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Article

Preliminary Evaluation of a Mobile Device for Dark Adaptation Measurement

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Purpose: We evaluated the feasibility of a smartphone application-based dark adaptation (DA) measurement method (MOBILE-DA).

Methods: On a Samsung Galaxy S8 smartphone, MOBILE-DA presented a 1.5° flashing stimulus (wavelength = 453 nm) between −1.15 and −4.33 log candela (cd)/m^2 at 8° eccentricity using an adaptive staircase, and logged timing of user response (tapping on the screen) whenever the stimulus became visible (monocularly). In a dark room, the smartphone was placed ≈40 cm from the subject, and a white smartphone screen at maximum brightness (≈300 cd/m^2) for 120 seconds was used for bleaching before testing. MOBILE-DA was evaluated in normally-sighted (NV) subjects (n = 15; age, 22–82 years). Additionally, a subject with myopic retinal degeneration (MRD; VA, 20/100; age, 62 years) and another with optic nerve atrophy (ONA; visual acuity [VA], 20/500; age, 40 years) were measured. Maximum test timing was capped at 20 minutes. Linear regression was performed to determine age-effect on DA parameters: rod-cone break time (t_{RCB}) and test-time (t_{term}). Use of the normalized area under the DA characteristics (AUC) as an outcome measure was explored.

Results: For NV, the repeatability coefficients for t_{RCB}, t_{term}, and AUC were ±2.1 minutes, ±5.4 minutes, and 4.4%, respectively, and aging-related delays were observed (t_{RCB}, R^2 = 0.47, P = 0.003; t_{term}, R^2 = 0.34, P = 0.013; AUC, R^2 = 0.41, P = 0.006). Compared to ONA and NV, DA was greatly prolonged in the MRD subject (52% larger AUC than the NV mean).

Conclusion: The age-effect was verified for MOBILE-DA measurements in NV subjects; impaired DA in a case with retinal-degeneration was observed.

Translational Relevance: This study establishes feasibility of the smartphone-based DA measurement method as a potential accessible screening tool for various vision disorders.

Introduction

Dark adaptation (DA) is the natural process through which our eyes adapt to low light or darkness after exposure to a bright light. In normally-sighted human observers, DA has been well characterized and its molecular bases have been studied extensively.[1–3] Typically, the DA process unfolds over a period of time (order of minutes) in a characteristic manner due to the differences in the light sensitivities and adaptation responses of rod and cone photoreceptors. Thus, when measured in a controlled manner, typical DA curves, obtained by plotting the sensitivity/stimulus threshold over time in dark, have somewhat distinct components corresponding to the cone and rod photoreceptors. Since it measures photoreceptor function, DA can be an important functional vision measure with significant clinical value.

The value of DA as a functional vision measure lies in the fact that it is affected noticeably in certain retinal disorders, such as age-related macular degeneration (AMD) and retinitis pigmentosa (RP) among others.[1,4] In case of AMD, most significant changes have been observed in the kinetics of the DA process (time-dependent parameters), particularly in the rod component of the DA characteristics, compared to age-matched controls with healthy eyes.[5–8] Importantly, these changes in DA are known to occur early

in the course of the disease, even before changes in other vision measures are noticed,[9] and they are correlated with the severity of the condition.[8,10] Thus, DA measurement can be used as a clinical test for early detection and for monitoring disease progression in patients with retinal disorders, such as AMD.

Current clinical practice for DA measurement involves exposing the subject's test eye (typically, a small portion on the macula eccentric to the fixation) to a bright light (bleach) so as to saturate the photoreceptors, followed by presenting flashing stimuli within the bleached area to record the time required for the photoreceptors to regain their sensitivity in the dark. The luminance of the stimulus progressively decreases as the eyes become adapted over time. The subject responds to the perception of the stimuli and the strength of the stimulus and time are recorded to generate DA characteristics and derive any clinically meaningful parameters. The test terminates after a fixed amount of time, or after the sensitivity target threshold is achieved, or when the luminance level of the stimulus threshold drops below a certain preset threshold.

Broadly following these steps (minor instrument-related variations in the protocol may exist), DA can be measured using dark-adapted chromatic perimetry instruments,[11] or with dedicated instruments (dark-adaptometers).[12] While shown to be effective in DA measurement in AMD patients,[10,13] clinical instruments for DA measurement are limited in their availability, face cost and accessibility barriers in their widespread use, and are not suitable for home-based monitoring. Modern mobile devices have hardware-level capabilities to adopt a feasible DA measurement protocol, while increasing access and reducing costs. A mobile device-based DA measurement application can potentially be used in primary care clinics for screening of certain retinal diseases, or even facilitate home-based measurements. We developed a mobile device-based DA measurement method, referred henceforth as MOBILE-DA (it collectively refers to the measurement protocol and the associated mobile application [app] that we developed). Our main motivation behind development this app was to explore whether DA measurement can be simplified and made more accessible so that it can be used more easily in clinics or at home for self-testing.

While DA measurement for clinical use was the chief motivation and long-term goal behind development of the MOBILE-DA, we described the first step toward that goal: determining feasibility of using a contemporary mobile device for DA measurement. This involved characterizing device capabilities, establishing measurement protocol, devising methods for data analysis, and determining whether the DA measurements are meaningful in a human subject study. We briefly described the MOBILE-DA method and its preliminary evaluation by examining whether we can reproduce some of the known effects on the DA characteristics measured using MOBILE-DA. Since it is well known that DA characteristics change with age,[14–17] we used this observation to verify whether DA characteristics obtained using a mobile device showed a similar effect. Additionally, we contrasted the DA measurements from two low vision patients, one with and the other without retinal damage, to further verify the validity of MOBILE-DA measurements.

