there may be strabismus. Because of a possibly abnormal afferent visual system, both the INS and any sensory deficit limit peak visual acuity. However, improvements in the foveation quality of INS waveforms will still translate directly into improvements in visual function regardless of the sensory deficit.

Two types of surgical INS therapy are possible for the patient who’s near acuity is not higher than at distance (A). For Case 4A i), where the gaze angle for VApk is small (<10°), a 2-muscle Anderson recession procedure combined with a T&R of the remaining 2 horizontal muscles will broaden the high-acuity, gaze-angle region (HAgar=LFD). For Case 4A ii), where the gaze angle for VApk is large (≥10°), the 4-muscle Kestenbaum procedure is the surgery of choice. It will have the same effects for large lateral VApk angles as the Anderson recession procedure combined with a T&R of the remaining 2 horizontal muscles has for small lateral VApk angles.

For either Case 4A i) or ii), either surgery will have variable effects on peak acuity (VApk ≤ NAFXpk) depending the NAFXpk pre-therapy value. If it is low (a), a large improvement results; if it is mid range (b), a small improvement results; or if it is high (c), no improvement results. However, peak acuity would be shifted from the prior lateral gaze angle to primary position. These results are equally applicable to all of the sensory possibilities listed (d-f). If strabismus is present, it should be corrected at the same time as the surgical procedure by suitable recessions and/or resections.

Also, for or either Case 4A i) or ii), soft contact lenses may have the similar positive effects on visual function but will not shift the peak-acuity gaze angle to primary position. As in Case 3, soft contact lenses may be used prior to surgery to determine which combination of OM and
sensory deficits applies and thereby, estimate the probable improvements in VApk (see Discussion of Case 3).

**Measured Visual Acuity**

![Graph showing Measured Visual Acuity](image)

Figure 4. Measured VA vs. Gaze Angle plots for Case-4 patients with low VApk ≤ NAFXpk at a small [i] VApk @ < 10° or large [ii] VApk @ ≥ 10° lateral gaze angle, and mid-range HAgar = LFD including: VAf = VAn, ± strabismus [Case 4A] or VAf < VAn, no strabismus [Case 4B]. The following possibilities are also included: a) low NAFXpk at far; b) mid-range NAFXpk at far; or c) high NAFXpk at near and far. Pre-therapy NAFX curves of equal LFD values and post-therapy VA curves for conditions b) and c) are shown in grey. Solid = pre-therapy VA and possible NAFX curves and dashed and dot-dashed = post-therapy A+T&R [Case 4A i) a-c)] or K [Case 4A ii) a-c)] and BMR±(A+T&R)/BOPr [Case 4B i)] or BMR+K [Case 4B ii)] curves respectively. Consistent with the Tables, s = small lateral angle (<10°), L = large lateral angle (≥10°), h = high NAFXpk (>0.6), m = mid-range NAFXpk (0.25 ≤ NAFXpk ≤ 0.6), and l = low NAFXpk (<0.25).

Figure 4 illustrates the expected improvements in VApk and HAgar resulting from either the A+T&R or K (for patients without convergence damping or with strabismus) or BMR+A+T&R (or BOPr) or BMR+K (for binocular patients) therapies. Because VApk is low, VA measurements are usually less than NAFX values; possible curves for high and mid-range
NAFXpk are shown in grey. The initial mid-range VAgar values (20°) should increase post-therapy to approximately 42° for A+T&R or K and >45° for BMR+A+T&R or BMR+K. For those patients without strabismus whose INS damps with convergence, BMR or BOPr may be expected to improve VApk and HAgar to a greater extent than the T&R. These patients should improve from being effectively blind when looking laterally to VApk to patients who substantially have their highest VApk across a wider range of gaze angles. Note that the expected results are the same regardless of the lateral extent of VApk.

**INS Therapy is indicated** in Case 4A because of the broadening of the range of gaze angles where the patient has the highest acuity. The shifting of the gaze angle with the highest acuity to primary position has both visual function and orthopedic benefits, making the surgical therapies preferable.

Case 4B is similar to Case 4A, requiring the consideration of different combinations of possible OM and afferent visual characteristics; however, measured acuity does improve at near. In addition, one must consider whether VApk is near (i) or far (ii) from primary position.

Three types of surgical INS therapy are possible for the patient who’s near acuity higher than at distance (B) and has no strabismus. For Case 4B i), where the gaze angle for VApk is small (<10°), a BMR procedure combined with a 2-muscle Anderson recession procedure plus T&R of the remaining 2 horizontal muscles will broaden the high-acuity, gaze-angle region (HAgar=LFD). Alternatively, the BMR alone may accomplish the same thing, since the broadening of the HAgar would effectively shift VApk to primary position. For Case 4B ii), where the gaze angle for VApk is large (≥10°), a BMR procedure combined with a the 4-muscle Kestenbaum procedure is the surgery of choice. It will have the same shifting effects for large lateral VApk angles as the Anderson recession procedure combined with a T&R of the remaining 2 horizontal muscles has for small lateral VApk angles. In this case, the BMR alone may not fully accomplish the same thing, since the broadening of the HAgar might not effectively shift VApk to primary position.

