

# Quantitative analysis of vitreous inflammation using optical coherence tomography in patients receiving sub-Tenon's triamcinolone acetonide for uveitic cystoid macular oedema

Sreekantam, Sreekanth; MacDonald, T; Keane, Pearse; Sim, Dawn; Murray, Philip; Denniston, Alastair

DOI:

[10.1136/bjophthalmol-2015-308008](https://doi.org/10.1136/bjophthalmol-2015-308008)

[10.1136/bjophthalmol-2015-308008](https://doi.org/10.1136/bjophthalmol-2015-308008)

License:

None: All rights reserved

*Document Version*

Peer reviewed version

*Citation for published version (Harvard):*

Sreekantam, S, MacDonald, T, Keane, P, Sim, D, Murray, P & Denniston, A 2017, 'Quantitative analysis of vitreous inflammation using optical coherence tomography in patients receiving sub-Tenon's triamcinolone acetonide for uveitic cystoid macular oedema', *British Journal of Ophthalmology*, vol. 101, no. 2, pp. 175-179. <https://doi.org/10.1136/bjophthalmol-2015-308008>, <https://doi.org/10.1136/bjophthalmol-2015-308008>

[Link to publication on Research at Birmingham portal](#)

## **Publisher Rights Statement:**

Eligibility for repository: Checked on 27/6/2016

## **General rights**

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

## **Take down policy**

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact [UBIRA@lists.bham.ac.uk](mailto:UBIRA@lists.bham.ac.uk) providing details and we will remove access to the work immediately and investigate.

1 **Quantitative Analysis of Vitreous Inflammation using Optical**  
2 **Coherence Tomography in Patients Receiving Sub-Tenon's**  
3 **Triamcinolone Acetonide for Uveitic Cystoid Macular Oedema**

---

4

5 **SUBTITLE** – OCT derived measurements vitreous inflammation decrease with  
6 clinical resolution of inflammation in CMO, providing a quantitative and objective  
7 marker of disease activity in uveitis.

8 **KEY WORDS** – uveitis, cystoid macular oedema, optical coherence tomography,  
9 imaging, outcome measures

10

11 Sreekanth Sreekantam\*<sup>1</sup>, Trystan Macdonald\*<sup>2</sup>, Pearse A Keane<sup>3</sup>, Dawn A Sim<sup>3</sup>,  
12 Philip I Murray<sup>1,4</sup>, Alastair K Denniston<sup>2,4</sup>

13

14 <sup>1</sup>Birmingham and Midlands Eye Centre, Sandwell and West Birmingham NHS Trust,  
15 Birmingham, United Kingdom

16 <sup>2</sup>University Hospitals Birmingham NHS Foundation Trust, Birmingham, United  
17 Kingdom

18 <sup>3</sup>NIHR Biomedical Research Centre for Ophthalmology, Moorfields Eye Hospital  
19 NHS Foundation Trust and UCL Institute of Ophthalmology, London, United  
20 Kingdom

21 <sup>4</sup>Academic Unit of Ophthalmology, Centre for Translational Inflammation Research,  
22 College of Medical and Dental Sciences, University of Birmingham, Birmingham,  
23 United Kingdom

24 \* These authors contributed jointly to this study and share the role of first author.

25 **Correspondence to –**

26 Mr. Alastair Denniston,

27 Consultant Ophthalmologist (Uveitis/Medical Retina) & Hon Reader

28 Institute of Immunology and Immunotherapy

29 College of Medical and Dental Sciences

30 University of Birmingham

31 Edgbaston

32 Birmingham

33 B15 2TT

34 UK

35 **Email - [a.denniston@bham.ac.uk](mailto:a.denniston@bham.ac.uk)**

36

37 **Abbreviations**

38 CMO – Cystoid macular oedema

39 EMA – European Medicines Agency

40 FDA – United States Food and Drug Administration

41 OCT – ocular coherence tomography

42 RPE – retinal pigment epithelium

43 STTA - Sub-Tenon's Triamcinolone Acetonide

44

45 **Disclosure**

46 Drs. Keane and Sim have received a proportion of their funding from the Department  
47 of Health's NIHR Biomedical Research Centre for Ophthalmology at Moorfields Eye  
48 Hospital and UCL Institute of Ophthalmology. The views expressed in the publication  
49 are those of the author and not necessarily those of the Department of Health.

50 Drs. Keane and Sim have received travel grants from the Allergan European Retina  
51 Panel.

52

53

54

55 **Abstract:**

---

56

57 **BACKGROUND/AIMS** : To evaluate the vitreous signals obtained on spectral  
58 domain optical coherence tomography (SD-OCT) in patients with uveitic cystoid  
59 macular oedema (CMO) and compare these signals before and after sub-Tenon's  
60 triamcinolone acetonide injection.

