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Objective Measurement of Vitreous Inflammation using Optical Coherence Tomography

Pearse A. Keane, MD FRCOphth¹, Michael Karampelas, MD FEBO^{1,2}, Dawn A. Sim, FRCOphth¹, Srinivas R. Sadda, MD³, Adnan Tufail, MD FRCOphth¹, H. Nida Sen, MD, MHSc⁴, Robert B. Nussenblatt, MD, MPH⁴, Andrew D. Dick, MD, FMedSci⁵, Richard W. Lee, MRCOphth, PhD⁵, Philip I. Murray, PhD FRCOphth^{6,7}, Carlos E. Pavesio, MD FRCOphth¹, and Alastair K. Denniston, PhD FRCOphth^{7,8}

¹NIHR Biomedical Research Centre for Ophthalmology, Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, UK

²Hinchingbrooke Hospital, Hinchingbrooke Health Care NHS Trust, UK

³Doheny Eye Institute and Department of Ophthalmology, Keck School of Medicine of the University of Southern California, Los Angeles, California, USA

⁴National Eye Institute, National Institutes of Health, Bethesda, Maryland, USA

⁵Bristol Eye Hospital, University Hospitals Bristol NHS Foundation Trust, Bristol, UK

⁶Academic Unit of Ophthalmology, University of Birmingham, Birmingham, UK

⁷Birmingham & Midland Eye Centre, Sandwell and West Birmingham NHS Trust, Birmingham, UK

⁸Queen Elizabeth Hospital Birmingham, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK

Abstract

Purpose—To obtain measurements of vitreous signal intensity from optical coherence tomography (OCT) image sets in patients with uveitis, with the aim of developing an objective, quantitative marker of inflammatory activity in patients with this disease.

Design—Retrospective, observational case-control series.

Participants—Thirty patients (30 eyes), with vitreous haze secondary to intermediate, posterior, or panuveitis; twelve patients (12 eyes) with uveitis but without evidence of vitreous haze; and 18 patients (18 eyes) without intraocular inflammation or vitreoretinal disease.

Correspondence and reprint requests: Alastair K Denniston, FRCOphth PhD, Queen Elizabeth Hospital Birmingham, University Hospitals Birmingham NHS Trust, Birmingham, United Kingdom. Tel: +44 121 6278568 Fax: +44 121 6278789 a.denniston@bham.ac.uk.

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Methods—Clinical and demographic characteristics were recorded, including visual acuity (VA), diagnosis, and anatomic type of uveitis. In each eye, the anterior chamber (AC) was graded for cellular activity and flare according to standardized protocols. The presence and severity of vitreous haze was classified according to the National Eye Institute system. Spectral domain OCT images were analyzed using custom software. This software provided an “absolute” measurement of vitreous signal intensity, which was then compared to that of the retinal pigment epithelium (RPE), generating an optical density ratio with arbitrary units (“VIT/RPE-Relative Intensity”).

Main Outcome Measures—Correlation between clinical vitreous haze scores and OCT-derived measurements of vitreous signal intensity.

Results—VIT/RPE-Relative Intensity was significantly higher in uveitic eyes with known vitreous haze (0.150) than in uveitic eyes without haze or in healthy controls (0.0767, $p=0.0001$). VIT/RPE-Relative intensity showed a significant, positive correlation with clinical vitreous haze scores ($r=0.566$, $p=0.0001$). Other ocular characteristics significantly associated with VIT/RPE-Relative Intensity included VA ($r=0.573$, $p=0.0001$), AC cells ($r=0.613$, $p=0.0001$), AC flare ($r=0.385$, $p=0.003$). Measurement of VIT/RPE-Relative Intensity showed a good degree of inter-grader reproducibility (95% limits of agreement: -0.019 to 0.016).

Conclusions—These results provide preliminary evidence that OCT-derived measurements of vitreous signal intensity may be useful as an outcome measure in patients with uveitis. If validated in future studies, such measures may serve as an objective, quantitative disease activity endpoint, with the potential to improve the “signal:noise” ratio of clinical trials in this area, thus enabling smaller studies for the same power. The incorporation of automated vitreous analysis in commercial OCT systems may, in turn, greatly facilitate monitoring and retreatment of patients with uveitis in clinical practice.