For either Case 4B i) or ii), either of the three surgeries will have variable effects on peak acuity (VApk ≤ NAFXpk) depending the NAFXpk pre-therapy value. If it is low (a), a large improvement results; if it is moderate (b), a small improvement results; or if it is high (c), no improvement results. However, peak acuity would be shifted from the prior lateral gaze angle to primary position and VAgar would be broadened. These results are equally applicable to all of the sensory possibilities listed (d-f). If strabismus is present, the BMR is contraindicated; the Anderson plus T&R (i) or the 4-muscle Kestenbaum (ii) should be performed and the strabismus corrected at the same time by suitable recessions and/or resections.

Also, for or either Case 4B i) or ii), soft contact lenses may have the similar positive effects on visual function but will not shift the peak-acuity gaze angle to primary position. As in Case 3, soft contact lenses may be used prior to surgery to determine which combination of OM and sensory deficits applies and thereby, estimate the probable improvements in VApk (see Discussion of Case 3).
INS Therapy is indicated in Case 4B because of the broadening of the range of gaze angles where the patient has the highest acuity. The shifting of the gaze angle with the highest acuity to primary position has both visual function and orthopedic benefits, making the surgical therapies preferable.

Illustrative Cases (Mid-Range Acuity, Table 3)
The cases below illustrate the considerations producing the therapeutic choices listed in Table 3, Cases 5 and 6; the Cases appear highlighted and superscripted in Table 3. In cases of mid-range VApk (≥0.25 to ≤0.6), we are limited to lower probability inferences about the patient’s NAFX and LFD for use in identifying the best INS therapy.
Table 3. INS Characteristics and Preferred Therapies for Mid Visual Acuity Patients

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<tr>
<th>Group 3 Types</th>
<th>VApk</th>
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<th>VApk</th>
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<th>INS Therapies</th>
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VApk = peak visual acuity; HAgar = high-acuity gaze-angle range; h = high (>25°); l = low (≤10°); m = mid range (10° ≤ mid < 25°); f = far; n = near; p = primary position; s = small lateral angle (<10°); L = large lateral angle (≥10°); S = strabismus; None = no therapy likely to make significant improvements; N = no; Y = yes; SCL = soft contact lenses; T&R = tenotomy and reattachment; SS = strabismus surgery; A = Anderson; K = Kestenbaum; BMR = bimedial recession; BOPr = base-out prisms

1 Based on the probability of highest percentage improvements

2 Depending on the breadth of HAgar, no peak may be discernable

Group identification letters simply reflect the “Y” responses in each column

<sup>3</sup> Case 5 (see text); <sup>5</sup> Case 6 (see text)
Case 5. A mid-range VApk in or near (< ±5°) primary position with a high HAgar (Table 3, Types mhfp, mhfps, mhnp, mhnpS)

A. far acuity ≥ near; ± strabismus (Table 3, Group 3, Types mhfp, mhfps)

Inferences:
OM →
- a) a low NAFXpk in or near primary position at distance (unchanged with convergence)
or
- b) a mid-range NAFXpk in or near primary position at distance (unchanged with convergence)
or
- c) a high NAFXpk in or near primary position at distance (unchanged with convergence) and
  a high LFD
Sensory →
- d) little/no afferent sensory deficit (e.g., OA + little foveal dysplasia) or
- e) moderate afferent sensory deficit (e.g., OA + some foveal dysplasia) or
- f) large afferent sensory deficit (e.g., OA + foveal aplasia)

INS Therapies:
T&R → some improvement in VApk (some increase in NAFXpk)
little or no broadening of the HAgar (unchanged LFD)
SCL → some improvement in VApk (some increase in NAFXpk)
no broadening of the HAgar (unchanged LFD)

B. near acuity > far; ± strabismus (Table 3, Group 3, Types mhnp, mhnpS)

Inferences:
OM →
- a) a low NAFXpk in primary position at distance (increased with convergence)
or
- b) a mid-range NAFXpk in primary position at distance (increased with convergence)
or
- c) a high NAFXpk in primary position at distance (increased with convergence) and
  a high LFD
Sensory →
- d) little/no afferent sensory deficit (e.g., OA + little foveal dysplasia) or
- e) moderate afferent sensory deficit (e.g., OA + some foveal dysplasia) or
- f) large afferent sensory deficit (e.g., OA + foveal aplasia)

INS Therapies:
BMR* → improvement in VApk (increased NAFXpk)
no broadening of the HAgar (unchanged LFD)
BOPr** → improvement in VApk (increased NAFXpk)
no broadening of the HAgar (unchanged LFD)
  * if strabismus, BMR is not an option and BOPr is usually not an option
  ** with -1.00 S added OU to refraction for pre-presbyopic patients and removed
  when the patient becomes presbyopic
SCL → some improvement in VApk (some increase in NAFXpk)
no broadening of the HAgar (unchanged LFD)

Discussion:
Case 5 patients have a mid-range distance visual acuity, both in primary position and in lateral gaze that is not (A) or is (B) greater at near. Therefore, the NAFXpk cannot be low (a) nor can
there be a severe afferent sensory deficit (f), as the strikethroughs indicate. The remaining possibilities are b&d,e and c&e.

For Case 5A, the 4-muscle T&R procedure is indicated. It will improve VApk ≤ NAFXpk but VAgar=LFD will remain unchanged. For Case 5B with no strabismus, either a BMR or BOPr are the best choices; they will improve VApk and leave VAgar high. For Case 5 (A or B) with strabismus, the 4-muscle T&R plus strabismus correction is preferred; it will improve VApk and leave VAgar high. Soft contact lenses can also be used in Case 5 (A or B).

