Objective Measurement of Vitreous Inflammation Using Optical Coherence Tomography

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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; 12 patients (12 eyes) with uveitis but without evidence of vitreous haze; and 18 patients (18 eyes) without intraocular inflammation or vitreoretinal disease.

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 were 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 with 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: The 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, $P = 0.0001$). The 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 ($r = 0.613$, $P = 0.0001$), and AC flare ($r = 0.385$, $P = 0.003$). Measurement of VIT/RPE-Relative Intensity showed a good degree of intergrader 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 end point, 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, facilitate monitoring and retreatment of patients with uveitis in clinical practice. *Ophthalmology 2014;■:1–9 © 2014 by the American Academy of Ophthalmology.*

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 have 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 is compared with a series of photographs representing various degrees of fundal vitreous haze. This assessment is recognized as a surrogate end point by the U.S. Food and Drug Administration 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 interobserver agreement; (2) noncontinuous, leading to 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+; and (4) limiting of sensitivity in a clinical trial context

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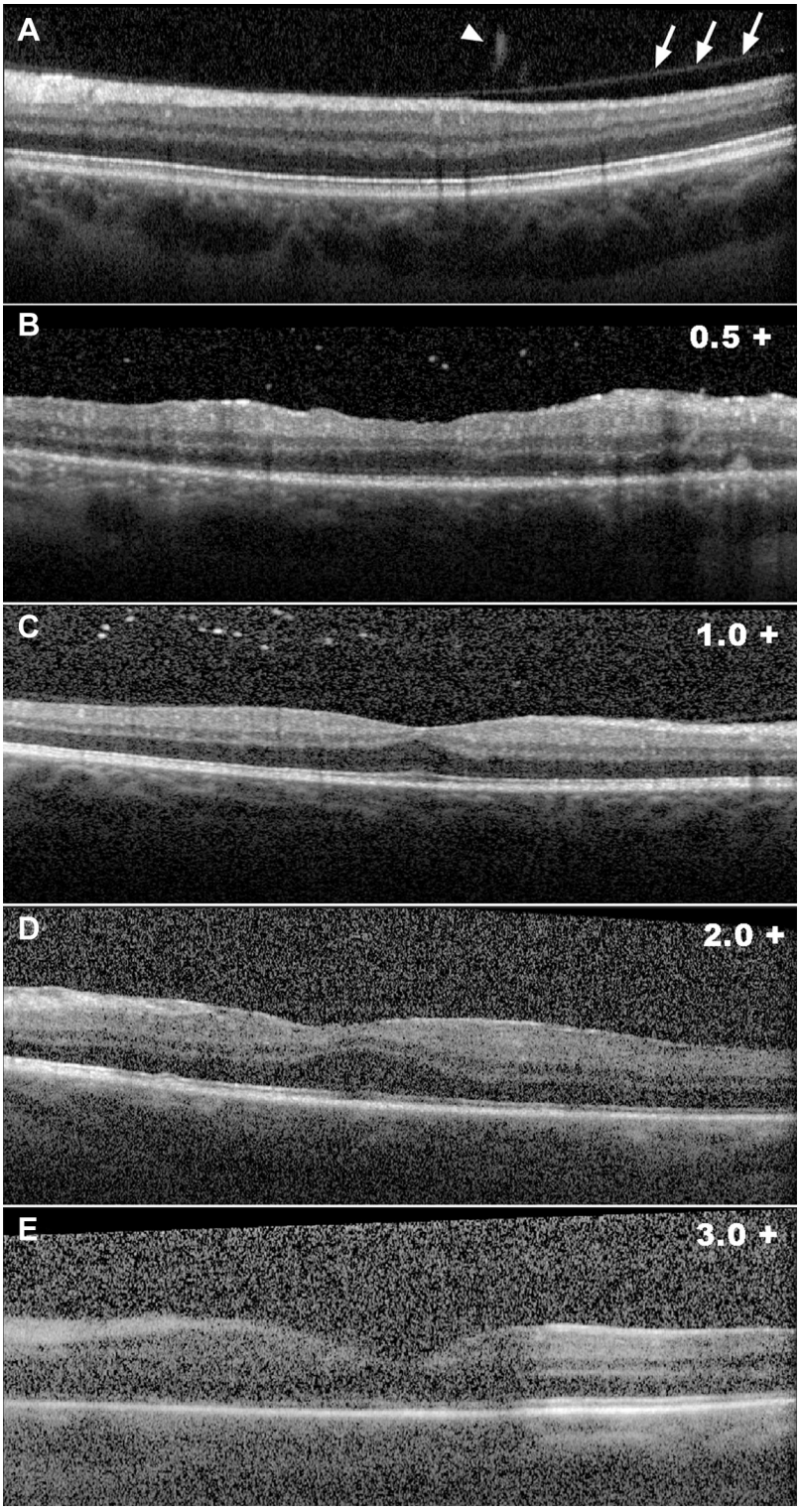

Figure 1. Visualization of age-related and inflammatory changes in the vitreous using spectral-domain optical coherence tomography (SD-OCT). **A,** An OCT B-scan obtained from a 74-year-old woman without uveitis demonstrating detachment of the posterior hyaloid face (*arrows*) and age-related vitreous condensation (*arrowhead*). **B,** An OCT B-scan obtained from a patient with birdshot chorioretinopathy demonstrating vitreous cells with minimal vitreous haze (clinical vitreous haze score +0.5, vitreous signal intensity/retinal pigment epithelium [VIT/RPE]-relative intensity 0.0783). **C,** An 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,** An 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,** An 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).