Keywords

Vitreous; Inflammation; Optical coherence tomography; Uveitis

Uveitis, a group of diseases characterized by intraocular inflammation, is an important cause of blindness worldwide.¹ The annual incidence of uveitis is between 17 and 52 per 100,000 of the population, with up to 35% of patients reported to suffer significant visual impairment or legal blindness.^{2–5} One of the greatest challenges in caring for patients with sight-threatening uveitis is the lack of objective markers of disease activity, whether in the context of routine clinical practice (to direct treatment), or for use in clinical trials (to establish efficacy of new therapies and standardization of care).⁶

The current gold standard for assessing vitreous inflammation in patients with intermediate and posterior uveitis is the National Eye Institute (NEI) system for grading of vitreous haze.^{7, 8} In this system, often referred to as the Nussenblatt scale, the patient’s eye is examined with an indirect ophthalmoscope and the appearance compared to a series of photographs representing various degrees of fundal vitreous haze. This assessment is recognized as a surrogate endpoint by the United States Food and Drug Administration (FDA) and has been adopted as a primary outcome in almost all recent studies of uveitis. Despite this, the technique has a number of limitations, notably that it is: 1) subjective, with only moderate inter-observer agreement; 2) non-continuous, leading to very large steps in

disease activity between categories; 3) poorly discriminatory at lower levels of vitreous haze, with most cases of active uveitis being scored at 0.5+ or 1+; 4) limiting of sensitivity in a clinical trial context (where a two point change is required to be counted as significant).^{9, 10}

In recent years, ophthalmology has been revolutionized by the introduction of a new imaging modality, optical coherence tomography (OCT).¹¹ OCT provides high-resolution, cross-sectional images of ocular tissues in a non-invasive manner. From an early stage in its development, OCT has also been pioneering in its attempts to provide automated measurements of disease morphology and thus objective markers for clinical care.¹² Until recently, OCT imaging has focused in large part on the neurosensory retina, allowing qualitative assessment of disease features such as cystoid macular edema (CME) and providing automated measurements of retinal thickness.^{13, 14} Lately however, the use of OCT for direct visualization of vitreous inflammatory cells in patients with uveitis has been described.¹⁵ In addition, quantitative assessment of OCT image sets has begun to evolve, from simple measurements of thickness or volume, to the assessment of more novel parameters such as optical density/signal intensity.^{16–22} Taken together, these advances present an opportunity to derive objective, OCT-derived measurements of inflammation in patients with uveitis.

In this exploratory study, we obtain measurements of vitreous signal intensity from OCT image sets obtained in cohorts of patients with intermediate and posterior uveitis. We correlate these findings with standard assessments of vitreous haze in an effort to develop an improved marker of inflammatory activity in patients with this disease.

Methods

Inclusion Criteria

For this study, OCT image sets from two separate patient groups, attending specialist uveitis clinics at Moorfields Eye Hospital and the Birmingham Midland Eye Centre, were retrospectively collected. In the first group, images from eyes with vitreous haze secondary to intermediate, posterior, or panuveitis, were included. These images were then compared to those of a second group obtained from eyes with uveitis in the absence of vitreous haze. A further control group consisted of OCT image sets obtained from healthy volunteers without evidence of intraocular inflammation or other vitreoretinal disease. Approval for data collection and analysis was obtained from a UK National Health Service (NHS) research ethics committee and adhered to the tenets set forth in the Declaration of Helsinki.

Clinical Data Collection

Information about age, gender, diagnosis, and anatomic type of uveitis, were gathered before clinical ophthalmic examination and OCT image acquisition. Best-corrected visual acuity (VA) was measured using Early Treatment Diabetic Retinopathy Study (ETDRS) charts. Clinical ophthalmic parameters assessed included: 1) visually significant keratic precipitates (KPs); 2) posterior synechiae; 3) cataract, and 4) posterior capsular opacification (in pseudophakic eyes). In each eye, the anterior chamber (AC) was graded for cellular activity

and flare according to standardized protocols by experienced observers (A.K.D. and M.K.). The presence and severity of vitreous haze was also classified by the same graders according to the National Eye Institute system.^{7, 8}

