heru

Expanding Clinical Care for AMD

Heru's Dark Adaptation Fills the Gap

Key Messages

- Age-related macular degeneration (AMD) is a progressive chronic disease of the central retina accounting for 8.7% of all blindness worldwide[1].
- Early AMD patients exhibit moderate to severe impairment of dark adaptation (DA) even in the absence of visual acuity loss[4–6].
- A test to probe rod function in dark adaptation can be used as a clinical outcome measure in studies tracking the progression of AMD, or more practically, a diagnostic tool targeting the identification of early AMD[4].
- A patient's rod function can be easily examined with Heru's dark adaptation test which is billable to insurance (CPT 92284) and co-billable with visual fields, OCT and/or office visits.

Introduction

Age-related macular degeneration (AMD) is a progressive chronic disease which affects the central vision and accounts for 8.7% of all blindness worldwide[1]. In developed countries, it is the leading cause of irreversible blindness in people of 50 years and over. The mechanisms underlying vision loss in AMD are multifactorial, with a complex interplay of genetic and environmental factors[2]. Early identification of AMD may help with the management of the disease.

AMD is characterized by degenerative changes that involve the retinal pigment epithelium (RPE), Bruch's membrane, and choriocapillaris. The change may lead to degeneration, dysfunction, and the death of photoreceptors, resulting in vision loss. However, lesions to the RPE/Bruch's membrane complex may not be visible until late in AMD, if ever at all[2]. Thus, the functional status of photoreceptors lends itself as the most direct bioassay to identify early AMD[3].

Early AMD patients exhibit moderate to severe impairment of dark adaptation (DA) even in the absence of visual acuity loss. Impairment of dark adaptation is related to disease severity; with slower DA associated with increasing AMD severity[4,7,8]. Delayed DA in older adults with normal macular health is associated with doubling the risk of developing AMD three years later[7,9]. A test to probe rod function in dark adaptation can be used as a clinical outcome measure in studies tracking the progression of AMD, or more practically, a diagnostic tool targeting the identification of early AMD[4].

Dark adaptation can be impacted in other diseases like glaucoma, cataracts, and diabetes[11,12]. Being able to detect impairment of dark adaptation can help doctors not only better understand their patient's functional vision but also allow them to make better optical recommendations and educate their patients about lifestyle changes.

Dark Adaptation and Current Instruments

Until recently, dark adaptometry utility was limited due to long test duration (over 60 minutes with 100 threshold estimates), patient burden and fatigue, and lack of standardized dark adaptometry. AdaptDx by MacuLogix (Middletown, PA) attempted to address these limitations by providing a shorter-duration, operator-friendly dark adaptometer while maintaining sensitivity and specificity. On a sample of normal subjects and AMD patients, AdaptDx had a diagnostic sensitivity of 90.6% and specificity of 90.5%[6,10].

The Heru Dark Adaptation Test

The Heru dark adaptation module is implemented on the Heru platform which leverages commercially available AR/VR head-mounted displays. Heru's dark adaptation does not require pupil dilation which may lead to enhanced patient comfort. Once the headset is placed on the patient a pre-test alignment is performed to ensure appropriate fixation. A light shield and a neutral density filter are used to create a dark testing environment within the headset. The pupil size is measured and a photoflash appropriate to that pupil size is administered 6 degrees below fixation using an LED device mounted in front of the wearable device. Repeated threshold measurements are then made at that same retinal location using a staircase thresholding algorithm, which starts with a stimulus intensity at 0.06 cd/m^2.

During the test, the Heru portal shows the test timer, fixation monitoring status, and most recent threshold values, allowing the operator to follow the patient's test progress. It also warns the operator when fixation losses are detected, when patients' eyes are closed, or if the patient was not properly fixated during the initial photoflash. This allows the operator to remedy the issues to ensure test accuracy and reliability.

A report is generated at the end of the test, which shows a plot of the measured sensitivity thresholds over time, as well as an Adaptation Index with reference ranges. Examples of the dark adaptation test report in normal eyes and eyes with AMD are shown in the figures below.

