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MULTISPECTRAL DIAGNOSTIC IMAGING OF THE IRIS IN PIGMENT DISPERSION SYNDROME

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Abstract

Purpose—To determine if wavelength selection with near infrared (NIR) iris imaging may enhance iris transillumination defects (ITDs) in pigment dispersion syndrome.

Methods—An experimental apparatus was used to acquire iris images in 6 African-American (AA) and 6 White patients with pigment dispersion syndrome. Light emitting diode (LED) probes of 6 different spectral bands (700 to 950 nm) were used to project light into patients' eyes. Iris patterns were photographed, ITD regions of interest were outlined, and region of interest contrasts were calculated for each spectral band.

Results—Contrasts varied as a function of wavelength ($P < 0.0001$) for both groups, but tended to be highest in the 700 to 800 nm range. Contrasts were higher in Whites than AAs at 700 nm but the opposite was found at 810 nm ($P < 0.001$).

Conclusions—Optimized NIR iris imaging may be wavelength dependent. Ideal wavelength to image ITDs in more pigmented eyes may be slightly longer than for less pigmented eyes.

Keywords

glaucoma; infrared iris imaging; pigment dispersion syndrome

Introduction

Near infrared (NIR) imaging techniques currently provide the most sensitive means to detect and record iris transillumination. The first reports of NIR iris imaging occurred during the 1970s by Saari et al. who described stereophotography of the normal iris¹ and an iris affected by Fuchs' heterochromic iridocyclitis.² Subsequent to these reports, NIR iris imaging received little if any attention for many years, possibly because these older methods required specialized equipment that was not typically available to the clinician. Later, in 1990, Alward et al.³ described an NIR videography technique to obtain real-time images of

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the iris, and in 1994 Haynes et al.⁴ described an NIR photographic method to quantify iris transillumination defects (ITDs) in pigment dispersion syndrome (PDS).

In the late 1990s, the older NIR videographic method was further explored to determine if it was useful to detect subclinical ITDs among the dark-brown irides of African-American PDS subjects.⁵ Because of disappointing results, follow-up work led to a simple, more efficacious digital camera method to detect and record ITDs.⁶ Afterwards, this method was used to conduct preliminary study of PDS and other conditions affecting iris translucency.^{7–9} In 2003, it was shown that the digital camera method could detect iridociliary cysts,⁷ and most recently a series of new clinical observations was published to demonstrate the diversity of potential clinical and research applications of the NIR iris imaging modality.⁹

Although the modified digital camera system is useful, the method explored lacks some efficacy with the most darkly-colored irides and it still requires adaptations to be truly practical in clinical and research settings. This has therefore led to continued exploration and refinement of the NIR imaging modality. To investigate optimization of the NIR modality, we performed an initial study of the effect of wavelength selection on ITD imaging characteristics in PDS subjects.

Methods

The apparatus used in this investigation was constructed by attaching a NIR (range <1000 nm) monochrome CCD camera with VGA resolution 640×480 to the frame of a slit lamp table top and frame that was stripped of its illumination components. The goal of this camera construction was to capture the iris transillumination images obtained with 6 different light emitting diode (LED) probes (700, 750, 810, 850, 910, 950 nm) that were individually used to project light into subject eyes by passing it through the infero-temporal eyelid skin (Figure 1). We initially narrowed the choice of spectral bands by trial and error and observing the upper and lower limits for which reasonable images were obtained. We then arbitrarily selected the specific wavelength increments, based partially on LED availability. A separate LED light probe was constructed for each of the six spectral bands. The spectral bandwidth (full width at half maximum λ - 'FWHM') for the LEDs was 20 nm. Prior to human experimentation with the LEDs, we confirmed that exposure levels to the LEDs operating at maximum rated power levels would be well within established safety limits that have been published in the literature.^{10–12} An optical power meter and optical spectrum analyzer was then also used to ensure that the output power levels of purchased LEDs were within acceptable exposure limits.

The camera was connected to a laptop computer through a Firewire interface that would allow for data transfer and camera control. A custom software module (electronic control module, ECM) was constructed that facilitated exploratory studies and optimization of illumination. The ECM would accept signals from the laptop computer and adjust the power level of the LEDs individually or turn them on or off as desired.

