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USAGE OF ADAPTIVE OPTICS FOR HIGH-RESOLUTION *IN-VIVO* IMAGING FOR PANUVEITIS AND POSTERIOR UVEITIS

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ABSTRACT

Introduction: Adaptive optics (AO) is a groundbreaking technology increasingly used for high-resolution in-vivo imaging in ophthalmology. Panuveitis and posterior uveitis are inflammatory conditions affecting various parts of the uveal tract, including the retina and choroid. These diseases often result in visual impairment and present challenges in early diagnosis, monitoring, and evaluating treatment outcomes. **Materials and Methods:** A prospective comparative study was conducted in the Department of Ophthalmology at a rural hospital in South India. Eighty eyes from 40 patients were analyzed, split into two groups: Control Group (n=40 healthy eyes) and Study Group (n=40 eyes with panuveitis or posterior uveitis). **Observations & Results:** Cone cell density in the central 4° of fixation was analyzed using ImageJ software. The average cone cell count in affected eyes (Group A) was 9,835, compared to 24,958 in healthy eyes (Group B), a 60% reduction. The spacing between cone cells was significantly larger in affected eyes. **Conclusion:** AO-based high-resolution imaging enables detailed visualization of retinal microstructures, offering unique insights into disease pathology in panuveitis and posterior uveitis. This technology has strong potential for improving clinical care by facilitating early detection and monitoring of therapeutic outcomes.

INTRODUCTION

Imaging the posterior segment of the eye with high resolution has become an indispensable tool in diagnosing, monitoring, and understanding retinal diseases. Adaptive optics (AO) technology has revolutionized this field by enabling cellular-level imaging of the retina *in vivo*. Adaptive optics, originally developed for astronomy to correct atmospheric distortion, has been adapted for ophthalmology to address wavefront errors in the eye. These wavefront errors are measured and corrected in real-time using a deformable mirror or other corrective optics, allowing for near-diffraction-limited imaging. While standard imaging modalities, such as fundus photography, optical coherence tomography (OCT), and fluorescein angiography, are widely used in the clinical setting, they have limitations in resolution and sensitivity. This gap in resolution has driven the integration of AO with imaging modalities to achieve unparalleled clarity and detail. This technique not only corrects all the static spatial modes but also corrects and measures the dynamic changes and allows for *in vivo* cellular imaging, the classification of individual photoreceptor cells, and enables psychophysical testing of human visual function at the neural level [1]. This technology facilitates early detection of disease progression, precise monitoring of therapeutic responses at a microscopic scale, and quantitative assessment of retinal changes caused by inflammation [2]. In the context of panuveitis and posterior uveitis,

AO-based imaging provides significant advantages. The inflammatory processes in these conditions often lead to subtle microstructural changes in the retina, such as photoreceptor loss, microvascular abnormalities, or immune cell infiltration. AO imaging enables clinicians and researchers to detect and quantify these changes at a cellular level, offering new insights into disease mechanisms and therapeutic targets. The purpose of this study is to evaluate the utility of AO imaging in patients with posterior and panuveitis associated with Behcet's disease, Vogt Koyanagi Harada's (VKH) Syndrome, and Serpiginous-like Choroiditis (SLC). AO enables the detailed visualization of retinal microstructures, such as photoreceptors, retinal pigment epithelium, and microvasculature, at a cellular level. AO aids in the detection of retinal vasculitis and microvascular anomalies in Behçet's disease. Occlusive retinal vasculitis and bilateral recurrent non-granulomatous panuveitis are the hallmarks of ocular involvement (Behçet's uveitis). Due to irreversible retinal damage and complications like macular scarring, macular atrophy, and optic atrophy, recurrent inflammatory episodes in the posterior segment may result in irreversible vision loss [3]. During active inflammation and treatment, AO allows for precise monitoring of choroidal changes and photoreceptor damage in VKH syndrome. With AO imaging, retinal pigment epithelium and choroidal lesions can be more clearly seen in cases of serpiginous-like choroiditis, which helps with accurate disease progression assessment. AO helps develop specialized treatment plans and improves knowledge of these disorders.

MATERIALS AND METHODS

Source: All the patients presenting to the Department of Ophthalmology in a rural hospital in South India.

Informed and written consent: Taken from each participant.

Ethical committee approval: Obtained.

Sample Size: 40 (20 case and 20 controls); a total of 80 eyes. Participants were categorized into two groups:

Study group (Group A, n = 40): Patients with Behcet's disease, Vogt Koyanagi Harada's Syndrome, and Serpiginous-like Choroiditis.