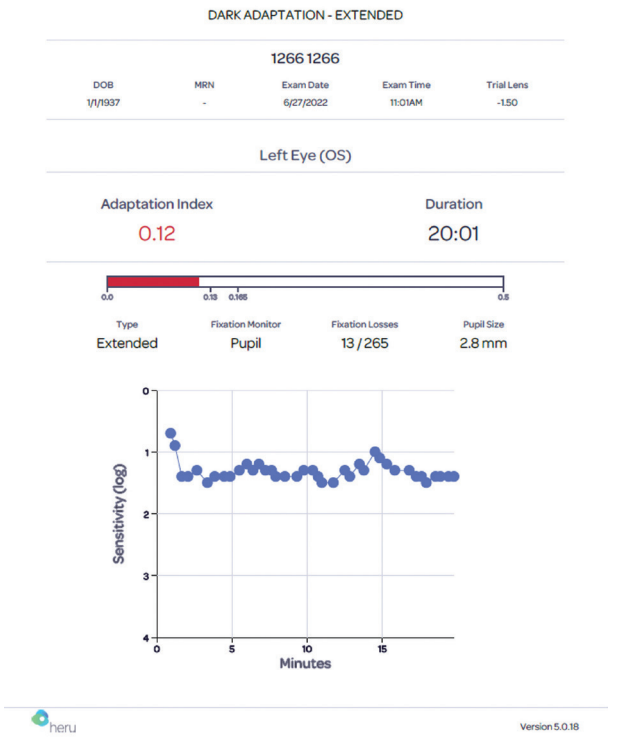
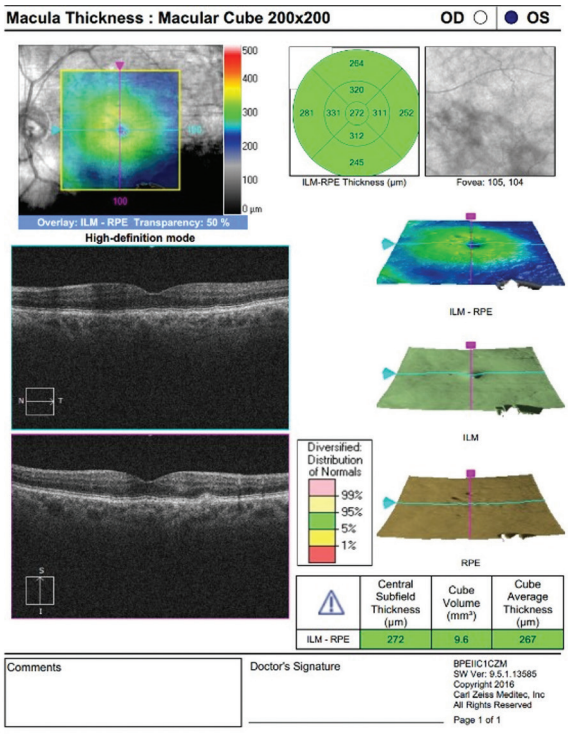
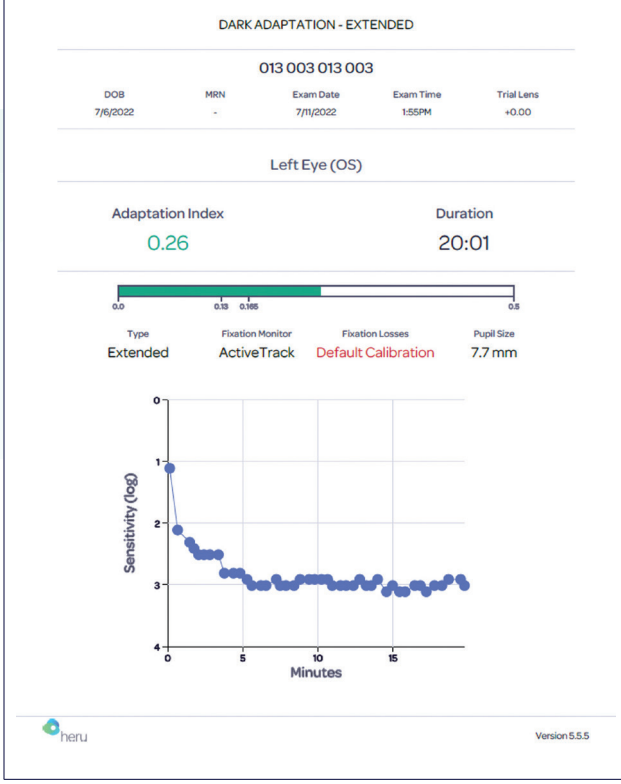
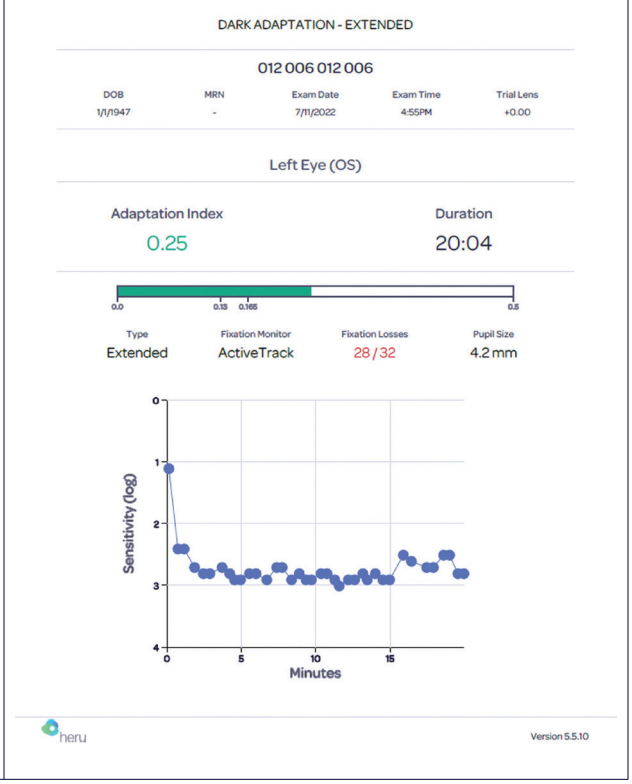
Example from an 85-year-old patient with intermediate dry AMD	Macular OCT from the same subject
	