61 **METHODS**

62 Design: Retrospective study with standardised longitudinal imaging pre- and post-  
63 intervention. The study cohort comprises 22 patients (22 eyes) with uveitic CMO  
64 receiving a Sub-Tenon's Triamcinolone Acetonide (STTA) injection. Post-hoc  
65 analysis of SD-OCT images using custom software provided an "absolute"  
66 measurement of vitreous signal intensity, which was expressed as a ratio to the  
67 retinal pigment epithelium intensity ("VIT/RPE-relative intensity") in arbitrary units.

68 Main Outcome Measure: Difference in VIT/RPE-relative intensity before and after  
69 treatment.

70 **RESULTS:** Treatment with STTA resulted in a significant reduction in VIT/RPE-  
71 Relative Intensity, which was associated with both a reduction in central retinal  
72 thickness (CRT) and improvement in visual acuity. Mean (SD) VIT/RPE-Relative  
73 Intensity pre-treatment was 0.139 (0.074) vs. 0.053 (0.028) post-treatment ( $p=3 \times 10^{-5}$ ).  
74 Mean (SD) CRT was 581 $\mu$ m (119 $\mu$ m) pre-treatment vs 333 $\mu$ m (95 $\mu$ m) post-  
75 treatment ( $p=2 \times 10^{-8}$ ); the mean reduction in CRT was 248 (95%CI: 189-306). The  
76 correlation coefficient between VIT/RPE-Relative Intensity and CRT was 0.534

77 (p=0.011) and between VIT/RPE-Relative Intensity and visual acuity was 0.702

78 (p=0.0001).

79 **CONCLUSION:** This study provides evidence that the OCT-derived VIT/RPE-  
80 Relative intensity may be useful as a quantitative and objective marker of disease  
81 activity and treatment response in uveitis complicated by CMO. This first longitudinal  
82 study of this novel OCT parameter is an encouraging step in the development of  
83 sensitive objective OCT-based endpoints for trials of efficacy in uveitis.

84

85

## 86 Introduction

---

87

88 Uveitis, a group of conditions characterised by intraocular inflammation, is a  
89 major cause of blindness worldwide (1). The commonest cause of sight loss in uveitis  
90 is cystoid macular oedema (CMO), which accounts for around a third of blindness  
91 caused by the disease (2). CMO may be reversible with prompt corticosteroid  
92 treatment (3) such as with Sub-Tenon’s triamcinolone acetonide (STTA), leading to  
93 visual recovery (4-6).

94 Vitreous inflammation can be seen on examination as a characteristic “haze”,  
95 caused by the presence of proteinaceous exudate in the vitreous. The level of  
96 vitreous haze is considered to be a good marker of inflammation in the underlying  
97 uveal tract. For this reason the National Eye Institute (NEI) “Vitreous Haze Score” is  
98 the trial endpoint most commonly accepted by regulatory bodies. The NEI scale is  
99 determined by examining the vitreous using an indirect ophthalmoscope with  
100 comparison to standardised photographs. Weaknesses are that it is subjective, non-  
101 continuous, poorly discriminatory at lower levels of inflammation and has low  
102 sensitivity in a clinical trial context (7-10).

103 Optical coherence tomography (OCT), an imaging modality that provides high  
104 resolution, cross sectional images of ocular tissues non-invasively is well-established  
105 in the measurement of macular pathology, including macular oedema (11-13). Most  
106 analysis of OCT images is qualitative, but quantitative analysis - such as the  
107 measurement of central macular thickness in macular oedema – provides an  
108 objective and sensitive measure of deviation from normal, change over time and  
109 response to therapy. We and others are using these principles to develop measures  
110 all the key components of intraocular inflammation, such that the clinical assessment

111 of uveitis may become more objective and reliable (8, 14-18). We have shown in two  
112 independent cohorts using two different OCT-platforms that measurements of  
113 vitreous inflammation derived from OCT scans are repeatable, reliable and  
114 correlated with clinical measures of disease activity, notably the NEI Vitreous Haze  
115 Score (17-18). To help ensure internal standardisation, we utilised the reflective  
116 intensity of the retinal pigment epithelium (RPE) as a reference, thereby producing a  
117 ratio ("VIT/RPE-Relative Intensity) (17-18)..

118           The aim of this paper is to further validate the use of the VIT/RPE-Relative  
119 Intensity as a marker of disease activity in uveitis by assessing whether it is capable  
120 of detecting changes in the vitreous pre-/post-STTA, and whether these correlate  
121 with other signs of reduction in disease activity.

122

123



## 124 **Materials and Methods**

---

125

### 126 **Study Population:**

127 This is a retrospective, longitudinal study comprising 22 patients with uveitic CMO  
128 attending a tertiary uveitis clinic at the Birmingham & Midlands Eye Centre, Sandwell  
129 & West Birmingham Hospitals NHS Trust, United Kingdom. All patients had a  
130 complete ophthalmic assessment including visual acuity, slit lamp examination,  
131 grading of anterior chamber inflammation, intraocular pressure measurement, fundus  
132 examination and grading of vitreous inflammation using the NEI Vitreous Haze  
133 Score. Approval for data collection and analysis was obtained from a U.K. National  
134 Health Service research ethics committee and adhered to the tenets set forth in the  
135 Declaration of Helsinki. All patients were consented for posterior STTA  
136 administration.