**Measured Visual Acuity**

![Measured Visual Acuity Graph](image)

Figure 5. Measured VA vs. Gaze Angle plots for Case-5 patients with mid-range VApk ≤ NAFXpk in or near primary position, high HAgar = LFD, including: VAF = VAn, ± strabismus [Case 5A] or VAF < VAn, no strabismus [Case 5B]. The following possibilities are also included: b) mid-range NAFXpk at far; or c) high NAFXpk at near and far. Pre-therapy NAFX curves of equal LFD values and post-therapy VA curves for conditions b) and c) are shown in grey. Solid = pre-therapy VA and possible NAFX curves and dashed and dot-dashed = post-therapy T&R [Case 5A b,c] and BMR±T&R/BOPr [Case 5B b,c]) curves respectively. Consistent with the Tables, h = high NAFXpk (>0.6) and m = mid-range NAFXpk (0.25 ≤ NAFXpk ≤ 0.6).

Figure 5 illustrates the expected improvements in VApk and HAgar resulting from either the T&R (for patients without convergence damping or with strabismus) or BMR (or BOPr) (for
binocular patients) therapies. Because VApk is mid range, VA measurements are ≤ NADEX values; the possible curve for high NADEXpk is shown in grey. The initial high VAgar values (35°) should not increase substantially (e.g., to 43°) post-therapy for A+T&R or K but should increase to approximately 56° for BMR. For those patients without strabismus whose INS damps with convergence, BMR or BOPr may be expected to improve VApk to a greater extent then the T&R. These patients should improve due to their higher VApk.

**INS Therapy is indicated** in Case 5 because VApk will increase and the high VAgar will be retained. There should be a greater increase with surgery than soft contact lenses (especially with the BMR procedure), making the surgical therapies preferable.

**Case 6. A mid-range VApk in far lateral gaze with a mid-range HAgar (Table 3, Types mmfL, mmfLS, mmnL, mmnLS)**

A. far acuity ≥ near; ± strabismus (Table 3, Group 3, Types mmfL, mmfLS)

VApk @ ≥ ±10° lateral gaze

**Inferences:**

**OM**

a) a low NADEXpk in far lateral gaze at distance (unchanged with convergence) or
b) a mid-range NADEXpk in far lateral gaze at distance (unchanged with convergence) or
c) a high NADEXpk in far lateral gaze at distance (unchanged with convergence) and a mid-range LFD

**Sensory**

d) little/no afferent sensory deficit (e.g., OA + little foveal dysplasia) or
e) moderate afferent sensory deficit (e.g., OA + some foveal dysplasia) or
f) large afferent sensory deficit (e.g., OA + foveal aplasia)

**INS Therapies:**

K → VApk shifted to primary position (also NADEXpk)
(b&d,e) improvement in VApk (increased NADEXpk)
(c&e) improvement in VApk (increased NADEXpk) and broadening of the HAgar (increased LFD)

SCL → some improvement in VApk (increased NADEXpk)
some broadening of the HAgar (increased LFD)

**B. near acuity > far; ± strabismus (Table 3, Group 3, Types mmnL, mmnLS)**

VApk @ ≥ ±10° lateral gaze

**Inferences:**

**OM**

a) a low NADEXpk in far lateral gaze at distance (increased with convergence) or
b) a mid-range NADEXpk in far lateral gaze at distance (increased with convergence) or
c) a high NADEXpk in far lateral gaze at distance (increased with convergence) and a mid-range LFD

**Sensory**

d) little/no afferent sensory deficit (e.g., OA + little foveal dysplasia) or
e) moderate afferent sensory deficit (e.g., OA + foveal dysplasia) or
f) large afferent sensory deficit (e.g., OA + foveal aplasia)

**INS Therapies:**

**BMR**+K → VApk shifted to primary position (also NAFXpk)
- b&d,e) improvement in VApk (increase in NAFXpk) or
c&e) little improvement in VApk (little increase in NAFXpk) and some broadening of the HAgar (increased LFD)

BMR→
- b&d,e) large improvement in VApk (some increase in NAFXpk) or
c&e) little improvement in VApk (little increase in NAFXpk) and some broadening of the HAgar (increased LFD)

BOPr** →
- b&d,e) improvement in VApk (increase in NAFXpk) or
c&e) little improvement in VApk (little increase in NAFXpk) and some broadening of the HAgar (increased LFD)

* if strabismus, BMR is not an option and BOPr is usually not an option
** with -1.00 S added OU to refraction for pre-presbyopic patients and removed when the patient becomes presbyopic

SCL →
- some improvement in VApk (increased NAFXpk)
some broadening of the HAgar (increased LFD)

**Discussion:**

Case 6 patients have a mid-range distance visual acuity in lateral gaze, decreases lateral to VApk ≤ NAFXpk, and is not (A) or is (B) greater at near. Therefore, the NAFXpk cannot be low (a) nor can there be a severe afferent sensory deficit (f), as the strikethroughs indicate. The remaining possibilities are b&d,e and c&e.