OCT Image Acquisition Protocol

For each eye, OCT image sets were obtained using a spectral domain OCT system (Spectralis OCT, Heidelberg Engineering, Germany). This system acquires 40,000 A-scans per second with an axial resolution, in tissue, of 7 μm , and a transverse resolution of 14 μm . In each case, volume scans centered on the fovea were obtained. The “enhanced depth imaging” (EDI) mode was not used in any case and the zero delay line, or the point of maximum sensitivity, was maintained on the vitreous side.²³

Qualitative Analysis of the Vitreous using OCT

For each OCT image set, the presence or absence of intravitreal cellular infiltrates was noted. These were defined as hyperreflective dots in the vitreous that were larger and of greater density than background speckle noise (as previously described by Saito et al.).¹⁵ These were differentiated from the larger, non-punctate, irregular condensations within the vitreous cavity, which appeared to reflect normal age-related vitreous synergetic changes. Examples of vitreous cells and flare, as seen on OCT, are presented for a variety of uveitic aetiologies in Figure 1.

Quantitative Analysis of the Vitreous using OCT

Raw OCT data were exported from the Heidelberg Spectralis OCT system and imported into validated custom grading software, entitled “OCTOR”.^{24, 25} This software enables easy navigation of spectral domain OCT volume scans and manual boundary annotation of each B-scan, or a subset of B-scans. Based on these boundaries, the intensity of all pixels in a morphologic compartment of interest (e.g., vitreous) can be summed, and mean OCT intensity values generated.^{26, 27} Image contrast was not adjusted either before or after export from the OCT system.

For each OCT image set, boundaries were manually segmented according to standardized OCT grading protocols (Figures 2 and 3).^{26, 28} In each case, 3–5 B-scans passing through the foveal central subfield (i.e., the 1 mm in diameter central subfield of the ETDRS grid) were analyzed. This typically required 5–10 minutes of grading time per image set. These boundaries consisted of: 1) “vitreous top”, the uppermost extent of the vitreous space as visualized on OCT, 2) internal limiting membrane (ILM), the inner boundary of the neurosensory retina, 3) retinal pigment epithelium (RPE)-inner, the inner boundary of the RPE, and 4) RPE-outer, the outer boundary of the RPE. The “vitreous” was defined as the space lying between the vitreous top and the ILM (except in cases of partial detachment of the posterior hyaloid face, or ERM, where the innermost boundary was chosen). The “RPE” was defined as the space lying between the inner and outer boundaries of the RPE. After completion of grading, mean intensity values were calculated for the vitreous space (termed “VIT-Absolute Intensity”) and the RPE space (termed “RPE-Absolute Intensity”) in the foveal central subfield. Intensity values for the vitreous and RPE spaces were then expressed as a ratio (termed “VIT/RPE-Relative Intensity”).

To examine the effects of scan localization on vitreous measurements, we also calculated VIT/RPE-Relative Intensity in a subset of cases across the total scan area (i.e., including every OCT B-scan in the volume scan rather than only those passing through the central subfield of the ETDRS grid). The resulting measurements were highly correlated with those obtained from the foveal central subfield alone ($n=40$ for all eyes in subset, $r=0.9419$, $p<0.001$ and $n=15$ for those eyes in the subset with uveitis and vitreous haze, $r=0.9213$, $p<0.001$).

Reproducibility of Vitreous Segmentation

All segmentation was performed by a single, reading center-certified, OCT grader (P.A.K.), masked to all clinical information at the time of grading. To assess reproducibility, the OCT image sets were also segmented by a second, experienced OCT grader, also in a masked fashion (M.K.).

Data Analysis and Statistical Methods

Clinical and imaging data were analyzed with frequency and descriptive statistics. For comparison of mean OCT intensity values between groups, non-parametric Kruskal-Wallis testing was used. For correlation of clinical vitreous haze scores with mean OCT intensity values, non-parametric Spearman testing was used. Multivariable regression was then used to model the effects of clinical characteristics on mean OCT intensity values.

Reproducibility, or inter observer variability, was assessed using Bland-Altman plots, using the mean OCT intensity values obtained by each grader. The mean difference and confidence intervals were calculated. Agreement between graders was also examined using Bland-Altman analysis, with the 95% limits of agreement (LoA) between graders calculated after confirming that the measurement differences were normally distributed using histograms.

