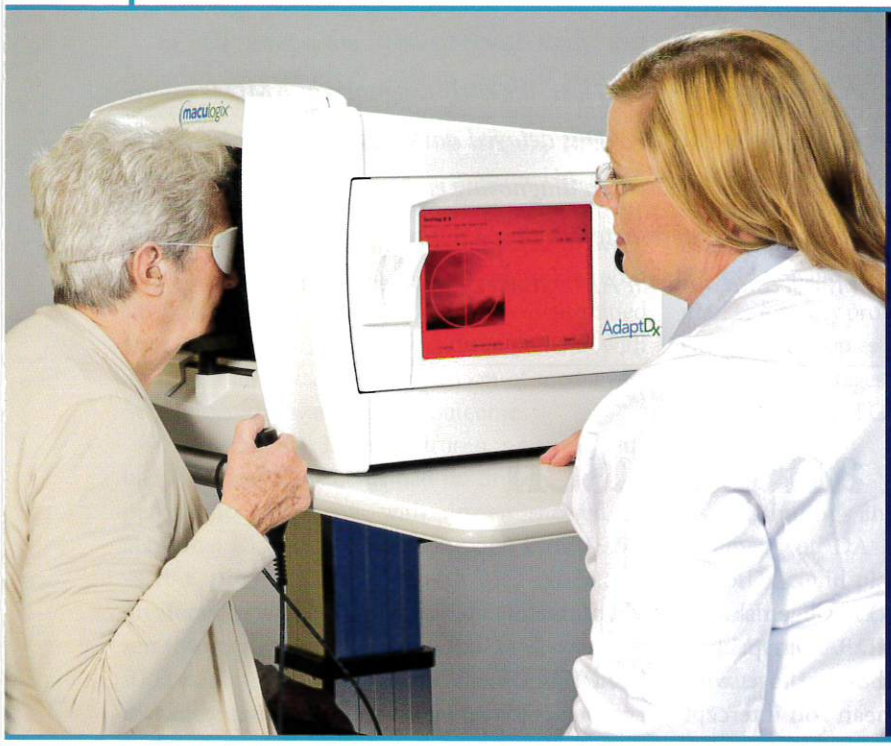
Dark Adaptation as a Clue to AMD

Clinical experience using a DA device to investigate the effect of drusen, disease subtypes and severities



INSIDE:

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Dark adaptation as a clue to AMD

Clinical experience using a DA device to investigate the effect of drusen, disease subtypes and severities.

To begin prompt treatment so as to halt further vision loss, the early diagnosis of AMD is essential. One characteristic that is indicative of early AMD is delayed dark adaptation (DA).

Here we present two authors' work with DA's role in diagnosing early AMD — with the help of MacuLogix's AdaptDx automated dark adaptometer. In the first, the connection between DA and drusen is discussed, and in the second, how an AMD diagnosis affects cataract patients.

AMD, DA and drusen

By Jordi Monés, MD, PhD

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Financial disclosure: Dr. Mones has no financial interests in MacuLogix, Inc.

Delayed dark adaptation (DA) has been shown to be indicative of early AMD. A prospective study of 325 patients found that those with abnormal dark adaptation (mean rod intercept = 15.1 minutes) were twice as likely to develop AMD after three years as those with normal DA (mean rod intercept = 9.1 minutes). The data from a recent study by lead author Cynthia Owsley, PhD, suggest that delayed rod-mediated DA could be a functional biomarker for early AMD.[1] Traditional DA testing can take up to an hour to complete, which is uncomfortable for the patient and reduces practice efficiency.

To overcome the limitations of traditional DA testing, MacuLogix, Inc. developed the AdaptDx, a dark adaptometer to screen for AMD and other conditions characterized by abnormal DA, such as retinitis pigmentosa. The main advantage of the AdaptDx is its ability to detect early functional impairment in patients whose macula appears anatomically normal.