137

### 138 **Procedure:**

139 Povidone iodine and oxybuprocaine drops were used to sterilize and anesthetize the  
140 eye before the procedure. The conjunctiva and sub-Tenons layer were lifted 10mm  
141 from the limbus superotemporally using blunt serrated forceps. The sub-Tenon's  
142 cannula was attached to a 2ml syringe containing 1ml of 40mg/ml triamcinolone  
143 acetonide, and inserted, advancing the needle 12-14mm into the posterior sub-  
144 Tenons space into which the full dose (i.e. 40mg triamcinolone acetonide) was  
145 administered (19).

146

### 147 **Image Acquisition:**

148 Optical coherence tomographic image sets were obtained using Heidelberg  
149 Spectralis OCT (Heidelberg Engineering, Germany). The images were obtained  
150 immediately prior to the procedure and at the first subsequent clinical review. The  
151 volume scan images were centred on the fovea and the TruTrack Active and  
152 AutoRescan features were used to ensure that follow-up scans were matched to the  
153 baseline scan.. The enhanced depth protocol was not used.

154

### 155 **Quantitative Assessment of Vitreous Signal Intensity:**

156 As per our previously published protocol, OCT scan images were imported into  
157 'OCTOR', a program for easy navigation and manual grading of the scans validated  
158 in previous studies (20-21). Masked to all clinical data, primary graders marked out 1)  
159 the uppermost extent of the vitreous space included in the scan - the "vitreous top",  
160 2) the internal limiting (ILM) membrane, 3) the inner layer of the RPE, and 4) the  
161 outer layer of the RPE on all the scans. This was done on five sections going  
162 through the central fovea subfield of the Early Treatment Diabetic Retinopathy Study  
163 (ETDRS) grid. The area between lines 1 and 2 was defined as the "vitreous  
164 space"(VIT), whilst the area between 3 and 4 was defined as the "RPE space"  
165 (RPE). The software then calculated the mean intensity values of all image pixels  
166 contained within each space as absolute values. A relative value, the VIT/RPE-  
167 Relative Intensity, could then be derived to minimise the potential effects of  
168 confounders such as lens opacities or anterior chamber inflammation (Figure 1).

169

### 170 **Statistical Analyses:**

171 Clinical and imaging data were analyzed with frequency and descriptive statistics.  
172 Snellen visual acuities were converted to LogMAR (logarithm of the minimum angle

173 of resolution) visual acuity for the purposes of statistical analysis. Spearman's  
174 correlation was used to assess the relationship between the VIT/RPE-Relative  
175 Intensity and clinical/retinal imaging parameter. The Mann-Whitney U test was used  
176 in independent samples and Wilcoxon Signed Ranks test in dependent samples.

177 Statistical analysis was performed using IBM SPSS software version 20.0 for  
178 Windows (SPSS, Inc, Chicago, Illinois, USA). P values < 0.05 were considered  
179 significant.

180

181

## 182 **Results**

---

183

### 184 **Baseline Characteristics:**

185 The study included 22 eyes of 22 patients, before and after treatment with STTA.

186 Their baseline characteristics are listed in Table 1.

187

### 188 **VIT/RPE-Relative Intensity**

189 Treatment with STTA was associated with a significant reduction in OCT-measured

190 VIT/RPE-Relative Intensity (Figure 2). The mean (SD) VIT/RPE-Relative Intensity

191 pre-treatment was 0.139 (0.074) vs. 0.053 (0.028) post-treatment ( $p=3\times 10^{-5}$ ).

192

### 193 **Mean Central Retinal Thickness**

194 Treatment with STTA was associated with significant reduction in the OCT-

195 measured mean central 1 mm of retinal thickness (CRT). Mean (SD) CRT was

196 580.5 $\mu\text{m}$  (119.4 $\mu\text{m}$ ) pre-treatment vs 332.7 $\mu\text{m}$  (95.4 $\mu\text{m}$ ) post-treatment ( $p=2\times 10^{-8}$ );

197 the mean reduction in CRT was 247.7 (95%CI: 189.1-306.3). The correlation

198 coefficient between VIT/RPE-Relative Intensity and CRT was 0.534 ( $p=0.011$ ; Figure

199 3).

200

201

### 202 **Visual acuities**

203 Treatment with STTA was associated with significant improvement in visual acuity

204 ( $p=0.0001$ ). The number of patients with a visual acuity greater than 6/12 increased

205 from 1 (4.54%) to 17 (77.3%) with a corresponding reduction in those with 6/12 or

206 worse from 19 (86.4%) to 5 (22.7%) (Fisher exact test,  $p=0.0001$ ). The correlation

207 coefficient between VIT/RPE-Relative Intensity and visual acuity was 0.702  
208 ( $p=0.0001$ ; Figure 4).