For Case 6A, the 4-muscle Kestenbaum procedure is indicated. It will shift and improve VApk ≤ NAFXpk and VAgar=LFD also broaden. For Case 6B with no strabismus, either a BMR+K, BMR, or BOPr are the best choices; they will improve VApk and broaden VAgar. For Case 6 (A or B) with strabismus, the 4-muscle Kestenbaum plus strabismus correction is preferred; it will improve VApk and broaden VAgar. Soft contact lenses can also be used in Case 6 (A or B).

Figure 6 illustrates the expected improvements in VApk and HAgar resulting from K (for patients without convergence damping or with strabismus) or BMR+K (for binocular patients) therapies. Because VApk is mid range, VA measurements are ≤ NAFX values; the possible curve for high NAFXpk is shown in grey. The initial mid-range VAgar values (20°) should increase post-therapy to approximately 42° for K and 56° for BMR+K. The initial mid-range VAgar values should increase post-therapy. For those patients without strabismus whose INS damps with convergence, BMR+K or may be expected to improve VApk and HAgar to a greater extent then the T&R. These patients should improve from being effectively blind when looking lateral to VApk to patients who substantially have their highest VApk across a wider range of gaze angles.

**INS Therapy is indicated** in Case 6 because VApk will increase and VAgar will be broadened. There should be a greater increase with surgery than soft contact lenses (especially with the BMR procedure), making the surgical therapies preferable.
Figure 6. Measured VA vs. Gaze Angle plots for Case-6 patients with mid-range VApk ≤ NAFXpk at a large [VApk @ ≥ 10°] lateral gaze angle, high HAgar = LFD, including: VAf = VAn, ± strabismus [Case 6A] or VAf < VAn, no strabismus [Case 6B]. The following possibilities are also included: b) mid-range NAFXpk at far; or c) high NAFXpk at near and far. Solid = pre-therapy VA and possible NAFX curves and dashed and dot-dashed = post-therapy K [Case 6A b,c)] and BMR+K [Case 6B b,c)] curves respectively. Consistent with the Tables, h = high NAFXpk (>0.6) and m = mid-range NAFXpk (0.25 ≤ NAFXpk ≤ 0.6).

Time-Varying Nystagmus
If a patient exhibits either a nystagmus that changes direction with time or alternate head turns, a definitive diagnosis should be made using the following clinical tests to allow determination of the proper INS therapy.

DIAGNOSIS
Approximately 9-30% of INS patients have asymmetric (a)periodic alternating nystagmus (APAN). Therefore, it is important to verify that it is APAN and not a change in the fixating eye that is causing the change in nystagmus or head turns.
1) Occlude one (the non-preferred) eye and observe the INS in primary position for at least 10 minutes. If there is a reversal, it is APAN. If not,
2) An alternate-cover test should identify the cause of nystagmus reversal or alternate head turns.
as secondary to a change in the fixating eye. If no nystagmus direction reversal occurs the patient has INS, if one occurs, the patient may have INS with a latent component, FMNS, or both. To distinguish between them, 3) Occlude one eye and observe the fixating eye from far abduction to far adduction. If a monotonic decrease with no reversal occurs, and you get the same results (no reversal) with the other eye fixating, it's probably FMNS but might still be INS with a large latent component (i.e., the occlusion shifts the null so far into adduction that it is not reached by adducting gaze). If a reversal occurs in adduction, it is INS with a latent component or both INS and FMNS (only eye-movement data can differentiate these two possibilities).

TREATMENT
If the clinical tests suggest APAN, four types of INS therapy are possible. Patients with APAN and no convergence damping (i.e., far acuity ≧ near) should be treated as follows.
1. Surgically, they should be treated in the same way as those with either no null or a null in primary position. The 4-muscle T&R procedure should improve waveforms (NAFX values) and may also alter the APAN periodicity. As with all INS cases, the amount of improvements in peak acuity and gaze-angle acuity will depend on the pre-surgical values of the NAFX and LFD functions. Without eye-movement data these cannot be predicted a priori but the numbers from our studies suggest some improvement in either one or both of these measures in most patients.
Patients with APAN plus convergence damping (i.e., near acuity > far) and no strabismus should be treated with either of the following two therapies.
2. Surgically, the BMR procedure may be expected to broaden the high-acuity, gaze-angle region (HAgar=LFD) with possible improvement in peak acuity (VApk ≤ NAFXpk).
3. Non-surgically, base-out prisms (7 PD) in both eyes with -1.00 S added OU to the patient’s refractive correction (if pre-presbyopic) will have similar effects.

For all APAN patients, the following non-surgical treatment is also possible.
4. Non-surgically, in all cases of APAN, soft contact lenses may have the same positive effects on the breadth of the high-acuity, gaze-angle region (HAgar=LFD) but may not raise peak acuity appreciably.

In APAN, the patient's acuity varies over time and may be very good during the neutral phase if the INS damps to near zero. Taking acuity measurements during the neutral phase and both the maximal jerk-left and jerk-right phases provides a baseline to compare against these values post-T&R. In APAN, the improvement in gaze-angle acuity should translate into longer periods of high acuity before and after the neutral phase of the APAN.

If the clinical tests suggest either INS with a latent component, FMNS, or both, the following are indicated.
1. Surgically, the 4-muscle T&R procedure should improve the nystagmus waveforms, subject to the same considerations as outlined above. Any required strabismus correction should be added into the same surgery.
2. Non-surgically, soft contact lenses may have the same positive effects on the breadth of the high-acuity, gaze-angle region (HAgar=LFD) but may not raise peak acuity appreciably.
INS Therapy is indicated in APAN (with or without a latent component) because of the broadening of the range of gaze angles where the patient has the highest acuity translates into increasing the time during the APAN cycle that acuity is highest. The possibility of additional improvement in the highest acuity makes surgical therapies preferable.