Methods

Characterizing Mobile Device Display Capabilities

Some of the main questions that must be addressed when designing a DA measurement method are related to the nature of the test stimuli to be presented, specifically the luminance range and its wavelength. Since human rod photoreceptors are sensitive to a different band of wavelengths and luminance range compared to the cones, establishing these values on the measurement bounds for the DA measurement apparatus was key for eliciting response from cone and rod photoreceptors. Until recently, the main roadblock in using mobile devices for DA measurement was that their displays had lower dynamic range, particularly at low luminance levels where rod sensitivity could be reliably tested. Also, the contrast between the stimulus and background at low luminance levels was inadequate because the displays could not really produce deep black colors (mostly because of the backlight). However, some of the recent smartphone displays, such as the Samsung Galaxy S8, consist of a matrix of organic light emitting diodes (OLED) that provide large luminance range with deeper black levels along with the option of choosing one of the primary colors for the test stimulus.

We characterized the display of Samsung Galaxy S8 smartphone using USB2000 spectrometer (Ocean-Optics). The OLED matrix in the display is made up of diodes belonging to three primary colors: red (peaking at 620 nm), green (520 nm), and blue (453

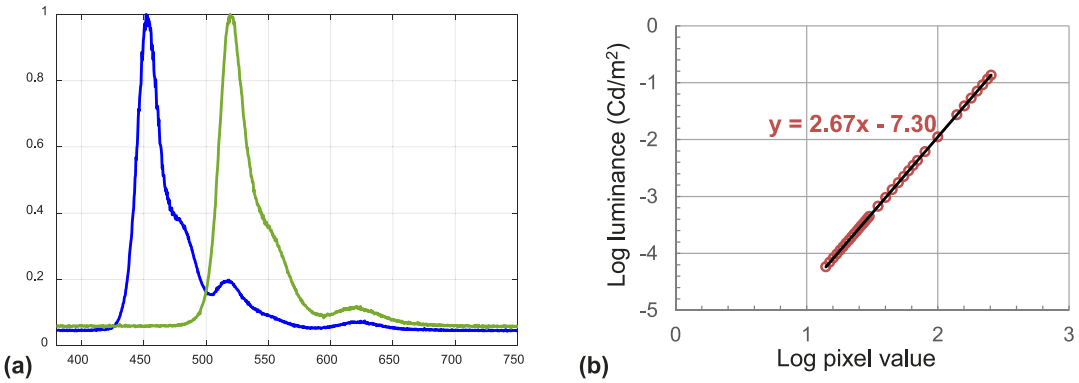

Figure 1. Samsung Galaxy S8 smartphone display characteristics measured using USB2000 spectrometer. (a) Color spectrum of the OLED display panel when showing *blue* and *green* colored screens. *Horizontal axis* shows the wavelength. *Blue color* channel peaks at ≈453 nm, whereas the *green* channel peaks at ≈520 nm. (b) Luminance characteristics of the display at minimum brightness setting for *blue* color channel for pixel values between (0, 0, 255) and (0, 0, 13). A lookup table was created in the software for pixel value - luminance relationship. Then a gamma function was fit to the data. While pixel values <13 were visible to dark-adapted normal eyes, they were below the measurement limit of the spectrometer and, hence, not shown here. The luminance decreased linearly with decreasing pixel values and the minimum luminance level that was measured was 4.64×10^{-5} cd/m^2. The smartphone can display luminance levels that are well below the known cone threshold in humans (≈ between −3 and −3.5 log cd/m^2). Thus, a part of the rod component of the DA characteristics could be measured using the smartphone.

nm) that can be turned on or off selectively depending on the display contents (Fig. 1a). We selected blue color for the stimulus as its spectrum had better overlap with the scotopic luminous efficiency function for human eyes.[18] Based on our measurements of the blue color channel, the overall luminance range of the Samsung Galaxy S8 smartphone was ≈10^6 cd/m^2, with a maximum of ≈300 cd/m^2 at maximum brightness setting with a white screen. The minimum luminance level measured for the blue channel was lower than 10^{-4} cd/m^2 (Fig. 1b). This allowed for the measurement of at least a part of the rod component of DA characteristics (generally considered to be $<10^{-3}$ cd/m^2). The ability of the display to produce deep black levels was empirically determined based on our experiments, where a full screen display of very low pixel levels (< pixel value of 6) was indistinguishable from the screen that was switched off in the dark after 30 minutes of adaptation.

DA Measurement Using a Mobile Device (MOBILE-DA)

The MOBILE-DA measurement protocol enabled DA measurement in a relatively straightforward manner. Using a contemporary mobile device (Samsung Galaxy S8 was used for the experiments), we could perform retinal bleaching (exposure to bright light), stimulus presentation, user response logging, and DA characteristics generation. The mobile device was placed at approximately reading distance (40 cm) from the test eye (for example on a desk as shown in Fig. 2a) in a dark room. Taking advantage of the high brightness level of the display in the smartphone, bleaching was done by presenting a white screen at maximum brightness setting for a preset amount of time before starting the DA measurement. Immediately after bleaching, the app presented a red fixation target and a flashing circular test stimulus (size set to 1.5° in our experiments) of blue color on a black background (Fig. 2b), whose luminance decreased from the highest to the lowest level. The test stimulus always appeared at a fixed eccentricity with respect to the fixation target (for example, 8° below the fixation assuming 40 cm viewing distance, as show in Fig. 2b, right, which would mean it appears in the superior visual field). The timing of the stimulus presentations and the luminance range (highest to lowest) could be configured within the app before starting the test.