P values < 0.05 were considered statistically significant. Statistical analysis was performed using commercially available software (Intercooled Stata for Windows, Version 9, Statacorp LP, USA).

Results

Baseline Characteristics

In the main study group (patients with uveitis and evidence of vitreous haze), 30 patients (30 eyes) were evaluated in our study. In the control group, 30 patients (30 eyes) were also evaluated, consisting of 12 patient (12 eyes) with uveitis but without vitreous haze, and 18 patients (18 eyes) without any evidence of uveitis or vitreoretinal disease. For each group, demographic features, visual acuities, and other clinical characteristics (including clinical vitreous haze scores), are summarized in Table 1.

OCT-derived Measurements of Vitreous Intensity

OCT-derived measurements of vitreous intensity for each group (“uveitis with vitreous haze” versus “uveitis with no vitreous haze” versus “normal eyes”), and for each grade of

vitreous haze are summarized in Figures 4 and 5. A significant difference in VIT/RPE-Relative intensity was found between those eyes with “uveitis with no vitreous haze” or “normal eyes” (median=0.0767, interquartile range (IQR)=0.0478), when compared those with “uveitis with vitreous haze” (median=0.150, IQR=0.135) ($p=0.0001$), and between each grade of vitreous haze ($p=0.001$).

A significant correlation was found between VIT/RPE-Relative Intensity and clinical vitreous haze scores ($r=0.566$, $p=0.0001$, Spearman non-parametric testing), VA ($r=0.573$, $p=0.0001$), and clinical AC cells ($r=0.613$, $p=0.0001$) and AC flare scores ($r=0.385$, $p=0.003$). VIT/RPE-Relative Intensity also showed a modest but significant correlation with retinal thickness in the foveal central subfield ($r=0.3246$, $p=0.038$). Of note, as the strength of the relationship between variables increases, so does the value of the correlation coefficient (r), with a value of 1 showing a perfect relationship. The relationship between VIT/RPE-Relative Intensity and the clinical vitreous haze scores is illustrated in Figure 6. When evaluated in a step-wise multivariable model examining factors governing media clarity (i.e. AC cells and flare) and other ocular characteristics such as VA and disease etiology (i.e. birdshot chorioretinopathy, Behçet’s disease, and idiopathic panuveitis), location of inflammation (i.e. anterior, intermediate, posterior, and panuveitis), VIT/RPE-Relative Intensity remained independently associated with clinical vitreous haze scores (R^2 -adjusted=0.292, $p=0.0001$).

Reproducibility of Vitreous Grading

Bland-Altman plots were used to illustrate the agreement between graders and 95% LoA are presented in Table 2 and Figure 7. It is expected that the 95% LoA include 95% of differences between the two graders and this is represented for visual judgment in the Bland-Altman plot. The smaller the range between these two limits the better the agreement is.

To examine whether the 95% LoA were significantly different between observers in controls and uveitic eyes, with and without vitritis, the variance of the interobserver measurement differences were calculated and the F statistic (variance ratio) presented (Table 3). The variance ratios between graders were not statistically significant in all groups, which suggest that VIT/RPE relative intensity measurements were reproducible in both controls as well as in eyes with vitritis. However, there was a trend towards a higher 95% LoA in eyes with vitritis compared to controls (0.0450 versus 0.0226 respectively).

Case Study

A 57 year-old man presented to the uveitis clinic and was diagnosed with active, non-infectious panuveitis affecting the right eye. At presentation he underwent spectral domain OCT imaging (Spectralis) which revealed widespread intravitreal cellular infiltrates and diffusely increased vitreous signal intensity (Figure 2A). Manual segmentation of vitreous and RPE in the image set from the affected eye was performed, resulting in a VIT/RPE-Relative Intensity value of 0.3550 (Figure 2B). He was commenced on oral prednisolone and followed closely. At one month post-treatment, there was no evidence of active inflammation on clinical examination, a finding in keeping with results from OCT analysis, where a VIT/RPE-Relative Intensity value of 0.1267 was determined.