A Paradigm Change
The past 50 years of detailed OM studies of INS have resulted in a paradigm change in the methods used to diagnose INS, evaluate both the OM and clinical characteristics of INS, determine the optimal therapy for each patient, apply each therapy, and estimate (pre-therapy) and evaluate (post-therapy) the therapeutic outcomes. The diagnosis must be specific (e.g., INS, FMNS, etc.) based on OM data; “nystagmus” is not a satisfactory diagnosis but merely a Greek word for the obvious eye oscillation. The evaluations should include OM data (e.g., the NAFX under different viewing conditions) and visual acuities taken at different gaze and convergence angles. The optimal therapy should improve either the peak acuity (VApk=NAFXpk), the range of high-acuity gaze angles (HAgar=LFD), or both. The application of therapies, especially surgical, should include all four EOM in the major plane of the INS, except for the BMR procedure in stereoscopic INS patients. Finally, the pre-therapy estimation and post-therapy evaluation of therapeutic outcomes should be made using the direct OM outcomes of NAFX and LFD improvements; secondary clinical outcome measures include percent improvements in VApk and HAgar. Using the guidelines in this tutorial, physicians can come closer to these goals when accurate OM data are unavailable. In some patients, it may even be possible to accurately estimate post-therapeutic improvements from clinical data alone.

Summary, Observations, and Conclusions
OM research has documented the following visual function improvements of INS therapies: improved peak visual acuity, broadened range of high-acuity gaze angles, and shortened target acquisition times; the latter two are never measured in the clinic. Although measuring target acquisition time is not easily done in the clinic, measuring acuities at different gaze angles is and should be, due to its importance in overall visual function. The major deficit in most INS patients is the sharp loss of acuity at lateral gaze angles. The complete clinical assessment of an INS patient must include VA measurements as gaze angles lateral to the angle where VApk occurs.

The range of gaze angles over which a person has good visual acuity is one of the least understood or appreciated factors in overall visual function; it is also the most important. The following is a test that all ophthalmology residents should be required to take (to discourage further dissemination of erroneous information about INS, I would also encourage some of their mentors to try it before their next INS lecture to those residents). Visual acuity “tunnel vision” causes a severe deficit in visual function; to illustrate it, one need only try to spend several hours (if they can last that long) viewing the world with their normal acuity (let’s be kind and say, 20/20) but through a small window of approximately 10° (i.e., ±5°). Again out of a sense of kindness, let’s place that window in primary position. This can be done in any of several ways: a translucent bag over the head with two small holes centered on the eyes; a pair of spectacles with the subject’s prescription and all but a small central hole covered with translucent tape, etc. Then, the subject should try to go about their normal routine including working at a desk, walking, talking to several people, or, if they are brave, catching a thrown ball. If at all masochistic, they could repeat the experiment with the small window of acuity placed laterally.
For comparison, they should use a plus lens just to blur their acuity slightly (i.e., one or two Snellen lines) over their entire visual field (i.e., without using the above window limitations). They should then ask themselves, “Would I rather have 20/20 vision in only a small island of my gaze field or 20/40 throughout that field?” I have no doubt the latter will be the choice. Now consider the therapies you might offer a patient with INS who is constricted by the deficits in visual function caused by the limited-gaze field condition. Where should your emphasis for improvement be? A line on the Snellen chart? Or broadening as much as possible the high-acuity gaze-angle field? Again, I think the answer will be obvious. That is why acuity vs. gaze angle must be part of the workup in INS, pre- and post-therapy and why the improvement in this factor should be a primary outcome measure in any study of INS therapies.

It is often heard from physicians that increasing peak VA “only a line or two” is not sufficient reward for therapeutic intervention. This author wonders how many of them would agree to spend the rest of their lives at 20/40 instead of the 20/20 that most of them presumably enjoy and which greatly enhances their ability to practice ophthalmology. The patients illustrated in Cases 1 and 2 are those with relatively good acuity (due to INS alone). Such patients (of which this author is an example) can improve 60% to 20/25 or even 20/20, making their lives as students much less stressful and opening all professions and sports to them. That doesn’t even include the more important improvements to their high-acuity range of gaze angles. The time is long overdue for physicians to rethink erroneous, condescending, or prejudicial attitudes towards improving the visual function and lives of all INS patients.

OM research into INS (including clinical trials) has demonstrated the key roles in visual function played by the characteristics of the nystagmus itself and their therapeutic independence from associated afferent visual deficits. That is, the amounts of improvement in each of the key outcome measures (NAFXpk and LFD) and of their clinical counterparts (VApk and HAgar) are dependent only on the pre-therapy values of NAFXpk and LFD and are not affected by the presence of associated sensory deficits. Thus, the current inclusion methods or patient groupings used in so-called “clinical trials” constitute fatal flaws in experimental design and guarantee a number of false negative results. By their nature, clinical trials do not ask important scientific questions and therefore, are not likely to reveal new understanding of either INS mechanisms or therapeutically important characteristics. Unfortunately, as presently carried out, they also cannot correctly answer the limited questions they do pose (e.g., how effective is a particular INS therapy?). Because patients in clinical trials are usually grouped in broad categories defined only by their associated sensory abnormalities, including those whose INS characteristics preclude any improvements from OM therapies, their results are hopelessly skewed towards negative results. Thus, such trials will fail to uncover effective therapies for the subsets of the INS population whose waveform characteristics allow for improvements from OM therapies.