The subjects responded to the perceived stimuli by tapping anywhere on the mobile screen. Responses registered only within a short time window after stimulus presentations were considered successful. After a successful response, the current stimulus luminance level and the time from the start of the test were recorded in the mobile device. Tapping led to vibration of the device to provide feedback to the user that the response has been registered by the device. Between the starting (highest) luminance level and −3 log cd/m^2, the stimulus luminance levels decreased by an average value of 0.17 log cd/m^2 after each successful response. After crossing −3 log cd/m^2,

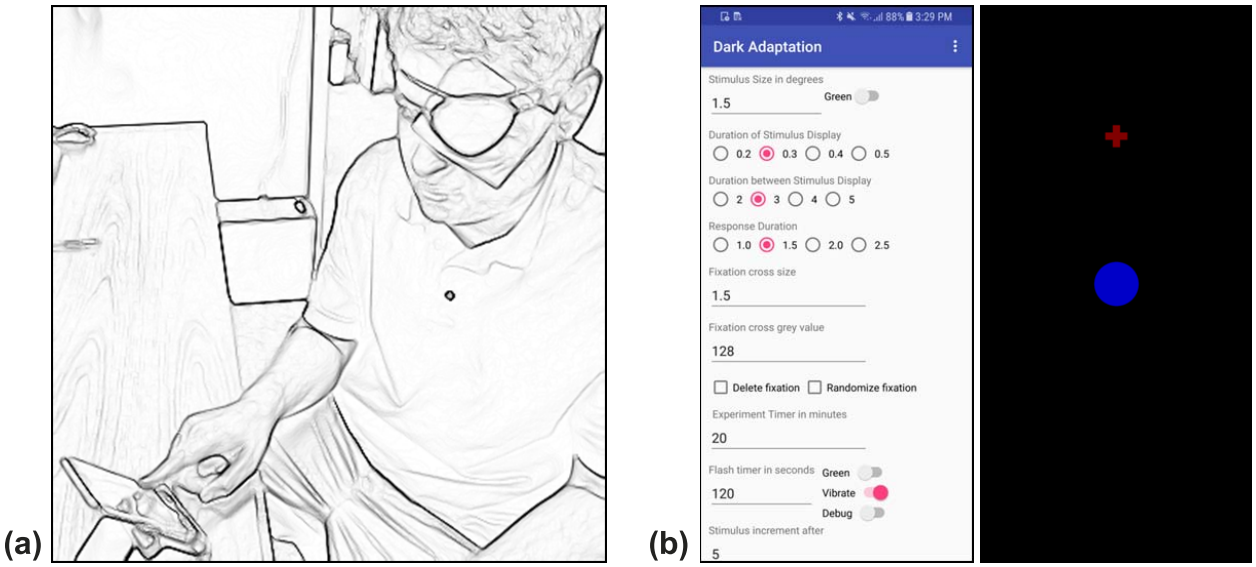

Figure 2. DA measurement using a smartphone. (a) Smartphone is placed at reading distance in front of the subject in a dark room. Bleaching is done by presenting a bright white screen for a predefined duration, after which the DA measurement trial commences. (b) Screenshots of the DA measurement app: configuration screen that allows setting of different parameters related to stimuli and fixation targets (*left*) and test screen that shows a red fixation cross and a flashing blue stimulus (*right*). The subject taps the smartphone screen whenever the blue dot becomes visible for a given luminance level. The time for the response (from the beginning of the test) is recorded for the presented stimulus and a new stimulus with lower luminance is presented at the same location. The logged data of the trial within the smartphone are processed to compute clinically relevant DA parameters.

the stimulus luminance decreased by an average value of 0.1 log cd/m^2 for each successful response until the lowest luminance level measured. If a successful response was not recorded after a fixed number of presentations at the same luminance levels, the stimulus luminance level was increased by 0.05 log cd/m^2 until a successful response was recorded. The period between successive stimulus presentations is configurable in the app (we set it at 3 seconds in our testing). The measurement process was terminated if the lowest stimulus luminance level was reached or the maximum allowable time for the test expired. The app allowed configuration of a wide range of measurement conditions, such as stimulus eccentricity (with respect to fixation target), size, and duration of presentation, luminance range, time of bleach, and maximum test time, among others (Fig. 2b). The configuration values for the app used in this study are shown in the Table.

Table. MOBILE-DA Configuration for Testing the Age-Effect on DA in Normally Sighted Subjects

Test Setting	Value
Stimulus size	1.5°
Stimulus eccentricity (with respect to fixation)	8°
Screen to eye distance	≈ 40 cm
Stimulus presentation duration	0.3 seconds
Response duration (after stimulus presentation)	1.5 seconds
Stimulus luminance range	−1.16 to −4.33 log cd/m^2
Time of bleach	120 seconds
Strength of bleach	≈ 300 cd/m^2
Maximum testing duration	20 minutes

Extraction of DA Parameters

The data recorded in the smartphone at the end of each trial consisted of pairs of values: luminance levels of the presented stimuli and the time when they were seen (time counted from the start of the test). The scatter of this data led to the generation of the DA characteristics (blue circles in Fig. 3). For this study, the data recorded on the smartphone were downloaded to the computer for further processing. Exponentially decaying functions, in one form or the other, have been used commonly to fit DA characteristics.[19,20] The raw DA data for any given trial were fitted with two exponential curves, separately for cone and rod components, via the nonlinear least squares method. To improve robustness, curve fitting for both