209

## 210 **Discussion**

211 This study provides the first ‘treatment-response’ data to support our proposal  
212 that OCT can be used to provide an objective measure of treatment response in  
213 uveitis based on changes in the vitreous. It builds on our previous feasibility study in  
214 which we demonstrated proof of concept that the VIT/RPE-Relative Intensity could  
215 provide an objective and quantitative measure of vitreous inflammation. Both that  
216 cross-sectional study and a validation study in an independent cohort showed that  
217 the VIT/RPE-Relative Intensity was higher in uveitic eyes with active inflammation  
218 than uveitic eyes without active inflammation or healthy controls, and that it  
219 correlated with the clinical NEI vitreous haze score (17-18). We also showed  
220 association with other markers of disease activity such as visual acuity, AC cells and  
221 AC flare. Importantly the VIT/RPE Relative Intensity was also shown to be a  
222 repeatable measure with high inter-grader reproducibility (17-18).

223

224 In this study we have demonstrated that the VIT/RPE-Relative Intensity  
225 decreases significantly in response to STTA and that this reduction was associated  
226 with improvement in another measurable sign of disease activity, CMO. Critically  
227 this study demonstrates VIT/RPE-Relative intensity is sensitive enough to measure  
228 changes in the vitreous undetectable using the clinical NEI Vitreous Haze Score. As  
229 highlighted by a number of authors, the poor discrimination of the NEI Vitreous Haze  
230 Score at lower levels has led most clinical trials in this field to require subjects to  
231 have a minimum NEI Vitreous Haze Score of 2+ for inclusion. This has significantly

232 limited enrolment (7-10,22). In an observational study comparing a photographic-  
233 based score to the NEI score, Hornbeak noted that had they used the traditional 'cut-  
234 off' 86% of participants would have been excluded. Although a significant proportion  
235 of that cohort were scored as 0 on the NEI Vitreous Haze Score it cannot be argued  
236 that all these cases were inactive as both the Hornbeak study and our current study  
237 indicate that an appropriately sensitive tool is able to discriminate within this group  
238 (9). Whereas the Hornbeak study was cross-sectional, our longitudinal study is the  
239 first to show a tool capable of detecting change in uveitis activity within these lower  
240 levels of inflammation, even when both the pre-treatment and post-treatment clinical  
241 Vitreous Haze Score was 0.

242

243         There is an urgent need to develop sensitive objective measures of  
244 inflammation in uveitis, for use as endpoints in clinical trials and to inform treatment  
245 decisions in routine clinical practice. The FDA advises that a trial endpoint must be  
246 'well-defined and reliable' and recommends that treatment benefit should be a  
247 measure of how a patient "survives, feels or functions". Other measures that do not  
248 capture these are regarded as "surrogate measures of benefit".

249

250         All measures of disease activity in uveitis are "surrogate measures". The FDA  
251 requires a surrogate to be "reasonably likely, based on epidemiologic, therapeutic,  
252 pathophysiologic, or other evidence to predict clinical benefit"., In the context of  
253 developing and assessing surrogate measures for use as trial endpoints in uveitis,  
254 we propose that they must meet two *essential criteria*: (1) The surrogate should be  
255 'biologically relevant' given our understanding of the pathophysiology of the disease;  
256 and (2) The surrogate should be 'functionally relevant' with evidence of a

257 downstream effect on visual function, but recognizing that this effect may be delayed  
258 and indirect. Provided a surrogate satisfies these criteria, it should then be assessed  
259 for *desirable criteria* such as objectivity, repeatability, and sensitivity,  
260

261 This study provides further evidence of the biological and functional relevance  
262 of VIT/RPE relative intensity..Its biological relevance is demonstrated by its  
263 association with other markers of inflammation such as the central retinal thickness.  
264 Its functional relevance is supported by its correlation with visual recovery, however  
265 it is recognized that this is largely indirect, the primary mechanism of improvement  
266 being the restoration of central macular architecture as the oedema resolves.  
267

268 The OCT-derived VIT/RPE-Relative intensity is the first instrument-measured  
269 marker of vitreous inflammation, and is an example of how extended applications of  
270 OCT and other imaging modalities have the potential to revolutionise our approach  
271 to the diagnosis, assessment and management of uveitis. Research into VIT/RPE-  
272 Relative intensity levels during the development of CME and its relation to vascular  
273 changes visualized on fluorescein angiography may inform our understanding of the  
274 natural history of this sight-threatening complication, and help guide treatment..  
275

276 Furthermore the sensitivity of this small study to detect a change at a highly  
277 statistically significant level ( $p = 0.00003$ ), shows how the acceptance of OCT-  
278 derived objective indices could transform our approach to effectiveness trials in  
279 uveitis. .The limitations of our current endpoints in uveitis provide major constraints  
280 to effectiveness trials (7-10,23), which may lead to a trial 'failing' (i.e. not meeting its  
281 primary endpoint) even in the presence of an effective therapy. This in turn

282 discourages further investment, and leads to an absence of high-quality trial data to  
283 inform clinicians, funders and policy makers with regard to main of therapies being  
284 considered for use in uveitis. The high sensitivity and reproducibility of instrument-  
285 based measures such as the OCT-derived VIT/RPE relative intensity can provide  
286 endpoints with much higher 'signal:noise' ratio than current clinical measures  
287 enabling smaller, faster, cheaper trials. Such endpoints can already be adopted as  
288 'signals' to inform investment decisions in early phase studies, but their adoption in  
289 later-phase licensing studies will depend on achieving the further validation required  
290 by regulatory bodies such as the FDA.