Control group (Group B, n = 40): Healthy individuals.

Inclusion Criteria: Confirmed diagnosis of one of these conditions based on clinical and/or imaging findings (with Fundus Fluorescein Angiography). Presence of active or resolved posterior segment inflammation affecting the retina or choroid. Adults or older adolescents who can provide informed consent and comply with imaging protocols.

Exclusion Criteria: Patients with pregnancy or hypersensitivity.

Study Method: Mean cone cell density of central four degrees of fixation was scanned and analyzed using **Image J software** and a **fundus camera**. Mean cone cell count and spacing between cone cells (in μm) were documented.

Adaptive Optics Imaging: Initially, confirmation of the diagnosis was done, and the patients were categorized into two groups. The procedure includes **pupil dilation** to maximize light entry, followed by **calibration of the AO system** using a wavefront sensor to detect and correct individual optical aberrations. Once calibrated, the **deformable mirror** adjusts the optics in real-time. The imaging system then captures detailed scans of the targeted retinal regions, such as photoreceptors, retinal vessels, or choroidal layers, using precise focus and stabilization techniques. **Multiple frames** are often averaged to enhance image quality

OBSERVATIONS &RESULTS

TABLE1– GENDER DISTRIBUTION

	Male	Female
GroupA	23	17
GroupB	21	19

In the study, 44 were male and 36 were female [Table1].

TABLE 2-AGE DISTRIBUTION

Age	Group A	Group B
21-30	10	07
31-40	09	11
41-50	13	15
51-60	08	07

In the study, most individuals fell under the age group of 41-50 (13 in Group A and 15 in Group B) [Table 2]

TABLE 3 –MEAN CONE CELL COUNT AND SPACING BETWEEN GROUPS

Diagnosis	Number of eyes	Mean cone cell count	p-value	Spacing between cones µm)	p-value
VKH	26	7905	Between affected eyes and non-affected eyes (0.05)	42.46	Between affected eyes and non affected eyes (0.05)
Bechet's Disease	22	3811		75.65	
Serpiginous-like Choroiditis	32	15546		9.34	
Healthy eyes	80	24958		7.06	

It can be noted that the mean cone cell count was 7905 in VKH, 3811 in Bechet's and 15546 in SLC.The same value in normal eyes was found to be 24958.The average cone cell count in each eye in GroupA was 9835.The average cone cell count in each eye in Group B was 24958. This shows that on an average, a single normal eye has around 60% more cone cells than when affected by either of VKH, Bechet's or SLC. [Table 3] The spacing between cones was 42.46 µm VKH, 75.65 µm Bechet's and 9.34 µm Serpiginous-like Choroiditis. The same in healthy eyes was 7.06 µm.Among the 40 cases in Group A, 13 were VKH with11 Bechet's disease and 16 SLC.

The average spacing between cone cells is 81% higher in normal eyes as compared to affected eyes. [Table 3]. Adaptive optics (AO) imaging has provento be avaluable toolfor studying posterior and panuveitis associated with Behçet's disease, Vogt-Koyanagi-Harada (VKH) Syndrome, and Serpiginous-like Choroiditis. These conditions often result in complex retinal and choroidal abnormalities that AO imaging can visualize with exceptional resolution .By compensating for the eye's natural aberrations, AO imaging enables the detection of cellular-level changes, such as photoreceptor damage, inflammatory cell infiltration, and alterations in the retinal

pigment epithelium (RPE). Withthe adaptive optics imaging system, cone subtypescould be identified inadditionto densitometry. Williams & Co. examined two normal human retinas to determine how three cone classes were arranged [6]. According to Cheung in his study, AO imaging has the potential to improve our understanding and perhaps the monitoring of cerebrovascular and neurodegenerative changes occurring in the retina [7]. Wolfing and colleagues reported Adaptive optics scanning laser ophthalmoscope (AOSLO) imaging in a patient with cone-rod dystrophy. Images were collected from various points of the retina where clinically identified bull's-eye lesions were present. Within the deteriorated zones, vast areas lacking wave-guiding cone structures were noticed. Contrastingly, areas seemingly untouched by clinical examination displayed a fully aligned cone arrangement. Nevertheless, in these unaffected zones, the cones were abnormally enlarged, resulting in a 6.6- fold decrease inthe regular peak cone density. (patient peak density: 30,100 cones/mm^2 , normal peak density: 199,200 cones/mm2) [8]. Our study showed peak density of 53987/mm^2 with Serpigenous choriditis.

