Catching Up with Ocular Imaging:
New Vision Tests Reveal Early Loss in Eye Disease

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I have no financial relationships to disclose.
I will not discuss off-label use and/or investigational use in my presentation.

Structural imaging, optical imaging and electrophysiology
- Spectral domain OCT
- Higher order aberrometry
- Multifocal techniques
- Outpacing clinical tests of visual function
- We are visualizing more than what we can measure functionally

The Dilemma

- New tests which go beyond “20/20 VA” to reveal subtle changes are needed
- Purpose is to describe new tests of contrast sensitivity, color vision and more which go beyond “20/20”
- Providing enhanced detection of hereditary and acquired ocular conditions and diseases.

What is Needed

- Visual acuity (VA) remains the cornerstone of clinical vision care.
- VA measures smallest letters one can read at distance (13 to 20 feet) or near.
- Adequate VA required for entrance/retention in military law enforcement driving piloting

Is 20/20 VA Enough?

- Visual acuity (VA) remains the cornerstone of clinical vision care.
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- Adequate VA required for entrance/retention in military law enforcement driving piloting

Introduction

- VA tested with black letters on white background
- But is 20/20 good enough?
- Can low contrast vision be decreased despite normal VA?

Is 20/20 Good Enough

- Optical/media conditions (refractive surgery, keratoconus, cataract)
- Eye, systemic or neurological disease (early glaucoma, diabetes, retinopathy)
- Operational stressors (night, smoke, altitude, fatigue)
A patient can have 20/20 visual acuity... (meet the current standard)

Patient's Performance = Normal Performance

But vision can be decreased!!

A CASE-IN-POINT

- PRK 5 years ago.
- Corneal haze in LE.
- Despite 20/20 acuity...
- Contrast sensitivity decreased.

Operational impact?

How does this patient see the world?
Operational Normal view

Clinical

Patient's view (despite 20/20 VA!)

Operational

Clinical

Loss of detail

Decreased sensitivity → (patient's view with left eye)

Loss of detail

Minimum difference in brightness between light and dark bars to detect patterns of

Increasing Pattern Fineness →

Contrast Sensitivity → Peak sensitivity

Less sensitive to coarse

Less sensitive to fine

High

Low

Sensitivity

Where is visual acuity on the contrast sensitivity function?

With visual acuity, we move along X-axis of CS function...

Increasing Pattern Fineness →

Where is visual acuity on the contrast sensitivity function?

A complete measure of vision!

Contrast Sensitivity Measures Sensitivity to a Range of Sizes

Increasing Pattern Fineness →

VA measures only one point on CS function!

Presenting letters smaller and smaller in size...

VA
**Letter CS in PRK:**
Effect of Higher Order Aberrations

<table>
<thead>
<tr>
<th>Normal mean</th>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>20/20</td>
<td>20/20</td>
</tr>
<tr>
<td>PRK</td>
<td>20/20</td>
<td>20/20</td>
</tr>
<tr>
<td>HOA: 1.9x &gt; normal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HOA: 2.3x &gt; normal</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- 0.5
- 1
- 1.5
- 2

Log contrast sensitivity

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**Exceptional Contrast Sensitivity After PRK**

- Trained pilot.
- PRK 1-year ago.
- Optics—better than normal.
- CS at or above mean performance.
- Letter CS “super-normal.”

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**Normal View**

- CS at baseline and 1-month after PRK
- Despite 20/20 VA...
- 3-fold increase in higher order aberrations.
- 2-fold decrease in CS 1-month post-op to PRK.

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**Return to Duty? When? QOV After PRK**

- High contrast VA
- 20/30 to 20/5
- 4X smaller than 20/20
- Low contrast CS
- 20/25 letters

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**Super Vision Test (SVT)**

- Separate sequence for each eye.
Super Vision Test (SVT)
- Includes dark green filter to simulate
- Color
- Brightness
- Of NVG display
- Produces same visual challenge.

Super Vision Test Normal Values

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Below Normal</th>
<th>Above Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual Acuity (photopic)</td>
<td>20/14</td>
<td>&lt; 20/19</td>
<td>&gt; 20/11</td>
</tr>
<tr>
<td>Visual Acuity (NVG)</td>
<td>20/18</td>
<td>&lt; 20/25</td>
<td>&gt; 20/13</td>
</tr>
<tr>
<td>Contrast Sensitivity (photopic)</td>
<td>1.05</td>
<td>&lt; 0.75</td>
<td>&gt; 1.35</td>
</tr>
<tr>
<td>Contrast Sensitivity (NVG)</td>
<td>0.70</td>
<td>&lt; 0.35</td>
<td>&gt; 1.05</td>
</tr>
</tbody>
</table>

Normative values based on validation study (n=20) and follow-up clinical application (n=95).