Discussion

In patients with uveitis, the onset of inflammation commonly leads to permeation of the vitreous with inflammatory cells and protein-rich exudate.²⁹ These changes typically reflect the degree, and to an extent the location and character, of the underlying uveal inflammation. Vitreous inflammatory cells can be directly visualized using slit-lamp biomicroscopy and, more recently, using OCT.¹⁵ However, in many cases of uveitis (e.g., pars planitis), vitreous cells may persist for extended periods even after resolution of their initiating inflammatory episode.⁷ In contrast, protein-rich exudate is only seen in the presence of active inflammation. This exudate may also be seen on clinical examination in the form of vitreous “flare” (i.e., the scattering of light by fine particles suspended in solution as described by the Tyndall effect).^{30, 31} As OCT is fundamentally a light scattering-based imaging modality, it is well suited to the visualization of this feature. Although OCT does not provide the exact composition of the vitreous compartment, higher vitreous signal intensity will be indicative of increased scattering of light and thus increased density of particles within the space. Conversely, lower vitreous signal intensity will reflect a relatively clearer vitreous composition with fewer suspended particles.

In this report, we first obtained an “absolute” measurement of vitreous signal intensity (“VIT-Absolute Intensity”), reflecting the mean intensity value for all image pixels contained within the vitreous compartment. In order to reduce the effects of OCT signal strength, anterior media opacities, and other confounding factors, we then compared this to a reference value (“RPE- Absolute Intensity”), and generated an optical density ratio with arbitrary units (“VIT/RPE-Relative Intensity”). The use of OCT-derived optical density ratios has previously been described for the assessment of intra- and subretinal fluid.^{16–21} In eyes with intraretinal fluid, increased signal intensity of cystoid spaces has been reported in diseases with active exudation (e.g., diabetic retinopathy) versus those without (e.g., cone dystrophies and idiopathic perifoveal telangiectasia).^{17, 18} Similarly, subretinal fluid in eyes with neovascular age-related macular degeneration (AMD) shows an increased OCT signal intensity relative to that seen in central serous chorioretinopathy (a finding the authors hypothesize is related to increased breakdown of the outer blood-retinal-barrier in the former condition).¹⁹

In the current study, we demonstrate that: 1) VIT/RPE-Relative Intensity is significantly higher in uveitic eyes with known vitreous haze than in uveitic eyes without haze or in healthy controls, 2) VIT/RPE-Relative Intensity values are higher with each incremental increase in clinical vitreous haze score, 3) VIT/RPE-Relative intensity values show a significant, positive correlation with clinical vitreous haze scores independently of other clinical characteristics, and 4) VIT/RPE-Relative Intensity scores can be calculated with a high degree of inter-grader reproducibility. These results are a preliminary step in the validation of this OCT-derived biomarker as an outcome measure in uveitis. This OCT-derived biomarker has important theoretical advantages over the current gold standard in that it is objective (vs subjective), continuous (vs ordinal) and has a high level of inter-grader reproducibility. If validated in future studies, OCT-derived measures of vitreous inflammation may prove useful as an objective, quantitative, disease activity endpoint in clinical trials of posterior segment uveitis. One of the key limitations in such trials currently

is the relatively poor ‘signal:noise ratio’ which renders a positive result unlikely except in the context of a highly effective treatment in a large-scale (and expensive) clinical trial. The reasons for this have been summarized elsewhere,⁶ but include the lack of an objective outcome measure with a high degree of discrimination. If the OCT-derived measures described here are validated, and are demonstrated to robustly predict visual function and clinical benefit in patients with uveitis, it may be possible for trialists and regulatory bodies to adopt such a marker as a surrogate endpoint in clinical trials of this disease.^{32, 33} In this manner, OCT-derived measurements of vitreous inflammation may be used to improve the sensitivity and efficiency with reductions in sample-size and cost for clinical trials in posterior segment uveitis.

It should be noted that whilst this study demonstrated a statistically significant association of VIT/RPE-Relative Intensity with the NEI Vitreous Haze score, the correlation was relatively weak at $r=0.566$. It should be recognized that both these tools are imperfect surrogate measures for the ‘true’ gold standard of intraocular inflammation as manifest in the vitreous cavity, and thus discordance between the two indices may reflect the limitations of either. Limitations in this OCT-derived vitreous reflectivity index will be explored further in subsequent studies and may be amenable to refinements in protocol, standardization in acquisition technique, and technical advances (discussed later). Some of the limitations in the NEI Vitreous Haze score have been assessed by Kempen et al.,³⁴ who noted an inter-observer agreement of $k=0.53$ (for exact agreement) and $k=0.75$ (for within 1 grade) and by Davis et al.¹⁰ Indeed, Davis et al., have addressed some of these issues by utilizing an extended nine-point graded photograph-to-photograph technique which was assessed in the Multicenter Uveitis Steroid Treatment (MUST) trial.¹⁰ Similarly to our study, whilst they note excellent interobserver and intraobserver intraclass correlations (correlation coefficients $0.84 - 0.93$), the correlation between the photographic and the NEI vitreous haze scores was much weaker ($r=0.51$; $P<0.001$).

