1. CHROMATIC PUPILLOMETER-BASED PERIMETRY IN PATIENTS WITH BEST MACULAR DYSTROPHY

2. CHROMATIC PUPILLOMETER-BASED PERIMETRY IN RETINITIS PIGMENTOSA PATIENTS

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Static automated perimetry

**Indications:** to detect visual field loss in:

1. Glaucoma (1%)
2. Neurological diseases
3. Retinal diseases
Subjective Perimetry

Goldman

Humphrey
Perimetry and its Limitations

• Patients’ cooperation is essential
• Can’t distinguish between damaged cells
• Qualified personnel
• Subjective

• It is easy to simulate neurologic field defects

(Deepta at el. Ophthalmology 2014)
Because of all those limitations there is a need to develop an **objective test** that requires a less cooperation from the patient.
Pupillary Light Reflex

The pupillary light reflex controls the diameter of the pupil in response to the intensity (luminance) of light that stimulates the retina

• The light stimulus activates the retina
• The retina activates the optic nerve
• The optic nerve activates the brain
• The brain constricts the pupil
The first chromatic multifocal pupillometer system

Skaat et al. IOVS 2013
First prototype limitations:

1. Only 13 locations
2. Some patient cooperation was required
3. Software
The second generation:

- The subjects look forward and stimuli are individually introduced at different VF locations.
- A smaller spot size is used with the aim of achieving better perimetric resolution.
The Chromatic multifocal pupillometer:

- objective perimetry
- 76 locations for blue and red stimulus

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The fovea is located in the center of the macula region of the retina. And responsible for sharp central vision.

3 main groups compose the retina:

1. Photoreceptors
2. Bi-polar cells
3. Ganglion cells

*Fig. 1.1. A drawing of a section through the human eye with a schematic enlargement of the retina.*
Photoreceptors

Within the retina 60-125 million rods and 3.2-6.5 million cones are distributed.

• No rods are present in the fovea.

• The cones are mainly concentrated in the fovea.
Perimetry based on Pupillary Light Reflex to multifocal chromatic stimuli

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<th>Cell Type</th>
<th>Stimulus</th>
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<td>Rods</td>
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<td>Ganglion</td>
<td>High intensity blue (482 nm)</td>
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Retinitis pigmentosa (RP)

- The most common cause of inherited blindness
- Progressive degeneration of the retina
- The rods are affected first leading to peripheral and night vision lost.

Retinal photoreceptors:

Bone spicule-shaped pigment deposits
RP – visual functions effects

Normal night vision

Night blindness

Normal night vision
RP – visual functions effects

- Reduction in the peripheral visual field up to tunnel vision
- Central (day) vision is subsequently lost leading to total blindness
RP patients - significantly reduced pupillary responses in nearly all perimetric locations in response to blue stimulus

Skaat et al. IOVS 2013
Study design:

- 9 retinitis pigmentosa patients

- 9 healthy age-matched volunteers

- Comparison between patients and healthy controls for all perimetry locations was performed using One-Way Analysis of Variance

- In RP patients, the chromatic pupillometer recordings were compared with their dark-adapted chromatic Goldmann
Average-long-wavelength stimulus
(622cd/m²)

Healthy

RP

18 degrees
Average short-wavelength stimulus (88 cd/m²)

Healthy

RP

18 degrees
Patient #1 - long wavelength

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<th>Pupil Response (% of Normal Value)</th>
<th>Chromatic Goldman</th>
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18 degrees
Patient #1 - short wavelength

Pupil Response
(% of Normal Value)

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Chromatic Goldman

18 degrees
Patient #2 - long wavelength

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Pupil Response (% of Normal Value)

18 degrees
Patient #2 - short wavelength

Pupil Response  
(\% of Normal Value)

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Chromatic Goldman

18 degrees
Conclusions

• RP patients demonstrated reduced pupillary responses to short wavelength stimuli

• Good correlation with Chromatic Goldman

• The new device will enable objective VF patient diagnosis and objective evaluation of treatment benefit
Hereditary dystrophies

• Hereditary dystrophies affecting the central retina
• represent a heterogeneous group of diseases.

• Genetic alterations may be responsible for:
  ➢ changes of the choroid
  ➢ changes of the retinal pigment epithelium [RPE] (Best's disease)
  ➢ changes of the photoreceptor outer segments (Stargardt's disease)
  ➢ Changes of the bipolar and Mueller cells (x-linked retinoschisis).
Best disease

• Autosomal dominant disease that affects the retinal pigment epithelium (RPE) at a very young age.
• Characterized by lipofuscin accumulation in the RPE.
• Atrophic changes of the RPE or scarring secondary to subretinal neovascular membranes with hemorrhage causes loss of central visual acuity.
• Typically, patients will present with an early central scotoma
• More dense scotomas will likely develop as the disease progresses
Best stages:

• Stage 1 is known as the pre-vitelliform stage, the macula looks normal, and there are only subtle RPE changes. Normally 20/20 vision is expected.

• Stage 2, the vitelliform stage, shows a yellow or orange elevated lesion which looks like an egg-yolk, Vision at this stage can range from 20/20 to 20/50.

• Stage 3, pseudohypopyon stage is when the yellow material breaks through the RPE and accumulates in the subretinal space forming a cyst of fluid. Vision remains stable at 20/20 to 20/50.
• Stage 4, vitelliruptive stage is known by its “scrambled egg” appearance. This is due to the vitelliform lesion breaking up. Vision may decrease to the range of 20/20 to 20/100.

• Stage 5 is the atrophic stage where the yellow material disappears and an area of RPE atrophy remains.

• Stage 6 follows the atrophic stage and presents with choroidal neovascular/cicatricial lesions. These lesions lead to subretinal fibrotic scars.

Vision at Stage 5 and 6 may deteriorate to less than 20/200.
Study design:

- 13 participants were recruited (4 BEST patients and 9 healthy individuals).

- A computerized infrared video pupillometer was used to record changes in pupil diameter in response to short- and long-wavelength stimuli (peak 485 nm and 620 nm, respectively).

- Target diameter was 2 mm, duration of stimulus was 1 sec.

- Stimuli were presented by 76 LEDs in a 18-degree visual field.

- Percentage change in pupil diameter was calculated.

- The pupillary responses of patients were compared with their findings on Humphrey's 24-2 perimetry and with the pupillary responses obtained from normal control subjects.
Average- short-wavelength stimulus (200 cd/m²)

Normal

BEST

18 Degrees
Average long-wavelength stimulus (622 cd/m²)

### Normal

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18 Degrees
Conclusions

• A good agreement was observed between the Humphrey's perimetry and the perimetry obtained by pupillary responses to short wave length stimuli.

• This study demonstrates the potential feasibility of using pupillometer-based chromatic perimetry for objective assessment of visual field defects and retinal function in patients with BEST vitelliform macular dystrophy.

• Perimetry testing based on pupillary responses to long wave length stimuli is more sensitive and may enable earlier detection of visual field defects in patients with central macular lesions.
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- Nir Levy
- Ron Chibel
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- Inesa Kelner

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- Dr. Skaat Alon
- Dr. Kinori Michael
- Dr. Attar-Ferman Gili

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- Dr. Treves Avi: Tel Hashomer, Israel
- Prof. Haratz Dror: Lipid Center, Tel Hashomer, Israel
- Dr. Shaish Aviv: Lipid Center, Tel Hashomer, Israel
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