ADAPTDX OVERVIEW

The AdaptDx provides a noninvasive, objective measure of retinal function, which is captured in the rod intercept (RI). It takes four minutes per eye without pre-adaptation or pupil dilation required.[2]

A multicenter clinical study undertaken by Jackson and colleagues enrolled patients with early to advanced AMD (n=127) and healthy eyes (n=21) as determined by clinical examination and grading of fundus photographs. The AdaptDx was used to measure DA in patients in each group. Patients were classified as having DA consistent with normal retinal health (rod intercept ≤ 6.5 minutes) or having dark adaptation consistent with AMD (rod intercept > 6.5 minutes). Findings showed that the screening test correctly identified 115 of 127 AMD patients and 19 of 21 of the healthy patients.

This data show that the AdaptDx has a high

diagnostic sensitivity and a specificity of 90% for detection of AMD.[3]

DA IMPAIRMENT IN PATIENTS WITH DRUSEN

The main advantage of the AdaptDx is its ability to detect early functional impairment in patients whose macula appears anatomically normal. However, at the Institut de la Màcula we are investigating the functional impairment induced by drusen in AMD. Therefore, while we began using the AdaptDx to examine differences between patients with drusen and healthy controls in terms of DA, it was mainly to explore any differences according to drusen type — namely types such as soft drusen and reticular pseudodrusen (RPD).

In this prospective, observational study that included 29 eyes of 29 patients aged 50 years or older, two masked graders classified fundus images as showing predominantly soft drusen, RPD or none. The AdaptDx was used to measure DA. Mean RI, defined as the time to recover visual sensitivity to 5x10-3 scotopic cd/m2, was compared between groups. As mentioned, an RI>6.5 minutes was considered abnormal. If the RI could not be determined after 20 minutes, we classified these patients with an RI>20 minutes. The comparison of median RI between groups was the main outcome.

Twelve patients had soft drusen, seven patients had RPD and 10 patients had no drusen. A larger percentage of patients with drusen showed an abnormal RI as compared to healthy eyes (89.5% vs 10%, $p = 0.001$). Patients with RPD exhibited a greater RI compared with patients with soft drusen (Mean RI: 17.58 vs 20; $p = 0.02$). All eyes with RPD exhibited an RI>20 minutes. After adjustment for sex and visual acuity, drusen ($p<0.001$) and age ($p=0.016$) were associated with a greater RI.

These findings indicate that patients with drusen had worse DA than healthy patients. In this sample, almost 90% of patients with drusen showed an abnormal RI. Further, the RI was >20 minutes in any patient with RPD, suggesting very poor DA in these patients.[4]

DIFFERENTIATING BETWEEN AMD SUBTYPES

In my experience, measuring DA impairment is most useful as a tool to help determine AMD severity, even in eyes that appear to have minor damage. We also use DA to differentiate between subtypes of intermediate AMD; it is a useful way to further characterize phenotypes. DA could also be very useful to properly stratify patients for clinical trials, which still mix different phenotypes in the same study groups. For example, patients with any geographic atrophy (GA) are typically placed in the same group.

This is not helpful because some patients with GA progress very quickly, others very slowly. Also, some have a lot of DA impairment, others do not.

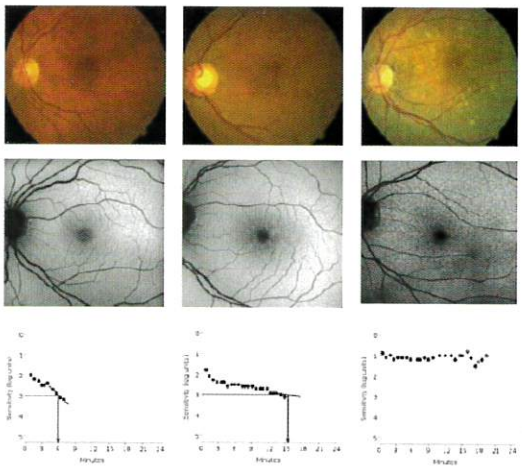

IMAGE COURTESY JORDI MONES, MD, PHD

Figure 1. Representative fundus autofluorescence images (top) and dark adaptometry (bottom) images from controls (left), soft drusen (middle) and reticular pseudodrusen (right) individuals.