To control fixation and to induce some degree of pupillary constriction, a red LED was attached to an articulated arm that could be used to project the light source directly toward the eye not being imaged without creating light scatter that might interfere with the iris transillumination image quality being obtained on the opposite eye. Because a darkened room is needed to conduct the iris imaging process, we also equipped the camera apparatus with a bright white LED that would provide ambient lighting of the subject's eye and face during initial light probe positioning and camera focusing. The white LED could be switched off just prior to image review and capture.

For the experiment, we selected a convenience sample of 6 African-American (AA) and 6 White PDS subjects and 12 race-matched normals. Each of the PDS subjects had been diagnosed based on the presence of a Krukenberg's spindle, moderate-to-heavy trabecular meshwork pigment, equatorial/posterior lens pigment accumulation (Scheie line), and the presence of midperipheral ITDs as detected via NIR iris imaging using a modified digital camera method that has previously been described.⁶ For purposes of this investigation and entry into the study, we did not require the presence or absence of a history of elevated intraocular pressure and/or glaucomatous optic neuropathy among the PDS subjects. However, subject status relative to these variables is shown in Table 1. Intraocular pressure and optic nerve status were also not used for purposes of the analysis since they were not critical to the analysis goals. All subjects were selected from a primary care clinic population at one facility, i.e., the Illinois Eye Institute. Each subject was required to have had a complete baseline ocular examination within one year of the study imaging in order to rule out ocular comorbidity besides PDS. Minimum examination required was ocular and medical history, extraocular muscle testing, pupil testing, confrontation visual field screening, slit lamp biomicroscopy, gonioscopy, Goldmann applanation tonometry, and dilated fundus examination. Subjects with a history of any type of previous intraocular surgery were excluded from the study. For eye color designations, we classified eyes according to one of three designations based on clinician judgment: brown, hazel, and blue. Hazel eye color was considered a "mixed" eye color, and this designation was used when an eye was not uniformly brown and not uniformly blue.

When subjects presented for the current study, their irides were imaged via the described multispectral NIR photographic technique. Following image acquisition using the six different spectral band light probes, ITD regions of interest (ROIs) were manually outlined with the aid of computer graphics software ("IDL", Interactive Data Language; ITT Visual Information Solutions; Boulder, Colorado, U.S.A.). No attempt was made to dissect large ITD regions into smaller ones; rather, each ITD "island" was completely outlined, even if it extended multiple clock hours circumferentially.

To measure the "visibility" of ITD ROIs, contrast values were calculated between each ITD ROI and a surrounding non-ITD region that consisted of an equal number of pixels automatically selected via computer algorithm (Figure 2). To perform ROI contrast calculations for each ITD and non-ITD ROI "pair", a computer algorithm then also determined the average pixel intensity of all of the ITD ROI pixels and the average pixel intensity of all of the surrounding, non-ITD pixels. Using the average pixel intensity values, we then used an analogy to the Michelson contrast formula¹³ to calculate our contrast values as follows: $Contrast = (I_{ROI} - I_{surround}) / (I_{ROI} + I_{surround})$, where I_{ROI} denotes the average light intensity of all of the pixels in an ITD ROI, and $I_{surround}$ denotes the average light intensity of all of the pixels of the appended surrounding pixels. For each ITD region, the contrast between each ROI pair was calculated for each of the six spectral bands tested during an imaging session. For control eyes, a computer algorithm was used to select random ROIs in the midperipheral iris, as well as corresponding "surround" areas so that average pixel intensities could be compared in a manner similar to the PDS eyes.

In order to provide some indication of repeatability of contrast measurements in the limited dataset, a convenience sample of 5 of the PDS subjects (3 White, 2 African-Americans) were re-imaged on another occasion within 6 months after their original imaging. Once the repeat images were obtained, they were inspected to confirm that the ITD patterns had not changed. The same person then manually outlined the ITD regions in the same manner as before, and the same process of computer selection of "surround" regions was conducted. The second ITD outlining was not performed in a masked fashion, i.e., without any visual reference to initial image outlining, since the goal was only to determine if contrast

measurements could be repeated reasonably from one imaging session to another. Contrast values were then calculated again in the same manner as before for each of the six different wavelength probes. After an initial assessment of simple correlations among the ROI measurements at each wavelength, we also tested whether the average differences between the first and second measurements were statistically and clinically significant from zero.¹⁸ This included an assessment of the 95% limits of agreement and whether repeatability measures varied as a function of mean contrast values.