Table 1: Extended dark adaptation example from an 85-year-old male with intermediate dry age-related macular degeneration. Dark Adaptation Index shows difficulty recovering.

Extended Dark Adaptation Curve from an eye of a 41-year-old healthy female	Extended Dark Adaptation Curve from an eye of a 75-year-old healthy male
	

Clinical Study

A clinical study was conducted to assess whether the Heru's DA test had a sensitivity and a specificity greater than 30% and 90% respectively. During the study, extended dark adaptation was measured for 20 minutes in subjects with normal retinal health and subjects with AMD. To evaluate Heru's rapid DA test, dark adaptation functions for subjects were truncated to 4.5 minutes and DA indices were then computed as the ratio of the mean threshold reached between 3 and 4 minutes to the mid-point between that time interval (i.e., 3.5 minutes). DA indices computed in this manner reflected the slope of DA functions, which is the change in thresholds per minute, where higher values indicated faster DA functions and vice versa. Similar to other studies, taking an average across multiple time points ensured a more reliable final threshold as the shape of DA curves measured across AMD subjects has been shown to be inconsistent[6]. Subjects with a DA index greater than or equal to 0.46 were classified as DA consistent with normal retinal health while subjects with DA index less than 0.46 were classified as DA consistent with AMD. Based on our eligible sample which included 25 normal adults (Age: mean=70, std=6.7, min=58, max=86) and 28 AMD subjects (Age: mean=76, std=9.7, min=50, max=97), the measured sensitivity and specificity of the rapid test were 64 % (lower bound 95 % CI = 49%) and 92% (lower bound 95% CI = 83%) respectively. These results suggest that the Heru's rapid DA test which takes 4.5 minutes can aid doctors in the detection of AMD while reducing the high patient burden associated with tests with longer durations.

Conclusion

Diagnosing early-stage AMD can be very challenging since patients are often asymptomatic with good visual acuity. Although dark adaptation is a useful test for aiding the diagnosis and assessing the risk of progression of AMD, the long duration of previous implementations limited its utility by clinicians. With Heru, a patient's rod function can now be easily tested with its new dark adaptation testing which is billable to insurance (CPT 92284) and co-billable with visual fields, OCT and/or office visits. Furthermore, Heru's AMD portfolio, which includes dark adaptation and contrast sensitivity, also offers the re:I Threshold 10-2 visual field test leveraging the same wearable platform to better detect and manage AMD. With Heru's AMD portfolio, doctors can quickly assess their patient's visual function and based on their findings, make important clinical decisions and recommendations to prevent further vision loss and improve visual functions of their patients.

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