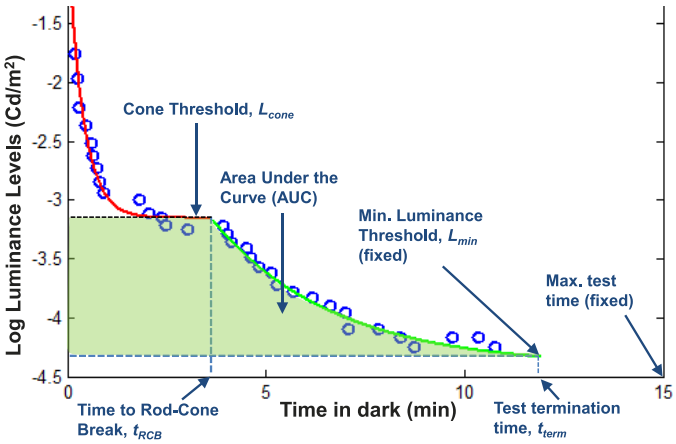

Figure 3. Extraction of DA parameters from the trial data logged by MOBILE-DA, which is a plot of the time in dark versus log stimulus luminance. Raw data for a single trial on NV subject (*blue circles*) recorded in the mobile device were fitted with two exponential functions, one for cone (*red curve*) and one for rod (*bright green curve*) components. The luminance range of the presented stimuli (on *y* axis) and the maximum time duration of the test (on *x*-axis) were fixed. The luminance value at which the cone curve levels off was determined to be the cone threshold. The intersection of rod and cone curves is the rod-cone break and the *x*-intercept was the time to rod-cone break (t_{RCB}). The *x*-intercept at the intersection of the rod component with the minimum luminance level was the test termination time. Together, these parameters define an AUC (*shaded green area*) that can be compared between individuals when normalized over the testing bounds.

components was done with the Random Sample Consensus (RANSAC) procedure: random subsets of points were iteratively fitted and the median curve parameters were obtained for each DA characteristic. The candidate locations for separating rod and cone components were identified by detecting sharp negative changes in the slope of the raw DA data. The exponential curve fitted to either component had three parameters and was of the form: $L = ae^{-bt} + c$, where L is the luminance level perceived at time t. This curve characterized the progressively decreasing luminance levels perceived as the time in the dark increased, up to a certain threshold denoted by the parameter c, with the shape and speed of the decay controlled by a and b.

Based on the curve fitting, the following DA parameters were extracted (Fig. 3): time to rod-cone break (t_{RCB}), time to test termination (t_{term}), and cone threshold (L_{cone}). Except in subjects who did not reach the lowest luminance level (L_{min}) before the maximum time limit of the test, t_{term} was computed by extrapolating the rod curve until it reached L_{min}. While t_{RCB}, t_{end}, and L_{cone} have been used commonly to describe DA characteristics, we explored the use of a new unifying parameter that could help describe the DA characteristics more succinctly: the normalized area under the DA curve (AUC). As shown in Figure 3 (shaded region), we defined AUC as the region between the cone threshold and L_{min} (fixed value for our setup), partly described by the rod-phase of the DA curve. Since the bounds on the luminance range of the stimuli (*y*-axis of the plot in Fig. 3) as well as the maximum test duration (*x*-axis) could be preset, the AUC can be normalized. Thus, the normalized AUC could be compared between different individuals, and can potentially serve as a surrogate parameter of DA kinetics. In subsequent sections, we examined how this parameter fares compared to other traditional DA parameters in summarizing the characteristics.

MOBILE-DA Evaluation

Evaluation of MOBILE-DA was primarily based on the examination of age effect on the DA characteristics in normally sighted (NV) subjects ($n = 15$), between 22 and 82 years old (mean ± standard deviation [SD] = 47 ± 22 years) with visual acuity (VA) 20/25 or better, and without diagnosis of any vitreoretinal conditions in the test eye. The test setup was similar to the one described previously (Fig. 1a). Each subject was tested in the same eye at least twice and a subset of subjects were tested three times ($n = 5$). A minimum interval of 30 minutes separated the two trials for a subject if they were done on the same day; otherwise, repeated measurements were taken on separate days. All subjects stayed indoors under standard room lighting (average illumination level of 120 lux) for at least 30 minutes before each trial. Eyes were not dilated. The test settings for the app are shown in the Table. Within-subject test–retest repeatability was determined using Bland-Altman coefficient of repeatability (CoR), which was computed as twice the standard deviation of the within-subject differences.[21] Effect of age on various DA parameters was analyzed using linear regression.

Additionally, we tested one patient with retinal damage due to myopic degeneration (MRD; VA, 20/100; age 62) and one with optic nerve atrophy (ONA; VA, 20/500; age 40) to verify whether the effect of retinal damage can be seen in the MOBILE-DA measurements. Both subjects had central scotomas; hence, unlike NV subjects, they could not fixate foveally. Therefore, they fixated eccentrically, while ensuring that the stimulus did not fall into the scotoma. The stimulus size and fixation target size