291

## 292 **Study limitations**

293 This study involves retrospective analysis of longitudinal OCT image sets  
294 obtained from a small number of patients with uveitis and OCT-confirmed CMO. It  
295 therefore has the limitations of a retrospective design, and we acknowledge that  
296 given the nature of this cohort the focus of the clinical assessments at the time will  
297 have been directed towards the CMO, and not on accurate grading of the clinical  
298 vitreous haze. We also note that visual acuity data were recorded as Snellen  
299 measurements rather than the preferred LogMAR notation. It should be noted  
300 however that the primary focus of this paper is on the post-hoc analysis of the OCT  
301 image sets and their change over time, rather than on the associated clinical  
302 changes.

303

304 The design of the study was pragmatic in using scans conducted under  
305 normal macular scanning conditions. We and others have proposed a number of  
306 techniques for optimising the visualisation of vitreous using current Spectral Domain



307 and emerging technology (8,10, 17-18). Increasing the proportion of the vitreous  
308 which is visualised is likely to improve this technique further, enhancing sensitivity  
309 and repeatability; it also enables anatomic localisation of foci of inflammation within  
310 the vitreous cavity related to the distribution and type of uveitis.

311

312 This study is based on a small cohort, with a range of uveitic diagnoses. This  
313 heterogeneity is common in uveitis studies (8,10), and indeed the consistent  
314 performance of the VIT/RPE relative intensity tool across this range of patients is  
315 very encouraging for its future usefulness as an outcome measure. Critically, despite  
316 its size and heterogeneity, the study achieved its primary endpoint at a high level of  
317 statistical significance .

318

319 A barrier to the potential adoption of our technique as described in this study  
320 is that it is time-consuming, taking around 3-5 minutes per scan. Recently however  
321 we have developed a software package for automation of this process. This custom  
322 software entitled VITreous ANalysis (VITAN) can segment and annotate the scans  
323 automatically, reducing the time taken to derive measures of vitreous reflectivity to a  
324 few seconds per scan, with benefits in speed, cost, and further reduction of  
325 subjectivity or human error in marking the boundaries of anatomical structures (24).

326

327 To conclude, in this study we have further demonstrated the relevance of the  
328 OCT-derived VIT/RPE-Relative intensity as a quantitative and objective marker of  
329 disease activity and treatment response in uveitis complicated by CME. This first  
330 longitudinal study of this novel OCT parameter is an encouraging step in the

331 development of sensitive objective OCT-based endpoints for trials of efficacy in  
332 uveitis.

333 **References:**

---

334

335 (1) Nussenblatt RB. The natural history of uveitis. *Int Ophthalmol* 1990 Oct;14(5-  
336 6):303-308.

337 (2) Rothova A, Suttorp-van Schulten MS, Frits Treffers W, Kijlstra A. Causes and  
338 frequency of blindness in patients with intraocular inflammatory disease. *Br J*  
339 *Ophthalmol* 1996 Apr;80(4):332-336.

340 (3) Levin MH, Pistilli M, Daniel E, Gangaputra SS, Nussenblatt RB, Rosenbaum JT,  
341 et al. Incidence of Visual Improvement in Uveitis Cases with Visual Impairment  
342 Caused by Macular Edema. *Ophthalmology* 2014 Feb;121(2):588-595.e1.

343 (4) Salek SS, Leder HA, Butler NJ, Gan TJ, Dunn JP, Thorne JE. Periocular  
344 triamcinolone acetonide injections for control of intraocular inflammation associated  
345 with uveitis. *Ocul Immunol Inflamm* 2013 Aug;21(4):257-263.

346 (5) Sen HN, Vitale S, Gangaputra SS, Nussenblatt RB, Liesegang TL, Levy-Clarke  
347 GA, et al. Periocular corticosteroid injections in uveitis: effects and complications.  
348 *Ophthalmology* 2014 Nov;121(11):2275-2286.

349 (6) Leder HA, Jabs DA, Galor A, Dunn JP, Thorne JE. Periocular triamcinolone  
350 acetonide injections for cystoid macular edema complicating noninfectious uveitis.  
351 *Am J Ophthalmol* 2011 Sep;152(3):441-448.e2.

352 (7) Madow B, Galor A, Feuer WJ, Altaweel MM, Davis JL. Validation of a  
353 Photographic Vitreous Haze Grading Technique for Clinical Trials in Uveitis. *Am J*  
354 *Ophthalmol* 2011 8;152(2):170-176.e1.