Statistical analyses were carried out using SAS[®] Statistical Program, Version 9.2 for Microsoft Windows (Cary, NC). The Wilcoxon Rank-Sum test was used for uncontrolled group comparisons of nonparametric contrast data, and Proc Genmod was used to assess variable relationships while controlling for the non-independence of the data.

Institutional Review Board approval was obtained for this investigation, and informed consent was obtained from all participants.

Results

The data of subjects evaluated are summarized in Table 1. Among right eyes, the 6 AAs (age range=48–71 years; all brown irides) had 48 ITD ROIs, and the 6 Whites (age range=34–58 years; 2 brown irides, 1 hazel, 3 blue) had 119. A collection of images, obtained using a single spectral band (Whites-700 nm, AAs-750 nm), from all of the PDS and normal subject right eyes is shown in Figure 3. The photos show the diverse nature of the ITDs among the PDS subjects. A few subjects had relatively classic midperipheral, spoke-like ITDs, but some ITDs had a more amorphous shape and were coalescent in nature. The amount of iris area affected by ITDs was also quite variable. The normal subject irides lacked abnormal ITDs and had a spectrum of appearances, sometimes with lighter areas corresponding to normal iris crypts. Example images from one of the African-American PDS subjects, across all 6 spectral bands, are shown in Figure 4. Contrast values for all 167 ITD ROIs among the PDS subjects are summarized in box plot graphs shown in Figure 5 where the contrast values are grouped according to spectral band and subject race. Median contrast values are also listed in Table 2 where they are statistically compared without controlling for non-independence of the data due to multiple ROIs being used from same subjects. In this analysis, contrast values were statistically higher for African-American subjects at the 810 and longer wavelengths ($P<0.0001$), but the contrast values were higher for Whites at the 700 nm wavelength ($P=0.0002$). As anticipated for the control eyes, contrast values between random midperipheral ROIs and corresponding “surround” areas approximated 0.00% at all wavelength levels for both AA and White groups (Figure 5).

Due to presumed large differences in iris pigment between the AA and White groups, we performed separate analyses to determine if ITD contrast values varied as a function of imaging wavelength. Here, adjusting for data dependence due to multiple ITD contrast measurements from same subjects, ITD contrast varied significantly as a function of imaging wavelength for both the AA and White groups ($P<0.0001$). In a separate analysis to assess whether there were any wavelength-related trend differences between the AA and White subjects, we found that there were no statistically significant differences ($P>0.05$) between the two groups using the entire dataset. Since it was clear though that any statistical differences could simply be overshadowed by trend similarities found with the longer wavelengths, we also performed a subanalysis using only data from the 700, 750, 810, and 850 nm wavelengths. When we excluded the two longest spectral bands, the adjusted analysis did in fact confirm wavelength-dependent differences, between the AA and White subject groups, that appeared evident relative to the shorter spectral bands ($P<0.0001$).

For the repeatability analysis, the simple correlation between the first and second measurements of the African-Americans (23 ROIs) ranged from $r=0.85$ to 0.98 ($P<0.0001$) for the 6 different spectral bands and from $r=0.74$ to 0.92 ($P<0.0001$) among the Whites (43 ROIs). For both groups the lowest correlation value occurred at the 950 nm wavelength. Bland-Altman¹⁸ “difference vs. mean” graphical assessments showed that although there were a few statistically significant differences between the first and second contrast measurements, mean difference values were typically small as reflected by the bias lines and 95% limits of agreement (Table 3). Also, inspection of “difference vs. mean” scatter plots did not reveal any consistent trend for mean differences to vary as a function of mean contrast values (Figure 6).