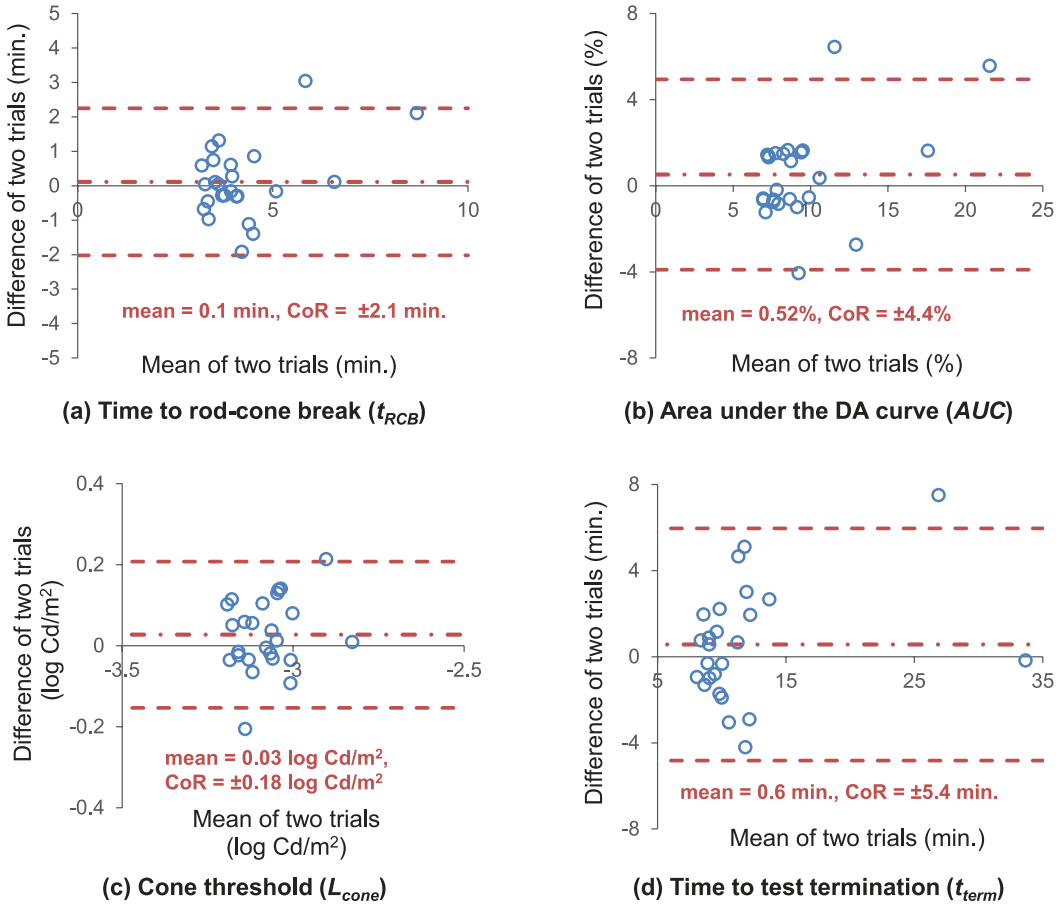

Figure 4. Test–retest repeatability of DA parameters obtained with MOBILE-DA. The plot shows the spread of the within-subject difference of DA parameters. The *dashed lines* indicate the 95% limits of agreement and the *dash* and *dot line* indicates the mean value of the difference.

used for testing both low vision subjects was increased to 2.5°, which was sufficiently large to be visible to the subjects (equivalent VA at 40 cm ≈ 20/600).

Testing was done in a dark room with no windows and with a padded door to stop stray outside light in the room. With the lights switched off, the room illumination was <0.01 lux, which was the measurement limit of a standard light meter (Konica Minolta T-10A). This study was done according to the tenets of the Declaration of Helsinki. All participants volunteered for the study and signed the informed consent form approved by the Human Subjects Committee of Massachusetts Eye and Ear. Instructions and training were provided to the subjects before the test with a brief demo of the working of the app.

Results

Within-subject test–retest repeatability of the DA parameters obtained using MOBILE-DA is shown in Figure 4. For subjects with more than two trials, all pairwise trial comparisons were considered, resulting in 25 total comparisons. Overall, the mean ± CoR between two trials for t_{RCB}, AUC, t_{term}, and L_{cone} were 0.1 ± 2.1 minutes, 0.52% ± 4.4%, 0.6 ± 5.4 minutes, and 0.03 ± 0.18 log cd/m^2, respectively. Presence of a few outliers affected the CoR for the DA parameters. The difference in t_{RCB} between two trials was <1 minute for 72% of the comparisons, and in 92% of trial comparisons the difference was <2 minutes. For t_{term}, 76% of comparisons were within 2 minutes. The AUC between two trials changed <2% in 84% of comparisons.

Qualitatively, the effect of age on the DA characteristics obtained from MOBILE-DA can be seen more evidently when comparing the characteristics of younger and older subjects (Fig. 5). For clarity, DA characteristics of only a subset of study participants are shown. Particularly, the 69-year-old subject can be seen with delayed DA characteristics (takes

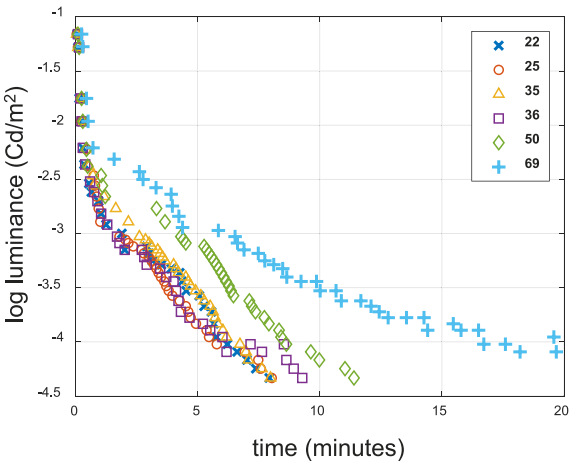

Figure 5. Raw DA characteristics obtained with MOBILE-DA for selected NV subjects. Overall, the older subjects took longer to complete a test trial compared to younger subjects, even as the difference among the DA characteristics of younger subject was not visually obvious.

longer to complete, elevated thresholds at the end of the test) compared to younger subjects. The DA characteristics of the relatively younger subjects are visually indistinguishable among themselves. A slight delay can be seen for the 50-year-old subject. A quantitative analysis of various DA parameters derived from these raw DA data can provide more insight.

Various DA parameters showed significant effect of age (Fig. 6). The data for a subject were combined across all trials. There was a significant increase in the t_{RCB}, AUC, and t_{term} with increasing age (t_{RCB}: $F[1,13] = 13.53$, $P = 0.003$, $R^2 = 0.47$; AUC: $F[1,13] = 10.75$, $P = 0.006$, $R^2 = 0.41$; t_{term}: $F[1,13] = 8.25$, $P = 0.013$, $R^2 = 0.34$). For two subjects who could not finish the test before the stipulated time limit, the time to test termination was extrapolated based on the intersection of the estimated rod curve with the lowest luminance level for the test. Excluding those subjects did not change the overall result as the time to test termination still significantly increased with age ($F[1,11] = 16.18$, $P = 0.002$, $R^2 = 0.56$; Fig. 6c). Contrary to the other extracted DA parameters, cone threshold did not change significantly with age ($F[1,13] = 0.49$, $P = 0.41$, $R^2 = 0.04$; Fig. 6d). As expected, the area under the DA curve was strongly correlated with t_{RCB} (Pearson's $r = 0.96$, $P < 0.001$) and with t_{term} (Pearson's $r = 0.93$, $P < 0.001$), but not with L_{cone} (Pearson's $r = 0.39$, $P = 0.06$; Fig. 7).