Clinical Application
Anterior Ischemic Optic Neuropathy
- Painless loss of vision in left eye
- Developed left quadrant field defect
- High contrast VA
  RE 20/12, LE 20/13 (exceptional in both eyes)
- Low contrast CS
  Exceptional in RE; 3x lower in the left eye

Super Vision Test in Clinical Conditions
(Decreased vision 3x more common at low contrast)

Super Vision Test in Clinical Conditions
(Enhanced vision more common at low contrast)
Normal Color Vision

- Normal color vision
- Based on red, green, and blue sensitive retinal cones

Color Vision Deficiency (CVD)

- Hereditary CVD
  - 8% of males
  - 1 in 200 females
- Acquired CVD occurs in eye disease

Color Deficiency

- CVD can
  - Decrease performance
  - Compromise safety
  - On real-world tasks increasing
  - Error rate
  - Time to complete tasks

Difficult When Color Only Cue!!

- Normal color vision depends on three cones (red, green, and blue)

The bottom line...

- Normal color vision depends on three cones (red, green and blue)
Normal color vision depends on three cones (red, green, and blue).

Color discrimination depends on the difference in cone stimulation.

Hereditary color deficiency
- 8% males
- 1 in 200 females

Lack of red cones
- 1% of males

Or green cones
- 1% of males

Or sensitivity shift
- 1% of males

Protan Dichromat
- 1% of males

Deutan Dichromat
- 1% of males

Protanomalous (red shifted toward green)
The bottom line…
• Or green toward red
  
Deuteranomalous (green shifted toward red)

The bottom line…
• Hereditary blue cone deficiency
• Quite rare (0.008%), but...

The bottom line…
• Blue cone sensitivity loss
• Occurs early in eye disease
  
Macular Degeneration  Diabetes  Glaucoma

• Making blue cone tests needed

The bottom line…

Color discrimination depends on the difference in cone stimulation

Small difference

\[ \begin{array}{c}
\text{B} \\
\text{G} \\
\text{R}
\end{array} \]

Small difference

5% of Males

\[ \begin{array}{c}
\text{B} \\
\text{G} \\
\text{R}
\end{array} \]

\[ \text{Look the same!} \]

Our research includes development and validation of new tests which go beyond 20/20 VA to better assess visual function.

- Goals include earlier detection, diagnosis and monitoring of ocular, systemic and neurologic diseases.

- Research to better predict real-world performance and to elucidate neural mechanisms of perception.
Cone Contrast Test (CCT)

- Letters visible only to red, green or blue cones
- Single colored letter appears 4 sec. on-screen
- Mouse used to match letter seen from display
- Program varies contrast up/down and measures lowest red, green & blue contrast seen

Protans Take Longer on Red CCT

- Red Color Deficiency
  - Takes >2X Longer to Recognize Red on Grey Letters

Deutans Take Longer on Green CCT

- Green Color Deficiency
  - Takes 2X Longer to Recognize Green on Grey Letters

Color Vision on iPad & iPhone

- The CCT was displayed on
  - iPad 2
  - iPad 3
  - iPhone 4
- Touch screen used to select letter seen.

Color Vision on iPad & iPhone

- There was no difference in performance between the four systems in CVNs (F=0.14, p>0.93).
**Red Cone (Protop) Deficiency**

Red Deficiency: Selective Decrease on Red Test. No difference between systems (F=0.27, p>0.84)

- Cone Test
  - Red
  - Green
  - Blue

CCT Score

**Green Cone (Deutan) Deficiency**

Green Deficiency: Selective Decrease on Green Test. No difference between systems (F=0.27, p>0.84)

- Cone Test
  - Red
  - Green
  - Blue

CCT Score

**Low Contrast Testing**

- 5% Low Contrast VA
- Small Letter (20/50) CS

**Carriers of Color Deficiency**

- Red (protopan) and green (deutan) CVD are X-chromosome linked conditions.
- Gene for CVD is on X-chromosome.
- CVD is passed from Mom to Son.
- Daughter acquires CVD from Mom and Dad.