355 (8) Denniston AK, Dick AD. Systemic therapies for inflammatory eye disease: past,  
356 present and future. *BMC Ophthalmol* 2013 Apr 24;13:18-2415-13-18.

357 (9) Hornbeak DM, Payal A, Pistilli M, Biswas J, Ganesh SK, Gupta V, Rathinam SR,  
358 Davis JL, Kempen JH. Interobserver agreement in clinical grading of vitreous haze  
359 using alternative grading scales. *Ophthalmology*. 2014 Aug;121(8):1643-8. doi:  
360 10.1016/j.ophtha.2014.02.018. Epub 2014 Mar 31. PubMed PMID: 24697913;  
361 PubMed Central PMCID: PMC4122589

362 (10) Barry RJ, Denniston AK. Controversies in the Pharmacological Treatment of  
363 Uveitis. *Curr Pharm Des* 2015 Sep 8. [Epub ahead of print] PubMed PMID:  
364 26350535

365 (11) Hee MR, Puliafito CA, Wong C, Duker JS, Reichel E, Rutledge B, et al.  
366 Quantitative assessment of macular edema with optical coherence tomography. *Arch*  
367 *Ophthalmol* 1995 Aug;113(8):1019-1029.

368 (12) Ouyang Y, Keane PA, Sadda SR, Walsh AC. Detection of cystoid macular  
369 edema with three-dimensional optical coherence tomography versus fluorescein  
370 angiography. *Invest Ophthalmol Vis Sci* 2010 Oct;51(10):5213-5218.

- 371 (13) Alasil T, Keane PA, Updike JF, Dustin L, Ouyang Y, Walsh AC, et al.  
372 Relationship between optical coherence tomography retinal parameters and visual  
373 acuity in diabetic macular edema. *Ophthalmology* 2010 Dec;117(12):2379-2386.
- 374 (14) Agarwal A, Ashokkumar D, Jacob S, Agarwal A, Saravanan Y. High-speed  
375 optical coherence tomography for imaging anterior chamber inflammatory reaction in  
376 uveitis: clinical correlation and grading. *Am J Ophthalmol* 2009 Mar;147(3):413-  
377 416.e3.
- 378 (15) Li Y, Lowder C, Zhang X, Huang D. Anterior chamber cell grading by optical  
379 coherence tomography. *Invest Ophthalmol Vis Sci* 2013 Jan 9;54(1):258-265.
- 380 (16) Sharma S, Lowder CY, VasANJI A, Baynes K, Kaiser PK, Srivastava SK.  
381 Automated Analysis of Anterior Chamber Inflammation by Spectral-Domain Optical  
382 Coherence Tomography. *Ophthalmology* 2015 Jul;122(7):1464-1470.
- 383 (17) Keane PA, Karampelas M, Sim DA, Sadda SR, Tufail A, Sen HN, et al.  
384 Objective measurement of vitreous inflammation using optical coherence  
385 tomography. *Ophthalmology* 2014 Sep;121(9):1706-1714.
- 386 (18) Zarranz-Ventura J, Keane PA, Sim DA, Llorens V, Tufail A, Sadda SR, Dick AD,  
387 Lee RW, Pavesio C, Denniston AK, Adán A; EQUATOR Study Group. Evaluation of  
388 objective vitritis grading method using optical coherence tomography: influence of  
389 phakic status and previous vitrectomy. *Am J Ophthalmol*. 2015 Oct 14. pii: S0002-  
390 9394(15)00637-6. doi: 10.1016/j.ajo.2015.10.009. [Epub ahead of print] PubMed  
391 PMID: 26476212.
- 392 (19) Venkatesh P, Kumar CS, Abbas Z, Garg S. Comparison of the efficacy and  
393 safety of different methods of posterior subtenon injection. *Ocular Immunology &*  
394 *Inflammation* 2008 Sep-Oct;16(5):217-223.
- 395 (20) Sadda SR, Joeres S, Wu Z, Updike P, Romano P, Collins AT, et al. Error  
396 correction and quantitative subanalysis of optical coherence tomography data using  
397 computer-assisted grading. *Invest Ophthalmol Vis Sci* 2007 Feb;48(2):839-848.
- 398 (21) Sadda SR, Keane PA, Ouyang Y, Updike JF, Walsh AC. Impact of scanning  
399 density on measurements from spectral domain optical coherence tomography.  
400 *Invest Ophthalmol Vis Sci* 2010 Feb;51(2):1071-1078.
- 401 (22) Lowder C, Belfort R, Jr, Lightman S, Foster CS, Robinson MR, Schiffman RM, et  
402 al. Dexamethasone intravitreal implant for noninfectious intermediate or posterior  
403 uveitis. *Arch Ophthalmol* 2011 May;129(5):545-553.
- 404 (23) Denniston AK, Holland GN, Kidess A, Nussenblatt RB, Okada AA, Rosenbaum  
405 JT, et al. Heterogeneity of primary outcome measures used in clinical trials of  
406 treatments for intermediate, posterior, and panuveitis. *Orphanet J Rare Dis* 2015  
407 Aug 19;10:97-015-0318-6.
- 408 (24) Keane PA, Balaskas K, Sim DA, Aman K, Denniston AK, Aslam T, et al.  
409 Automated Analysis of Vitreous Inflammation Using Spectral-Domain Optical  
410 Coherence Tomography. *Transl Vis Sci Technol* 2015 Sep 16;4(5):4.