Visually, the DA characteristics of the LV subject with myopic retinal degeneration differed greatly from the characteristics of the patient with optic nerve atrophy (Fig. 8a). Despite the low vision, the DA characteristics of the ONA patient had cone and rod components and the DA parameters were relatively close to the age-matched NV subject (ONA subject: $t_{RCB} = 6.4$ minutes, $t_{term} = 11.9$ minutes, AUC = 11.3%; 40-year-old NV subject: $t_{RCB} = 4.2$ minutes, $t_{term} = 10.5$ minutes, AUC = 9.2%). On the other hand, the rod component was missing from the DA characteristics of the MRD subject (blue dashed curve in Fig. 8a), as the luminance threshold levelled off at what can be considered as the cone threshold. Unlike the ONA subject, the MRD subject could not reach L_{min} (which was in the scotopic range) in the allotted test time. Consequently, the AUC was higher for the MRD subject compared to the ONA subject. Relative to the NV subjects, the AUC for the MRD subject was outside of the 99% observation bounds for the data, whereas it was not significantly different for the ONA subject (Fig. 8b).

Discussion

The main finding of this study is that DA measurement is feasible with a contemporary mobile device. By measuring the OLED display characteristics of the Samsung Galaxy S8 smartphone, we showed that it theoretically should be possible to display stimuli in scotopic range on a deep black background and consequently measure the rod component of the DA characteristics. We developed a mobile app and associated measurement method (MOBILE-DA) and showed that repeatable DA measurements can be obtained with this method in normally-sighted human subjects. Importantly, we also showed the validity of the DA measurements obtained using MOBILE-DA by verifying the age-related delay and retinal damage-related impairment in the measured DA characteristics.

The MOBILE-DA method was developed with the ultimate goal of making the measurement process easier, potentially enabling self-testing in the future. This necessitated changes in the methodology compared to traditional perimetry or dark adaptometry, such as absence of high intensity spot bleach, absence of a fixed head position using a head-chin rest, not dilating the pupils, and lack of fixation monitoring to ensure that the test stimulus is presented on a bleached location. It is typical in existing clinical protocols for DA measurement to dilate the eyes, which increases the retinal illuminance and possibly leads to a higher level of initial bleaching. However, the tradeoff is less expediency in the measurement

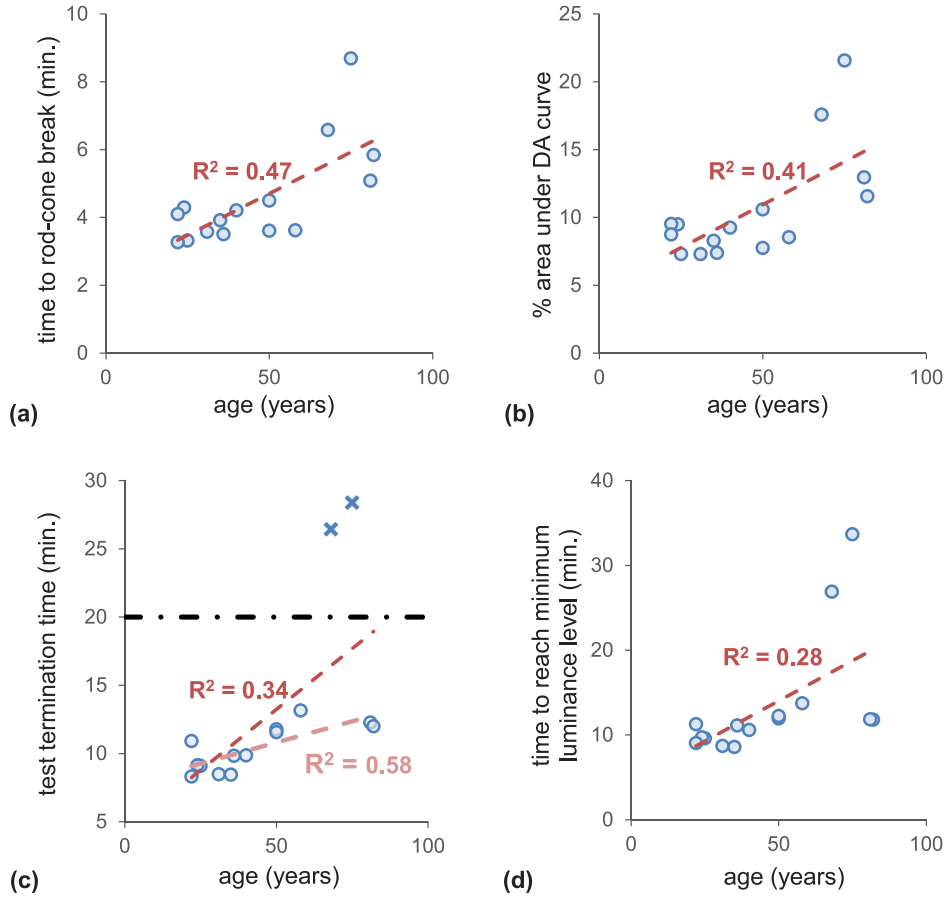

Figure 6. Effect of age on various DA parameters. The time to rod cone break (a), normalized AUC (b), and time to test termination (c) increased significantly with age, whereas there was no significant change in the cone threshold (d). Significant effects are overlaid with a *red dashed line* showing the linear regression fit. The *dotted red line in* (d) shows not significant regression ($R^2 = 0.038$). The *horizontal black dashed and dotted line* in (c) shows the maximum test termination time used in the study (20 minutes). Two subjects did not finish the test in this preset time limit and, thus, the time to reach minimum luminance level in their case was extrapolated (shown as 'x'). The lighter toned regression line shows the fit when excluding these two subjects, which is still significant.