Cases 1 and 2 illustrate how significant improvements in the visual function of patients with isolated (unassociated) INS may be improved. Cases 3 - 6 illustrate how, despite severe afferent deficits limiting VApk, significant, life-changing improvements in the visual function of these patients is not only possible but also probable.

Finally, there are a number of misimpressions, including demonstrably false statements about INS that have appeared in the literature and been repeated so often that they have assumed the
undeserved status of “current knowledge.” Indeed, resident examinations still contain questions couched in the resulting misleading and erroneous terminology and require “correct” answers that have been shown to be false. The statements to which I refer are: 1) there are two different kinds of INS, “sensory” and “motor;” 2) “sensory” INS has pendular waveforms; 3) “motor” INS has jerk waveforms; 4) any of a number of sensory deficits present in a patient is the “cause” of their INS; 5) if no sensory deficit is found, the cause of the INS is unknown and the term “idiopathic” should be used; 6) INS therapy does not improve VA; 7) surgical repositioning of the INS “null” is temporary and the null later reappears at some lesser gaze angle; 8) if an INS patient has a severe sensory deficit, INS therapy is contraindicated; 9) the T&R surgery does not change INS; and 10) the T&R surgery has only temporary effects. Published research has shown that each of these “ophthalmological myths” is false. Their continued use (especially the misnomer, “idiopathic”) suggests a failure to fully understand that research; the denial of effective treatment to INS patients is both contradicted by the peer-reviewed literature and medically indefensible.

**Key to Abbreviations:**

- **AN**: acquired nystagmus
- **BCVA**: best-corrected visual acuity
- **EOM**: extraocular muscles
- **FMNS**: fusion maldevelopment nystagmus syndrome
- **HAgar**: high-acuity, gaze-angle range
  - \( \text{low} \leq 10^\circ; 10^\circ < \text{mid} \leq 25^\circ; \text{high} > 25^\circ \)
- **INS**: infantile nystagmus syndrome
- **LFD**: Longest Foveation Domain
- **NAFX**: eXpanded Nystagmus Acuity Function
- **NAFXpk**: peak eXpanded Nystagmus Acuity Function
  - \( \text{high} > 0.6; 0.6 \geq \text{mid} \geq 0.25; \text{low} < 0.25 \)
- **NBS**: nystagmus blockage syndrome
- **OA**: ocular albinism
- **OM**: ocular motor
- **SNS**: spasmus nutans syndrome
- **VApk**: peak visual acuity
  - \( \text{high} > 0.6; 0.6 \geq \text{mid} \geq 0.25; \text{low} < 0.25 \)

**Non-Surgical Therapies:**

- **BOPr**: base-out prisms
- **SCL**: soft contact lenses

**Nystagmus Surgeries***:

- **A+T&R**: 2-muscle Anderson (2 muscles recessed) + 2-muscle T&R
- **BMR**: recession of both medial rectus muscles (“artificial divergence” procedure)
- **K**: 4-muscle Kestenbaum (2 muscles recessed and 2 resected)
- **T&R**: 4-muscle tenotomy and reattachment
- **SS**: strabismus surgery

*** All INS surgeries except BMR (for binocular patients) should be 4-muscle surgeries of the muscles in the main plane of the INS (usually the 4 horizontal rectus muscles). In the event of multiplanar INS, first operate on the muscles in the plane of predominant nystagmus and then, if
necessary, operate on the muscles in the other plane after allowing 4-6 months to pass to prevent ischemia.
Appendix

Figures D.1 and D.2 in Appendix D of the above-referenced book, are flowcharts outlining the "eye-movement-based" steps to the definitive differential diagnosis of the various types of nystagmus in childhood. In the absence of eye-movement data that definitively establishes the diagnosis of INS, that diagnosis may be made in some cases based on clinical data alone. By combining the standard measures of distance (in primary position and at lateral gaze angles), near, and binocular vs. monocular acuity measures and the other tests commonly administered to patients with nystagmus with the observations and tests ("clinical pearls" below), the diagnosis of INS can be made (or excluded) with some certainty in many cases. Figure A1 is a flowchart outlining the clinical steps to the differential diagnoses of INS, FMNS, NBS, and SNS. Although not always definitive, many clinically based diagnoses may be made with reasonable confidence. This tutorial presumes that INS has been correctly diagnosed and describes the treatments of INS with and without strabismus.