Discussion

A primary conclusion that can be derived from this experiment is that wavelength selection can be important in optimizing NIR iris imaging quality. Although the “quality” of an NIR iris image may be judged differently depending on the structures and conditions of interest, we chose to evaluate the ITD contrast in PDS subjects for this investigation because we had early interest in detecting ITDs that might otherwise be invisible in dark-brown irides. There may be a host of unknown factors that influence the ideal imaging wavelength, but it is suggested here that iris pigment density can be considered when attempting to optimize NIR iris images and the detection of ITDs. As noted, we found that, on average, ITDs in very dark irides might be enhanced with slightly longer spectral bands as compared to optimal ITD enhancement in less-pigmented irides. This was illustrated graphically in Figure 5 which showed higher ITD contrast values for the African-American eyes compared to the White subject eyes at all of the tested wavelengths except at 700 nm.

An interesting observation made by Alward et al.³ during experimentation with an infrared videography method in 1990 was that better images tended to be produced via a combination of “visible” and “infrared light.” Although the authors did not specify numeric specifications of any filter(s) they used to block light, their observation might in fact be supported by the multispectral data in our investigation since we found, on average, optimal ITD contrasts using light sources in the 700–800 nm range.

Depending on the literature source, the visible spectrum is usually considered to extend from about 360–780 nm,^{14–15} and the NIR spectrum is considered to extend from about 700–1400 nm.^{15–17} Since these graphical representations actually represent gradual transitions, variation in reported cutoff values are not unexpected. We have imaged eyes that showed nonexistent or minimal transillumination at 700 nm, but there were definitely eyes that showed excellent transillumination at the 700 nm spectral band. Decision to include 700 nm as the shortest wavelength was based simply on initial judgment, but perhaps there are certain eyes for which optimal images could be obtained with even shorter wavelengths. Regardless, these data demonstrate that optimal imaging spectral bands may in fact span the range including longer wavelength “visible light” and shorter wavelength “NIR light.” Using an optimal spectral band may help produce higher quality images by eliminating bands that actually detract from image quality. Perhaps though, certain iris pathologies might actually be optimized by using wider ranges of wavelengths because of variable imaging characteristics within the same iris. This will require further study.

A limitation of this study is the inclusion of a small number of subjects with a single ophthalmic condition, i.e., PDS. The simple goal here though was to perform an initial investigation into the potential effects of wavelength selection on ITD visibility, and it is evident that wavelength parameters may influence ITD contrast in some subjects. More study will obviously be needed to more precisely elucidate how wavelength may interact

with any number of different subject and condition parameters that influence imaging characteristics.

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Figure 1.
Infero-temporal position of light probe during imaging.

Figure 2.

Example photo showing iris transillumination defect regions of interest (ROIs) (red pixels) and non-iris transillumination defect zones (green pixels), which were used to calculate contrast values. The regions of interest and the surrounding non-iris transillumination defect zones have the same number of pixels. The surrounding regions were automatically selected via computer algorithm.

Figure 3.

Right eye images from all of the control and pigment dispersion subjects, obtained using 700 nm for the Whites and 750 nm for the African-Americans. Some show classic mid-peripheral iris transillumination defect spokes but others are more amorphous and/or coalescent.

Figure 4. Near infrared transillumination images of the same iris acquired at different wavelengths for an African-American pigment dispersion subject. Contrast differences can be visualized with the different wavelengths. This subject's 360° iris transillumination defect pattern was not detectable without near infrared imaging.

Figure 5.

Region of interest contrasts grouped by wavelength and subject group for the pigment dispersion subjects (top) and normal subjects (bottom). Boxplots denote the range of contrast values between the 25th and 75th percentiles, with whiskers extending to the 10th and 90th percentiles. Dashed and solid lines connect mean region of interest contrast values across all wavelengths for the White and African-American groups respectively. Peak contrast occurred at 750 nm for the African-American pigment dispersion eyes, but it was 700 nm for Whites.

Figure 6.

Example “mean vs. difference” plots of two selected imaging wavelengths that reflect region of interest contrast results calculated from two separate imaging sessions.

Table 1

Characteristics of study subjects.