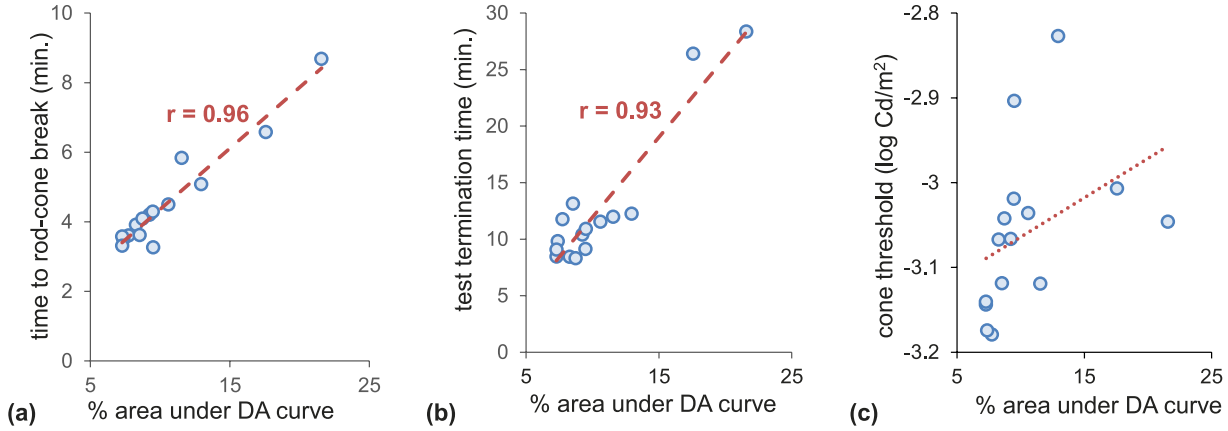

Figure 7. Correlation of the AU) with other DA parameters. AUC was strongly correlated with t_{RCB} (a) and t_{term} (b), whereas it was not correlated with the cone threshold (c). Significant correlation is shown by *red dashed line* and correlation coefficient. *Dotted line* shows nonsignificant regression ($r = 0.39$) in (c).

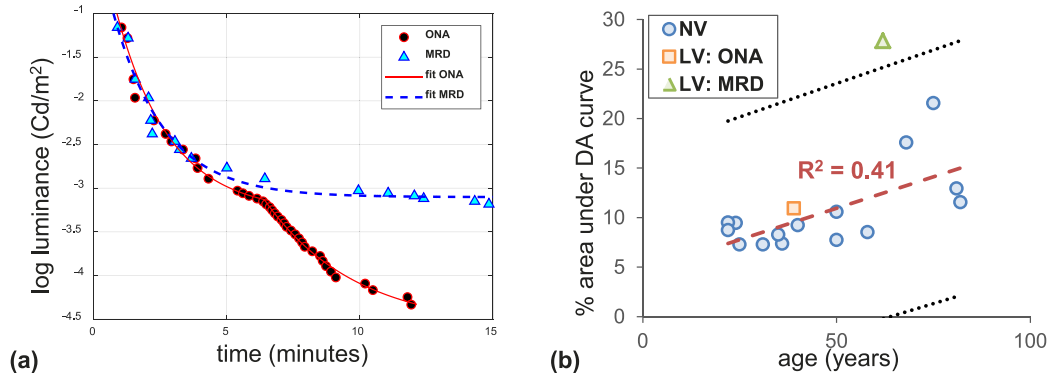

Figure 8. DA measurement in 2 low vision (LV) patients. (a) The DA characteristics of the subject with MRD was impaired with the rod component missing (*dashed blue line*) and the curve leveled off at −3.1 log cd/m^2. On the other hand, the DA characteristics of the patient with ONA appeared to be similar to the characteristics of NV subjects, as it had rod and cone components and the subject reached the minimum luminance threshold set for the test within the allotted time. In both subjects, the Figure shows the average of two trials. (b) The plot of age versus AUC from Figure 6b, overlaid with the AUC data points for the two LV subjects. As a consequence of the difference in DA characteristics, the MRD subject (*green triangle*) recorded a large AUC (outside the 99% observation bound of the NV population, indicated by the *black dotted lines*) compared to the subject with ONA (*red square*).

protocol, which is a main concern for our approach. In our experiments, retinal bleaching was performed using the bright screen of the mobile device on undilated eyes. Since the entire phone screen is turned bright, the retinal area bleached is large compared to spot bleaching (as done in clinical dark adaptometers[12]). Hence, unintended changes in fixation location during the test due to small head movement would not cause the stimulus to be outside of the bleached region. It should be noted that the subjects were instructed not to make large body movements during the test, but small head movements were probably inevitable since a head-chin rest was not used. While simplifying the measurement method, use of a mobile screen to bleach meant that the maximum luminance level would be much lower that the luminance of flash-based bleaching apparatus. Thus, the bright screen was presented for a longer duration (in our case 120 seconds) to bleach sufficient photopigment for generating valid DA characteristics. This kind of prolonged bleach has been used previously in some of the DA measurement instruments.[11] The resultant DA characteristics show the typical biphasic shape (due to cone and rod components), despite the lower luminance level of bleaching light.