In a study, we identified three major subgroups of GA patients who differed in terms of atrophy growth and fundus features.[5] If we can demonstrate that DA impairment can be used to differentiate between various disease subtypes, then it could be used for proper patient eligibility in clinical trials.

Additionally, we may be able to use DA as a biomarker for early proof-of-concept studies evaluating emerging therapies for AMD, specially treatments to target early stages of the disease, such as preventing progression of GA associated with drusen.[6]

CONCLUSION

As our findings and those of others show, measurement of DA using a device such as the AdaptDx could play an important role in AMD research and management. Consequently, DA should not be limited to use as a screening tool for early-stage disease. **OM**

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The impact of subclinical AMD on cataract outcomes

DA changes the choice of lens for cataract patients.

By Mark F. Pyfer, MD

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His disclosures, as of May 2017, include Abbott, Alcon, BioTissue and Maculogix.

While fundus autofluorescence, intravenous fluorescein angiography, OCT and OCT angiography provide a clearer view of the retina by allowing identification of structural defects or drusen even a few microns in size, these instruments still measure structure only. They can offer a false sense of security, namely when screening for AMD prior to cataract surgery. The reason: The appearance of drusen alone does not lead to a diagnosis of AMD. Even if these tests do, the disease has usually progressed past the earliest stage.

After discovering this in my own practice, I began looking for cases of subclinical AMD. It's often had a direct impact on the IOLs I choose.

SIMILAR COMPLAINTS

I practice comprehensive ophthalmology and specialize in cataract and refractive surgery. The era of presbyopia-correcting IOLs has excited me professionally and contributed to my practice's growth. I perform roughly 30 cataract surgeries per week using several premium lens technologies.

Many of our patients are 50 years and older, so many either have early cataracts or at least dysfunctional lens syndrome. These patients' complaints are nearly identical to early AMD symptoms, such as night vision issues.

Before acquiring the AdaptDx, we would hear these complaints, and then we would look for clinical signs of AMD. We sometimes would see drusen on fundus exam or OCT, but we often couldn't diagnose the disease in these patients until several years later when the disease had progressed. This led me to invest in AdaptDx. With it, we can detect subclinical AMD at least three years earlier than it is clinically evident.[1]

THE TEST

While the correlation between early AMD and impaired DA function has been known for some time, we only recently have had access to an effective, patient-friendly way to measure DA in the clinical setting. The test is easy for technicians to learn. As for the patient, who does not have to deal with pupil dilation or prolonged adjustment time, they continuously focus on a fixation light, and are exposed to a mild bleaching flash and asked to indicate when a progressively dimmer stimulus light appears. By complementing our advanced structural imaging capabilities with a quick, effective functional test of a patient's DA, we get a more complete picture of retinal health.

LENS SELECTION — GETTING IT RIGHT

In our practice, we primarily use the AdaptDx to diagnose early disease when the structure is normal. About 10% of the patients tested fall into this category — meaning that 10% have a clinically normal exam yet have abnormal DA.

Abnormal DA can limit a patient's outcome and, at the very least, requires special counseling. I don't want to backtrack later and say, "You're not doing as well as we hoped because you have AMD, which we couldn't see through your cataract." Thanks to this test, I can educate patients when they have a greater likelihood of still experiencing night vision impairment after surgery.

Multifocal lenses split the incoming light into a near and distance focal point, resulting in a symptomatic loss of contrast in patients with less-than-optimal retinal function. Patients pay out-of-pocket for premium lens, so they tend to have justifiably higher expectations. It is our job to do everything we can within reason to meet or exceed those expectations.

Mildly abnormal DA doesn't necessarily rule out a multifocal or extended depth-of-focus lens, but I avoid putting one in a patient with significant impairment — even if the clinical exam is normal. For these patients, I usually suggest a monofocal lens. **OM**

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