Our study has a number of strengths, combining detailed clinical assessments of ocular characteristics by uveitis specialists with novel, standardized qualitative and quantitative assessments of OCT images by a senior grader certified for image interpretation in clinical trials. Of note, our study was performed using standard volume scans obtained from the current generation of commercially available spectral domain OCT systems (i.e., without the need for specialized hardware). Although our study required the use of custom image analysis software employed at the Doheny Image Reading Center, similar forms of analysis are possible using free, publically available, image analysis tools (e.g., ImageJ, National Institutes of Health, Bethesda, MD; available at <http://rsb.info.nih.gov/ij/index.html>, accessed December 22nd 2013), or commercial software (Photoshop, Adobe Systems, San Jose, CA).^{15, 21} As such, this form of analysis may be applied retrospectively to any large-scale clinical trial of uveitic conditions where spectral domain OCT was employed. As manual segmentation of the vitreous using this approach typically requires 5–10 minutes, it is perhaps less likely to be used in routine clinical practice. Fortunately however, development of automated segmentation solutions is unlikely to prove challenging (especially given the progress in recent years of automated analysis of more challenging morphology on OCT, such as choroidal neovascularization (CNV))^{35–37} – such software would have the potential to facilitate real-time clinical decision-making.

Our study also has a number of limitations. In particular, it involves cross-sectional analysis of OCT image sets obtained from a small number of patients. As a result, our study contained no eyes with a clinical vitreous haze score of 4+ and it is unknown whether reliable measurements of VIT/RPE-Relative Intensity are possible at this level. In the future, longitudinal studies involving larger patient cohorts, and potentially other imaging modalities (e.g., fluorescein angiography), will be required to validate the clinical significance of our findings. Of note, no image sets were acquired using the EDI mode of the device – i.e., in all cases, the point of maximum imaging sensitivity was at the vitreoretinal interface rather than at the choroid, and only minimal B-scan averaging was performed.²³ In future studies, it will be interesting to examine the effects of increased B-scan averaging on VIT/RPE-Relative Intensity levels, and to determine whether the associated reductions in image speckle noise will result in increased accuracy of measurements. Similarly, future studies should evaluate the use of reflectivity references other than the RPE, particularly in those patients with uveitis where there is putative involvement of this layer.

The design of the study was pragmatic in utilizing scans conducted under normal macular scanning conditions, rather than attempting to optimize for vitreous – for example, it is possible for the operator to increase the amount of vitreous imaged by pulling back on the joystick during image acquisition.³⁹ Even employing this technique, the depth of vitreous that can be imaged is still limited to the scanning range of the Spectralis OCT system (1.9 mm).⁴⁰ As a result, only the posterior aspect of the vitreous is directly visualized. Although this is a significant shortcoming for the assessment of vitreous cells, it may be less of a disadvantage when assessment is of diffuse vitreous permeation with protein-rich exudate. Moreover, the next generation of “swept source” OCT technology will allow for greatly increased scanning ranges.⁴¹ In fact, the introduction of vertical cavity surface-emitting lasers (VCSEL) already allows “whole eye” OCT image sets with visualization of the vitreous in its entirety.⁴² To date, these systems have only been used for simple applications such as ocular biometry;⁴³ their potential for vitreous imaging in uveitic disease is intriguing, particularly if combined with measures such as VIT/RPE-Relative Intensity.