Cone cell density may be reduced in pan-uveitis and posterior uveitis because of inflammation and associated retinal damage. In these conditions, inflammation affects the retina and choroid, which are critical for supporting the function of cone cells.The immune response
leads to the release of pro-inflammatory cytokines, recruitment of immune cells, and increased oxidative stress, all of which can directly damage cone cells. This damage disrupts the photoreceptor layer, leading to apoptosis (cell death) of cone cells and affecting the structural integrity of the retina.

Additionally, chronic inflammation in pan-uveitis and posterior uveitis may impair the Retinal Pigment Epithelium (RPE), which plays a vital role in supporting photoreceptors, including cone cells. The RPE is responsible for nutrient transport, waste removal, and photoreceptor maintenance. Dysfunction of the RPE, along with compromised blood-retinal barriers, can lead to insufficient support for cone cells, further contributing to their degeneration. Overtime,this process can result in a reduction in conecell density,which manifests as decreased visual acuity, loss of color vision, and central visual field deficits. Agarwal et al studied the adaptive optics imaging in white dot syndrome and found that there is decrease in cone cell count in inactive lesions compared to active lesions which is correlating with our study where cone cell count is decreasing in patients with panuveitis and posterior uveitis. He showed the mean photo receptor density was 7331±4628 cones/mm^2overlying 16 active lesions and 6546 ±3775 cones/mm^2 overlying 19 inactive lesions (*P*=.896).Mean retinal sensitivity(9.37±5.34dB)showed modest correlation with photoreceptor density ($\rho = 0.42$, $P = .03$).

According to a study by Shinetal, Cone density was significantly reduced in patients with BD compared to controls[10]. It is also the same with our study where the mean cone cell counts decreases in patients with Behcet's disease.

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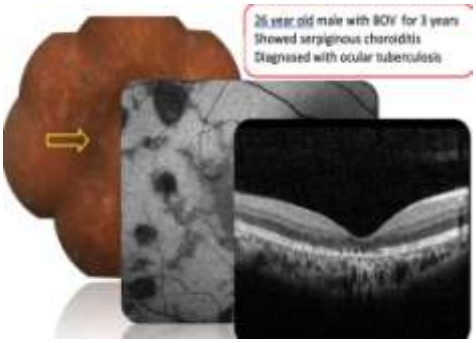

IMAGE1-SERPIGENOUS CHOROIDITIS

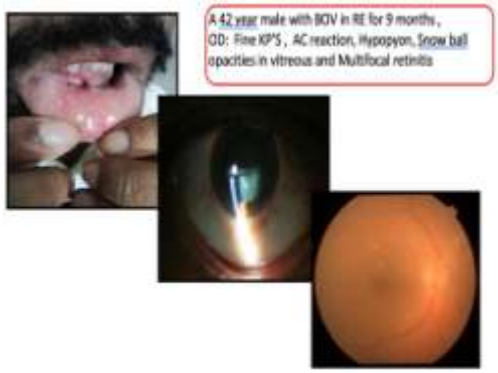

FIGURE2-BEHCET'S DISEASE

CONCLUSION

Adaptive Optics Imaging can be used as an additional quantifying imaging modality to studythephotoreceptorsdensityandspacingtoa ssessthefovealchangesinBehcet's,VKH,SLC. It has emerged as a powerfultoolfor studying posterior and pan-uveitis associated withBehçet's disease, VKH syndrome, and serpiginous-like choroiditis. By providing cellular-level resolution of retinal and choroidal structures, AO imaging enables detailed assessment of disease-related changes such as photo receptor damage, vascular inflammation, and choroidal granulomas. It aids in diagnosing these complex inflammatory conditions, tracking disease progression, and evaluating treatment responses. Importantly, modalities, enhancing our understanding of the pathological processes underlying these uveitic diseases. Its non-invasive nature and

high sensitivity make it invaluable in both clinical practice and research. Future advancements in AO imaging may further refine its role in personalized medicine for patients with uveitis. Adaptive Optics imaging in VKH and Behcet's has not been reported till now.

LIMITATIONS: Inpatients with hazy media, like Cataract, Vitreoushaze, Macular edema and small pupil size photoreceptors cannot be visualized. No tall cases of VKH, Bechet'sand SC present with both panuveitis and posterior uveitis which makes it hard to assess .The sample size is also small which can be expanded later for more cases.

CONFLICTOF INTEREST: All the authors declare that there is no conflict of interest noted.

AUTHOR CONTRIBUTIONS: All the authors declare that the contribution is equal in all aspects.

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