412 **Tables and figures:**

413 TABLE 1: Baseline Characteristics

<b>Age</b>	47.4 years ( 23y – 74y)
<b>Gender</b>	
Female	17 (77%)
Male	5 (23%)
<b>Anatomical Site of Uveitis</b>	
Panuveitis	10 (45%)
Intermediate Uveitis	8 (36%)
Anterior Uveitis	4 (18%)
<b>Aetiology</b>	
Idiopathic	14 (64%)
Sarcoidosis	4 (18%)
TINU	1 (5%)
Behcet's	1 (5%)
Reiter	1 (5%)
VKH	1 (5%)
<b>AC Cells</b>	

0	6
0.5+	6
1+	4
2+	4
3+	0
4+	0
Not available	2
<b>AC Flare</b>	
0	12 (54.54%)
0.5+	2 (9.09%)
1+	6 (27.27%)
2+	0
3+	0
4+	0
Not available	2 (9.09%)
<b>Vitreous haze</b>	
0	15 (68.18%)
0.5+	0
1+	2 (9.09%)
2+	1 (4.54%)
3+	0
4+	0
Not available	4 (18.18%)

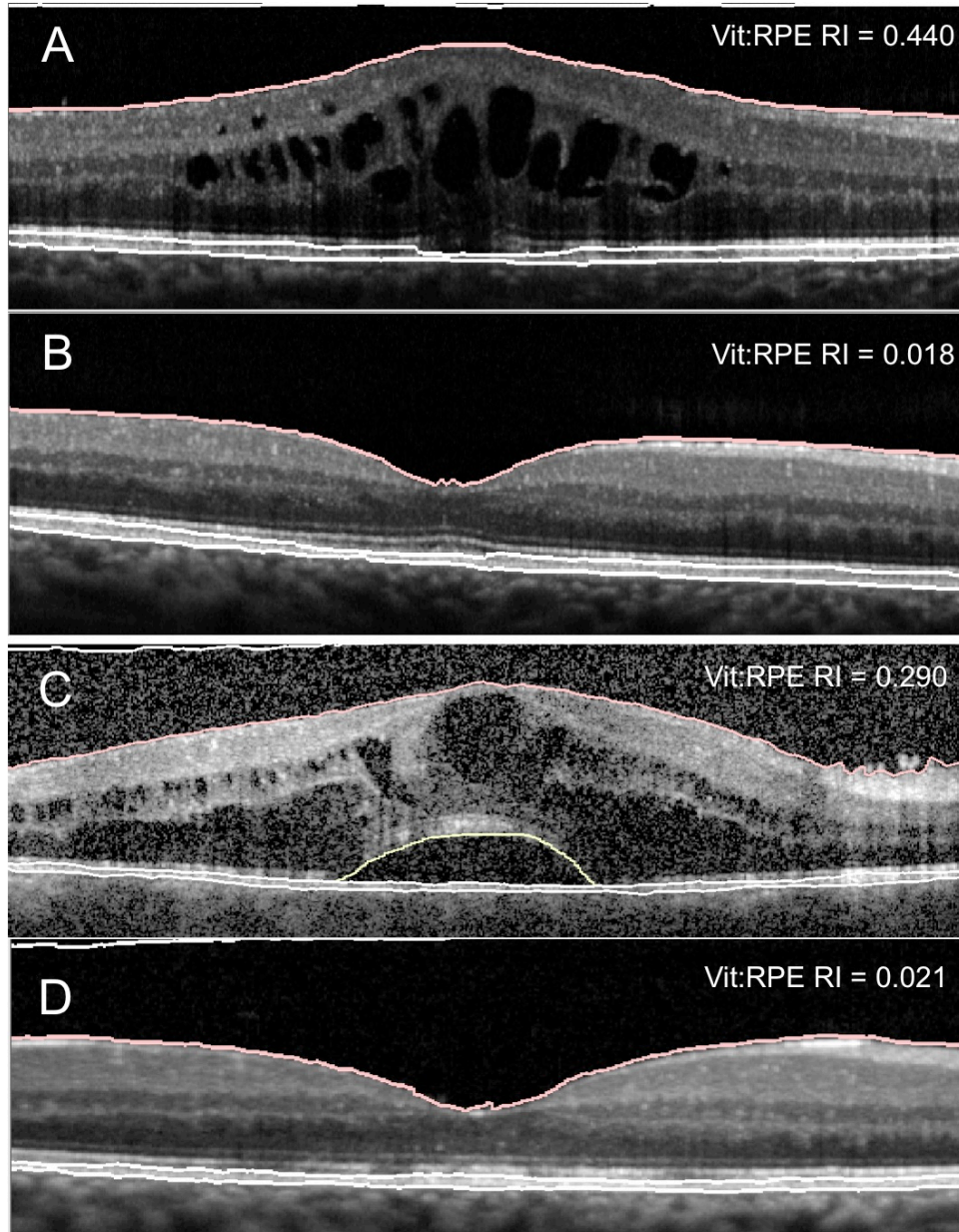
<b>Timing of Post-Intervention Review</b>	
Median (range) duration to follow-up OCT scan and review post-treatment	7 weeks (4 – 19 weeks)