Systemic drug therapies for INS act centrally to reduce the centrally generated nystagmus signal from the brain stem. When used in conjunction with peripheral therapy (surgery, prisms, etc.), the effects of both are multiplicative. That is, if the drug reduces the nystagmus signal to 50% of its original value, the peripheral therapy reduces the eye-muscle response to that signal by 50%; the net result is a nystagmus that is 25% (0.5 x 0.5 = 0.25) of its pre-therapy value. However, the use of systemic drugs for INS has always been problematic. Originally, their side effects made them less than desirable; but even with new drugs like memantine or acetazolamide, whose side effects are minimal, they are less than optimal. First, drugs need to be taken for the patient’s (usually a child) lifetime if INS waveforms are to be consistently improved. That poses risks since the long-term effects of newly developed drugs are unknown. Second, these drugs may have undesirable side effects. Third, life-long drug therapy is economically draining on either the patients, their parents, or their insurance companies compared to either a single payment for outpatient surgery, prism glasses, or soft contact lenses. Fourth, life-long drug therapy suffers from compliance problems. Given the low-risk of outpatient extraocular muscle (EOM) surgery or the no-risk use of prism glasses or soft contact lenses, I regard life-long systemic drug therapy for a child with INS as the least conservative medical approach and, for that reason, it is not included as a preferred therapy in this tutorial.
Figure A1. Flowchart demonstrating how clinical observations and tests may be used to arrive at a nystagmus diagnosis. Note that, unlike when using waveform analysis, all paths do not lead to a definitive diagnosis and there is no reliable path to acquired nystagmus. AN, acquired nystagmus; FMNS, fusion maldevelopment nystagmus syndrome; INS, infantile nystagmus syndrome; NBS, nystagmus blockage syndrome; SNS, the spasmus nutans syndrome; VN, vestibular nystagmus. [From Figure D.3, Hertle, R. W. & Dell’Osso, L. F. (2012) Nystagmus in Infancy and Childhood. Current Concepts in Mechanisms, Diagnoses, and Management. Oxford University Press: Oxford.]

The possibility of peripheral drug therapy for INS, administered to the EOM proprioceptors either via microinjection or eye drops, is a much more attractive alternative. First, they are likely to be faster acting than systemic drugs. Second, they are unlikely to have the undesirable side effects of the latter. Third, if administered as eye drops, they can be used, as needed, by the patient (e.g., when a student is attending a lecture or for sports). At present brinzolamide eye drops, which did not have the undesirable side effects of systemic acetazolamide in the subject we tested, show some promise. More research into this and other peripherally administered INS drugs is currently under way and if the results are positive, eye-drop therapy will need to be added to those in the Tables in parts 1-3 of this tutorial.
Figure A2 is a flowchart showing the therapeutically exploitable clinical characteristics of INS. It serves as the foundation to the detailed consideration of specific characteristics and recommended therapies in this tutorial.

**Therapeutically Exploitable Clinical Characteristics**

Figure A2. Flowchart demonstrating how clinical observations and tests may be used to determine therapeutically exploitable characteristics of infantile nystagmus syndrome (INS). The relevant therapies may be surgical or nonsurgical. Note that when the peak is high and the range of high-visual acuity (Hi VA) gaze angles is broad, their values cannot be significantly increased and, therefore, no waveform foveation improvements are possible; only under these simultaneous conditions is nystagmus therapy precluded. BMR, bimedial recession; m, muscle; Rec, recession; R&R, recess and resect; Strab, strabismus; T&R, tenotomy and reattachment. [From Figure D.4, Hertle, R. W. & Dell’Osso, L. F. (2012) Nystagmus in Infancy and Childhood. Current Concepts in Mechanisms, Diagnoses, and Management. Oxford University Press: Oxford.]

This tutorial is not intended to be a “cookbook” combination of patients’ clinical signs and the therapeutic options available, although the three Tables summarize all the permutations of the relevant INS characteristics of three groups of patients whose INS does not vary with time (see “Time-Varying Nystagmus” above). Table 1 is for patients with high peak visual acuities (Group 1), Table 2 is for those with low peak acuities (Group 2), and Table 3 is for those with mid-range peak acuities (Group 3). Once the proper Table for a given patient is determined (based on the magnitude of VApk), the characteristics of HAga, far visual acuity vs. near visual acuity, location of VApk, and the presence or absence of strabismus may be used to determine the available choices of INS therapies for that patient. Like stereotypes, such treatment pathways/diagrams often lack the important nuances that distinguish the individual (INS patient) from the clinical group to which that patient seems to belong. Blind adherence to cookbook descriptions and therapies (including those in the Tables) may, in certain cases, result in
minimally effective, ineffective, or even inappropriate therapies. The physician should always take into account all facets of each patient’s visual, OM, and other characteristics and signs. The relevant scientific bases for each INS therapy choice are included in this tutorial to serve as a bridge from the knowledge gained during the past 50 years of INS research using OM data to the improvements in diagnoses, therapies and clinical outcomes that are now possible and which have been demonstrated in many INS patients.

As is evident from the Tables, there are only a limited number of effective INS therapies; thus, they appear repetitively, albeit in different preference orders, depending on the particular INS characteristics of the patient. Post-therapy percent improvements in VApk and HAgar will ultimately depend on the quality of the pre-therapy waveforms, as shown in Figure A3, and do not depend on either age or the presence or severity of associated afferent visual deficits. Our research has demonstrated that the most therapeutically effective INS surgery is the BMR procedure; non-surgically, the use of BOPr (with -1.00S added for pre-presbyopic patients) has the same beneficial effects. Unfortunately, these therapies are limited to the subset (<10%) of INS patients who are binocular (no strabismus) and whose INS damps with convergence (i.e., acuity at near is higher than at far). BMR is also used to correct esotropia but that strabismus surgery does not induce convergence or significantly damp INS. Also, to obtain the maximum damping effect of a four-muscle procedure for null regions at small lateral gaze angles, the Anderson procedure (2 rectus-muscle resections) accompanied by T&R of the other two lateral rectus muscles is recommended over the two-muscle Anderson procedure alone. It remains to be shown if the NAFX and LFD improvements from an Anderson procedure alone are equal to those shown in Figure A3; justification for eliminating the additional T&R procedure on the two non-recessed muscles requires such a demonstration.