In conclusion, in this pilot study, we describe a method for quantitative analysis of vitreous signal intensity on OCT. We apply this method to a cohort of patients with uveitis, both with and without vitreous haze, and to healthy controls. As a result, we describe a new OCT-derived biomarker: “VIT/RPE-Relative Intensity” with potential for use as an objective marker of disease activity in patients with uveitis. Measurements of this biomarker can be made using existing, commercially available OCT devices, both prospectively, and in image sets that have already been collected. The incorporation of automated vitreous measurements in commercial OCT software would allow use of this parameter in routine clinical practice. Moreover, assessment of the vitreous in patients with uveitis may be an important clinical application of the next generation of “whole eye” swept source OCT systems.

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Abbreviations

OCT	optical coherence tomography
CME	cystoid macular edema
NEI	National Eye Institute
FDA	Food and Drug Administration
NHS	National Health Service
ETDRS	Early Treatment Diabetic Retinopathy Study
KP	keratic precipitate
AC	anterior chamber
EDI	enhanced depth imaging
CR	coefficient of repeatability
ICC	intraclass correlation coefficient
LoA	limits of agreement
IQR	interquartile range
AMD	age-related macular degeneration
MUST	Multicenter Uveitis Steroid Treatment
CNV	choroidal neovascularization
VCSEL	vertical cavity surface emitting laser

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Figure 1.

Visualization of age-related and inflammatory changes in the vitreous using spectral domain optical coherence tomography (OCT). [A] OCT B-scan obtained from 74-year-old woman without uveitis demonstrating detachment of the posterior hyaloid face (arrows) and age-related vitreous condensation (arrowhead). [B] OCT B-scan obtained from a patient with Birdshot chorioretinopathy demonstrating vitreous cells with minimal vitreous haze (clinical vitreous haze score +0.5, Vitreous (VIT)/Retinal Pigment Epithelium (RPE)-Relative Intensity 0.0783). [C] OCT B-scan obtained from a patient with sarcoid-related panuveitis

demonstrating vitreous cells in combination with moderate vitreous haze (clinical vitreous haze score +1.0, VIT/RPE-Relative Intensity 0.2222). [D] OCT B-scan obtained from a patient with idiopathic panuveitis demonstrating vitreous cells in combination with moderate to severe vitreous haze (clinical vitreous haze score +2.0, VIT/RPE-Relative Intensity 0.2701). [E] OCT B-scan obtained from a patient with idiopathic panuveitis demonstrating vitreous cells in combination with more severe vitreous haze (clinical vitreous haze score +3.0, VIT/RPE-Relative Intensity 0.3818).

Figure 2.

Quantitative assessment of the vitreous using spectral domain optical coherence tomography (OCT) at initial presentation in a 57 year-old patient with idiopathic panuveitis (clinical vitreous haze score 2+). **[A]** OCT B-scan revealing widespread intravitreal cellular infiltrates and diffusely increased vitreous signal intensity. **[B]** OCT B-scan following manual segmentation of the vitreous compartment (boundaries: vitreous top to internal limiting membrane (ILM)) and the retinal pigment epithelium (RPE) (boundaries: RPE-inner to RPE-outer), with a resulting Vitreous (VIT)/RPE-Relative Intensity of 0.3550.

Figure 3. Quantitative assessment of the vitreous using spectral domain optical coherence tomography (OCT) following treatment with oral corticosteroids in a 57 year-old patient with idiopathic panuveitis. **[A]** OCT B-scan revealing a significant reduction in both vitreous haze and inflammatory cells. **[B]** OCT B-scan following manual segmentation of the vitreous compartment, with a resulting Vitreous (VIT)/Retinal Pigment Epithelium (RPE)-Relative Intensity of 0.1267.

Figure 4.

Box plots illustrating Vitreous (VIT)/Retinal Pigment Epithelium (RPE)-Relative Intensity measurements in “uveitis with vitreous haze” versus “uveitis with no vitreous haze” versus “normal eyes”. The horizontal lines within each box represent the median for each group; the ends of the boxes are the upper and lower quartiles, and the whiskers represent minimum and maximum values.

Figure 5.

Box plots showing Vitreous (VIT)/Retinal Pigment Epithelium (RPE)-Relative Intensity measurements for each clinical grade of vitreous haze. The horizontal lines within each box represent the median for each group; the ends of the boxes are the upper and lower quartiles, and the whiskers represent minimum and maximum values.

Figure 6.