**Carriers of Color Deficiency**

- Heterozygous carriers of CVD (e.g., daughter of CVD father) typically pass standard color tests.
- Some carriers show mild CVD...
- Which is likely due to expression of CVD cone along with the three normal cones.

**Cone Contrast Test in Carriers**

- Right Eye
- Left Eye
  - Normal
  - Carriers
  - Protan
  - Deutan
  - Normal Red
  - Normal Green
Color Vision in Dim Light

- Color testing conducted under daytime light levels
- Less is known about performance of under decreased lighting...
  - Dusk
  - Night
  - Fog
- Is color vision decreased at decreased light levels?

Compared B/W to Color CS

Normal vs. Color Deficiency

B/W CS: Normal vs. Deficiency

S Cone CS: Normal vs. Deficiency

Retina: Macular Degeneration
**Diabetic Macular Edema**

Decreased color vision despite normal & equal VA

**Central Serous Retinopathy**

- Common in pilot population
- Local detachment of retina.
- Can resolve without treatment.

**Surface Wrinkling Retinopathy**

More advanced in LE

**Tilted Optic Discs**

Nonselective decrease in color vision

**Left Optic Neuropathy**

RE 20/20, LE 20/40
**Advanced Glaucoma in Right Eye**

- RE & LE 20/20
- Visual Field Loss in RE

**CCT Score**

- Red Cone stimulation
- Green Cone stimulation
- Blue Cone stimulation

**Non-arteritic Ischemic Optic Neuropathy**

- Standard color tests (PIP, D15, FM 100 Hue, anomaloscopes)
- NORMAL in both eyes!
- Cone Contrast Test
  - RE: normal (low normal on green)
  - LE: below normal on green & blue CCT

**Diagnosis?**

- 20-year-old healthy white male
- Decreased vision OD while deployed
- Medic prescribed drops; got better…
- But still not normal
- VA 20/15 OD, OS
- Subtle APD OD
- Fundi WNL

**Optic Neuritis: Early Sign of MS**

- Resolved Optic Neuritis of RE
- MRI and CSF: Probable MS

**VEP in Optic Neuritis**

- Pattern Reversal VEP
- Resolved Optic Neuritis of RE; RE & LE 20/15

**Multiple Sclerosis without Optic Neuritis**

- 42 yo female
- 2-year history of MS
Multiple Sclerosis without Optic Neuritis

33 yo female—10-year history of MS

No history of acute or chronic visual loss

Mean 2 SDs

Cone Contrast Test

Red Green Blue

Cone stimulation

Color Vision in MS

Cone Contrast Test

Red Green Blue

Cone stimulation

Color Vision in Eye Disease

CCT Score

CCT Score

Red Green Blue

Cone Contrast Test

Hereditary & Acquired Color Deficiency

Hereditary deuteranomaly confirmed by anomaloscope

Optic nerve head drusen, greater in left eye with atrophy

Consistent acquired protan defect in the left eye

What is Stereo-Depth?

Perceived depth between two objects

Distance between objects in space

Imaged on retina of each eye as a horizontal line of stimulation

Slight difference in length of the lines of stimulation is used by the brain to perceive depth

Computation of Stereopsis

\[ \text{Stereo} = \frac{PD(\Delta d)}{d^2} \]

\[ \text{Stereo} = \angle a - \angle b \]

\[ \tan(a) = \frac{PD}{d_1} \]

\[ \tan(b) = \frac{PD}{d_2} \]

ThusStereo = PD(d_1 - d_2)

Stereo = PD(d_2 - d_1)

Stereo = PD(\Delta d)

Brain compares \( a \) to \( b \) length in right eye to \( a \) to \( b \) length in left eye to perceive depth between points \( a \) and \( b \) in real space.
**Standard Near Test**

Near Stereo Test

Polaroid glasses allow presentation of slightly offset images to each eye (1 of 3 circles) to produce stereo depth. Subject identifies the finest stereo target she/he can see.

**New Distance Test**

Distance Stereo Test

Red-green glasses present slightly offset images to each eye (1 of 4 circles) to produce stereo. Remote used to select circle which appears closest.

**No Difference Between Tests**

Stereo Threshold (sec of arc)

<table>
<thead>
<tr>
<th>Distance</th>
<th>Near</th>
</tr>
</thead>
<tbody>
<tr>
<td>15.7”</td>
<td>15.9”</td>
</tr>
</tbody>
</table>

Mean values, n=20, p>0.9

**Neuro-Vision Card**