Subject No.	Diagnosis		Age	Race	Gender	Iris Color	#Regions of Interest (ROIs)
	R	L					
1	Normal	Normal	34	African-American	Female	Brown	-
2	Normal	Normal	32	African-American	Female	Brown	-
3	Normal	Normal	37	African-American	Female	Brown	-
4	Normal	Normal	38	African-American	Female	Brown	-
5	Normal	Normal	51	African-American	Female	Brown	-
6	Normal	Normal	57	African-American	Female	Brown	-
7	Normal	Normal	32	White	Female	Blue	-
8	Normal	Normal	33	White	Female	Brown	-
9	Normal	Normal	44	White	Male	Blue	-
10	Normal	Normal	54	White	Male	Blue	-
11	Normal	Normal	55	White	Female	Blue	-
12	Normal	Normal	60	White	Female	Hazel	-
13	†PDS	PDS	48	African-American	Female	Brown	10
14 *	PDS	PDS	50	African-American	Male	Brown	5
15 *	PDS	PDS	55	African-American	Female	Brown	5
16 *	PDS	PDS	64	African-American	Female	Brown	5
17 *	PDS	PDS	68	African-American	Female	Brown	14
18 *	PDS	PDS	71	African-American	Male	Brown	9
19	PDS	PDS	28	White	Female	Blue	16
20	PDS	PDS	34	White	Female	Brown	7
21 *	PDS	PDS	51	White	Male	Blue	42
22 *	PDS	PDS	52	White	Male	Brown	10
23	PDS	PDS	57	White	Male	Hazel	20
24	PDS	PDS	58	White	Male	Blue	24

[†]Abbreviations: PDS, pigment dispersion syndrome.

^{*} One or both eyes had history of glaucomatous optic neuropathy (based on optic nerve cupping along with repeatable visual field defect) and/or elevated intraocular pressure >21 mm Hg on two or more occasions.

Table 2

Iris transillumination defect (ITD) contrast values comparison: African-American vs. White.

Imaging Wavelength (nanometers)	Median Contrast (minimum, maximum)		*P-value
	African-Americans N=48 Regions of Interest (ROIs)	Whites N=119 Regions of Interest (ROIs)	
700	0.11 (−0.05, 0.22)	0.14 (−0.01, 0.40)	0.0002
750	0.14 (0.01, 0.54)	0.13 (0.02, 0.45)	0.2341
810	0.11 (−0.13, 0.40)	0.06 (−0.05, 0.32)	<.0001
850	0.08 (0.03, 0.34)	0.05 (−0.08, 0.23)	<.0001
910	0.06 (−0.004, 0.24)	0.03 (−0.02, 0.15)	<.0001
950	0.04 (0.01, 0.22)	0.02 (−0.04, 0.11)	<.0001

* Wilcoxon Rank-Sum test

Table 3

Repeatability analysis summary showing mean of first and second contrast measurements, the mean of their differences, and 95% limits of agreement.

Imaging Wavelength (nanometers)	$\bar{\dagger}$ Mean Contrast ($\bar{\ddagger}$ Mean Measurement Difference $\pm$ 1.96 SD)		
	All Subjects N=5, 66 Regions of Interest (ROIs)	African-American N=2, 23 Regions of Interest (ROIs)	Whites N=3, 43 Regions of Interest (ROIs)
700	0.109 (** 0.014 $\pm$ 0.053)	0.097 (0.007 $\pm$ 0.035)	0.115 (** 0.018 $\pm$ 0.06)
750	0.121 (−0.004 $\pm$ 0.047)	0.169 (** −0.019 $\pm$ 0.028)	0.096 (0.005 $\pm$ 0.046)
810	0.101 (0.000 $\pm$ 0.063)	0.135 (** 0.013 $\pm$ 0.035)	0.083 (−0.006 $\pm$ 0.070)
850	0.080 (0.004 $\pm$ 0.037)	0.105 (0.005 $\pm$ 0.038)	0.066 (0.003 $\pm$ 0.038)
910	0.048 (0.000 $\pm$ 0.024)	0.065 (** 0.005 $\pm$ 0.021)	0.039 (−0.002 $\pm$ 0.023)
950	0.036 (0.002 $\pm$ 0.031)	0.054 (** −0.007 $\pm$ 0.027)	0.026 (** 0.006 $\pm$ 0.031)

** Statistically significant differences between first and second measurements (P<0.05)

$\bar{\dagger}$ Mean of measurement 1 plus measurement 2

$\bar{\ddagger}$ Mean of measurement 1 minus measurement 2