Scatter plot comparing clinical vitreous haze scores with Vitreous (VIT)/Retinal Pigment Epithelium (RPE)-Relative Intensity scores, in uveitic patients with vitreous haze (n=30) and without vitreous haze (n=12). The solid line represents the regression line.

Figure 7.

Bland-Altman plot of difference in Vitreous (VIT)/Retinal Pigment Epithelium (RPE)-Relative Intensity measurements obtained by Graders 1 and 2, versus the mean VIT/RPE-Relative Intensity score obtained by Graders 1 and 2. The solid horizontal line corresponds to the mean difference (-0.002 arbitrary units) while the dashed horizontal lines correspond to the 95% limits of agreement (-0.019 to 0.016 arbitrary units).

Table 1

Baseline Clinical and Demographic Characteristics

	Uveitis with vitreous haze (n=30)	Uveitis without vitreous haze (n= 12)	Healthy controls (n=18)
Age, mean $\pm$ SD (years)	49 $\pm$ 18	44 $\pm$ 14	67 $\pm$ 8
Visual acuity, mean $\pm$ SD (log MAR)	0.53 $\pm$ 0.73	0.19 $\pm$ 0.30	0.02 $\pm$ 0.10
Disease association, no. (%)			
Idiopathic	17 (57)	6 (50)	N/A
Birdshot	5 (17)	2 (17)	
Toxoplasma	2 (7)	0 (0)	
Sarcoidosis	2 (7)	0 (0)	
Other	4 (12)	4 (33)	
Anatomic type of uveitis, no. (%)			
Anterior	3 (10)	4 (33)	N/A
Intermediate	5 (17)	1 (8)	
Posterior	7 (23)	2 (17)	
Panuveitis	15 (50)	5 (42)	
Keratic precipitates, * no. (%)	2 (7)	0 (0)	N/A
Posterior synechiae, * no. (%)	3 (10)	2 (17)	N/A
Cataract, * no. (%)	7 (23)	5 (42)	5 (28)
Posterior capsular opacification, * no. (%)	2 (7)	0 (0)	0 (0)
Anterior chamber cells, no. (%)			N/A
0	11	9	
0.5+	6	2	
1+	4	0	
2+	7	1	
3+	1	0	
4+	0	0	
n/a	1	0	
Anterior chamber flare, no. (%)			N/A
0	14	11	
1+	11	1	
2+	4	0	
3+	0	0	
4+	4	0	
n/a	1	0	
Vitreous haze, no. (%)			N/A
0	0 (0)	12 (100)	
0.5+	4 (13)	0	
1+	13 (43)	0	

	Uveitis with vitreous haze (n=30)	Uveitis without vitreous haze (n= 12)	Healthy controls (n=18)
2+	10 (33)	0	
3+	3 (10)	0	
4+	0	0	

SD = standard deviation; logMAR = logarithm of the minimum angle of resolution; N/A = not applicable

* Presence of factors thought to be significantly limiting posterior segment visualization

Table 2

Reproducibility of VIT/RPE-Relative Intensity Values in Patients with Vitritis and in Controls as assessed using Bland-Altman plots.

	VIT/RPE - Relative intensity		
	Interobserver Mean Difference	95% CI	95% Limits of Agreement
Uveitis with Vitreous Haze (n=30)	−0.00164	−0.00593 to 0.00264	0.0450
All Controls (n=30)	−0.00158	−0.00373 to 0.000566	0.0226
Normal Eyes (n=12)	0.00301	−0.00193 to 0.00795	0.0305
Uveitis without Vitritis (n=18)	0.000633	−0.00129 to 0.00255	0.0151
All (n=60)	−0.00161	−0.00394 to 0.000711	0.0353

VIT = vitreous; RPE = retinal pigment epithelium; CI = confidence interval

Table 3

The Variance Ratio (F Statistic) of Intergrader Differences in VIT/RPE-Relative Intensity Measurements in Eyes with Vitritis and Controls.

	<i>F</i> Test	<i>P</i> Value
Uveitis with Vitreous Haze (n=30)	1.06	0.88
All Controls (n=30)	1.07	0.86
Normal Eyes (n=12)	1.00	1.00
Uveitis without Vitritis (n=18)	1.07	0.90
All (n=60)	1.04	0.87

VIT = vitreous; RPE = retinal pigment epithelium; *F* Test = variance ratio test