Despite these differences in the experimental setup compared to dedicated dark adaptometers, the evaluation results indicated that MOBILE-DA measurements are valid. First, within-subject DA measurements are repeatable (Fig. 4). Test–retest differences in the DA parameters show low bias (mean close to 0), with CoR values that are comparable to previously reported data. For example, for AdaptDx dark adaptometer and for the computer-based approach of Patryas et al.,[22] the CoRs for time to rod cone break were 3.2 ($n = 14$, older subjects) and 3.6 ($n = 33$, young and old subjects) minutes, respectively, whereas for MOBILE-DA it was 2.1 minutes ($n = 15$). Second, MOBILE-DA measurements reflect aging-related changes in DA characteristics.

Aging affects DA, possibly due to the interplay of various factors that influence molecular mechanisms within the retinal layers controlling rhodopsin regeneration: impaired vitamin A metabolism, accumulation of byproducts of metabolism in the retinal layers, and thickening of retinal layers, such as Bruch's membrane.[1,11,15] These age-related changes in the retina manifest in terms of overall delays in the DA process (delayed rod cone break and rod recovery,[14] and even cone recovery[17,20]) and loss of photoreceptor sensitivity.[16] Based on the findings of these studies, our goal was to evaluate the validity of MOBILE-DA measurements by trying to reproduce a similar age-effect on DA characteristics within our study population. The evaluation results clearly show that time-dependent DA parameters (t_{RCB}, t_{term}, and AUC) showed a significant effect of increasing age (Fig. 6), and were consistent with the findings of previous studies.[14,17,22] These results showed the validity of MOBILE-DA measurements.

We did not find a significant effect of age on the cone threshold. For the rod component, luminance thresholds were elevated at the end of the test for some of the older participants, but we were unable to

clearly determine the extent of age-effect on rod threshold due to the limitations of the measurement setup (because the lower bound on the luminance range of the device did not include absolute rod threshold).

In this study, we explored the use of using the AUC as an outcome measure, in addition to or as an alternative to the traditional DA parameters, such as time to rod cone break, rod recovery, among others. As defined (Fig. 3), the AUC encapsulated the region between cone threshold and L_{min}. A large AUC could be due to delayed t_{RCB}, elevated L_{cone}, slower rod recovery (which in turn, included slower slope of recovery and longer duration to reach the minimum threshold), or all of these factors. In our study population, the AUC was strongly correlated with t_{RCB} and t_{term} (Fig. 7). Thus, by combining the effects of the traditional DA parameters, a single parameter of AUC could signal the overall delays in DA characteristics. Using AUC to describe DA characteristics can be particularly advantageous in situations where testing is bounded, which means there are limits on the time and luminance thresholds measured. Therefore, the AUC can be normalized and compared between subjects, irrespective of the inter-subject differences in the absolute photoreceptor sensitivities. Additionally, MOBILE-DA can be used to determine discrete photoreceptor sensitivity values after a predefined period of DA, in cases where entire DA characteristics are either not feasible or not necessary. For example, if we are interested to know whether a subject can achieve a particular luminance threshold after a fixed amount of time in dark, such a test can be easily configured on MOBILE-DA. Thus, not being able to measure the absolute rod sensitivities does not limit MOBILE-DA as a test of DA. Furthermore, short duration measurement protocols can be potentially devised using AUC as the primary outcome measure.

Another advantage of using AUC as an outcome measure is that it also can handle cases where the thresholds at the end of the test (when maximum allotted test time expires) are higher (i.e., subjects who do not reach the minimum threshold before time expires). Such cases will register a high value of AUC compared to those who reach minimum threshold within the time limit. This can be seen in the case of the subject with myopic retinal degeneration, where the DA characteristics were impaired to an extent that rod component was missing and the luminance threshold at the end of the test was highly elevated compared to NV subjects (Fig. 8). Comparison of two low vision subjects, one with retinal damage who was expected to have impaired DA characteristics, was done as a verification exercise. A large difference in the DA characteristics of these two subjects, which is visually noticeable, can be quantified in terms of AUC. While far from conclusive, the ability to differentiate obvious cases of retinal damage is a further piece of evidence suggesting that MOBILE-DA can provide valid DA measurements.

A feature that is inherently afforded by smartphones is the ability to easily configure various test parameters, which could potentially make MOBILE-DA a useful research and teaching tool. For example, stimulus size can be increased depending upon the screen size and viewing distance restrictions, to investigate how the rod sensitivities change with increasing stimulus size. Similarly, other measurement parameters, such as flashing frequency of the stimulus and its eccentricity with respect to fixation can be varied as required. While the measurements reported in this work were specific to the Samsung Galaxy S8, different OLED displays have broadly similar characteristics (our luminance and color measurements generally agree in terms of broad trends with previous studies[23,24]), which means that MOBILE-DA can potentially work on different devices with minor changes. While DA measurement may seem to be feasible only for OLED displays and not for LCD screens, many of the latest mainstream mobile devices models feature OLED displays. When using mobile devices that do not have sufficient dynamic range in their displays, neutral density goggles (for example, gray tint sunglasses) can be used to improve the range and enable testing of rod function. A similar approach of using neutral density filters was followed in previous DA measurement studies that used computer screens with limited display range for stimulus presentation.[20,22]

At present there are some limitations of the study particularly related to the understanding of the effect of changing various measurement parameters, such as stimulus size, as well as the effect of variation in pupil size on the DA characteristics. However, our goal was to determine whether we can measure DA in humans using a contemporary mobile device, with a relatively simple setup. For this purpose we used the fact that DA is affected by age or retinal damage to evaluate our DA measurement method. While preliminary in nature, our results clearly showed that it not only is possible to use mobile devices for DA measurement, but also that the measurement setup involved can be made simple enough so that the subjects could potentially perform the test by themselves in future.

Thus, in addition to the possible clinical use, MOBILE-DA potentially can be used by the public in mass screening in the future. Given the simplification of the testing method using a smartphone, there may be tradeoffs in accuracy and precision of the measured DA parameters, which are yet to be determined and will be the subject of future work.

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