The curves in Figure A3 are the results of several studies of the T&R procedure applied to different groups of INS and AN patients. These improvements in peak NAFX and LFD were then used to estimate the respective improvements in subsequent patients based on their pre-therapy values. As would be expected, both curves demonstrate that high initial values leave no room for improvement whereas lower values produce ever increasing percent improvements. Their independence from patient age or the presence, type, or extent of associated afferent sensory deficits is the source of their predictive therapeutic power.
The following “clinical pearls” are the practical results of ocular motor, nystagmus research. They contain clinical observations and tests that facilitate differential diagnosis and aid in determining the most therapeutically effective surgery.

**Differential Diagnosis**

**INS vs. FMNS vs. APAN: Head Postures**
Patients with INS and two static (or multiple) head postures should be examined for a latent component, FMNS or APAN.

**INS vs. FMNS vs. AN: Cover Test**
To distinguish between benign (non-neurologically threatening), infantile, primary-position, jerk nystagmus, and that which is neurologically threatening, first verify that there is no periodic alternation in direction and then perform bilateral, sequential, cover-uncover testing. If the cover test causes a reversal in the nystagmus direction consistent with FMNS, the nystagmus is benign (FMNS or INS with a latent component). If not, attempt to rule out INS (by history, clinical signs, and waveforms).
INS vs. FMNS: Cover Test
If the results of an alternate-cover test indicate a benign, infantile, primary-position, jerk nystagmus (i.e., it causes a reversal in the nystagmus direction consistent with FMNS or INS with a latent component), perform the test again but in far adduction of the fixating eye (e.g., far left gaze when the left eye is occluded). If the nystagmus again reverses (i.e., becomes jerk left in left gaze with left eye occluded), it is INS with a latent component. Repeat the test in adduction of the other eye fixating. If the nystagmus remains in the direction of the fixating eye, it may be either FMNS or INS with a large latent component.

APAN
Occlude the non-preferred eye and examine the preferred eye with the head straight and gaze in primary position over at least 5–7 minutes. A regular or irregular changing oscillation intensity and/or direction indicates APAN.

INS vs. AN: Head Tremor
Point out the head tremor to the patient. If it stops, the nystagmus is that of INS; if it persists, both are more likely acquired.

INS vs. SNS: Head Nodding
Based on the observation that head nodding is compensatory in the SNS, if further research on the eye movements of the “SN-like” nystagmus associated with brainstem gliomas demonstrates that these patients exhibit no head nodding, the presence of deliberate, compensatory head nodding is an indication of SNS and is benign.

**Terminology and Characteristics**

**INS Terminology**
Based on the research of the past 50 years, the INS in all patients is directly caused by instability in smooth pursuit damping plus a variable amount of tonic imbalance in the visualvestibular system. Thus, INS is a motor oscillation with known motor causes, making the adjective “motor” (e.g., motor nystagmus or congenital motor nystagmus) redundant. Similarly, the terms “sensory” and “idiopathic” are both incorrect and misleading. None of these terms should be used in describing INS.

**INS: Nulls, & Reading**
Patients who (taking advantage of their null) move their heads word to word across the line while reading (even those with high acuity) may have INS with a narrow range of gaze angles where their acuity is highest.

**INS & Fixating Eye**
When the preferred fixating eye is kept in abduction, the nystagmus is most probably IN, not FMN. Caveat: It might still be FMN if the patient has exotropia or an angle kappa.

**INS: Near Acuity & Convergence Damping**
Patients with INS whose near visual acuity is greater than distant may have INS that damps with convergence.
APAN: Visual Acuity
Patients with INS whose measured visual acuity changes from one office visit to the next may have short periods when the nystagmus stops and acuity peaks; this is an exaggerated form of APAN.

Therapies
INS Therapy & Associated Sensory Deficits
INS therapy is not contraindicated in patients with associated visual sensory deficits; in fact, these patients have the greatest chances for significant (i.e., life-changing) improvements in their visual function.

INS & SCL
Contact lenses are not contraindicated in INS and can provide better acuity than spectacles in patients whose nystagmus damps with afferent stimulation. Plano soft contact lenses can be used if no refractive correction is required. Four advantages of contacts in the INS patient are better optical quality, improvement in nystagmus foveation, move with eye to utilize eccentric gaze null, and ability to decrease light sensitivity/interference via tinting or painting.

INS Surgery: Recession & Resection Determinations
Determination of the amounts of recession and resection needed to rotate the eyes using bilateral recession and resection of the horizontal recti (A-K procedure) may be best accomplished by dividing the total amount of surgery (indicated by the curve given in Dell’Osso and Flynn, 1979) in two and applying those equal amounts to the two antagonist muscles.

Nystagmus & Strabismus Surgeries
When performing simultaneous nystagmus and strabismus surgery, the procedure is determined by a combination of moving the eccentric null (straightening the head) using the preferred eye and correcting the remaining strabismus using the non-preferred eye.

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