414

415

---

416



418

419

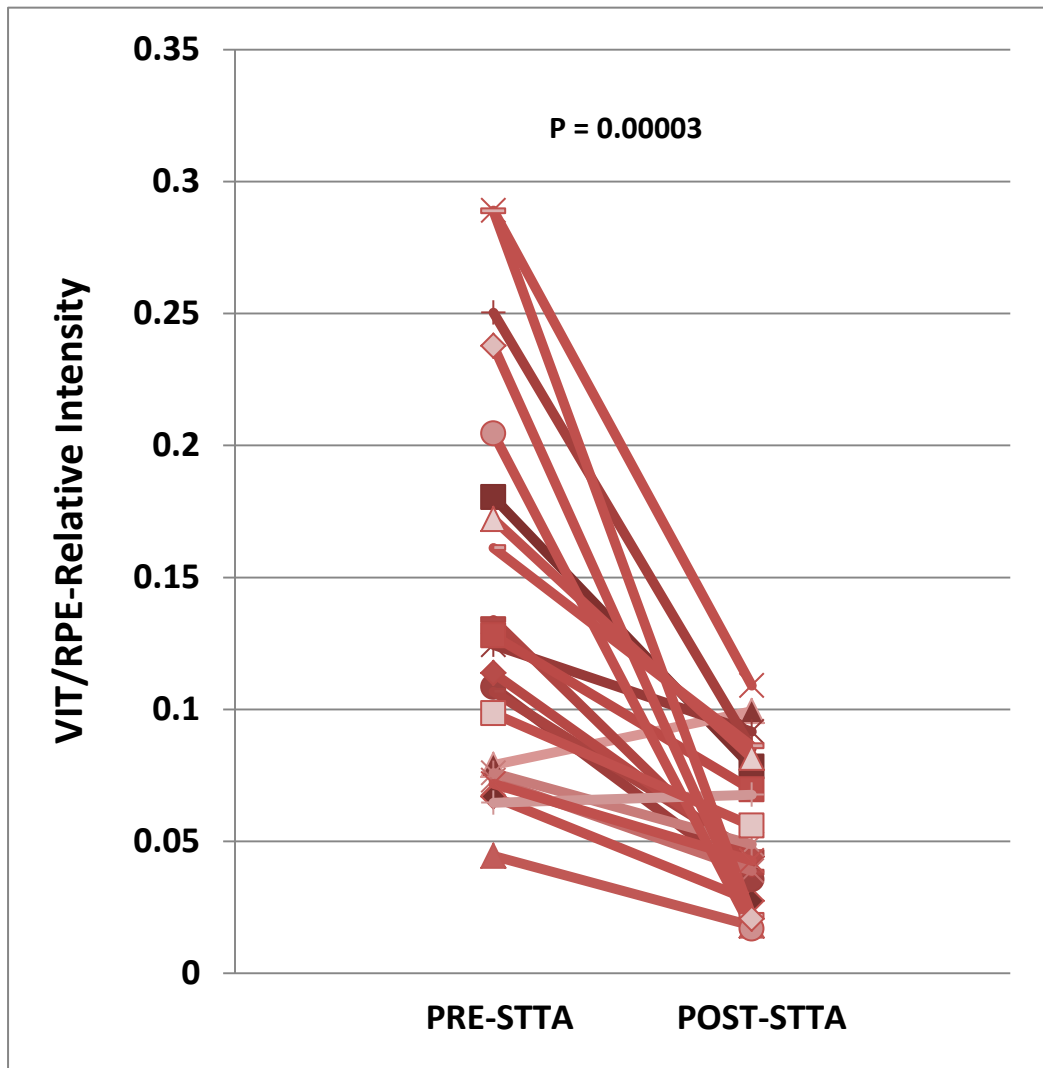
420 Figure 1. Quantitative assessment of the vitreous using OCT  
421 demonstrated in a 47 year old male with intermediate uveitis (A,B) and a  
422 48 year old female with panuveitis (C,D). Both patients were assessed



423 by standard macular-focussed OCT both before (A,C) and after (B,D)  
424 treatment with Sub-Tenon's Triamcinolone Acetonide (STTA), with  
425 calculation of the Vitreous/RPE-Relative Intensity (Vit/RPE RI)..

---

426

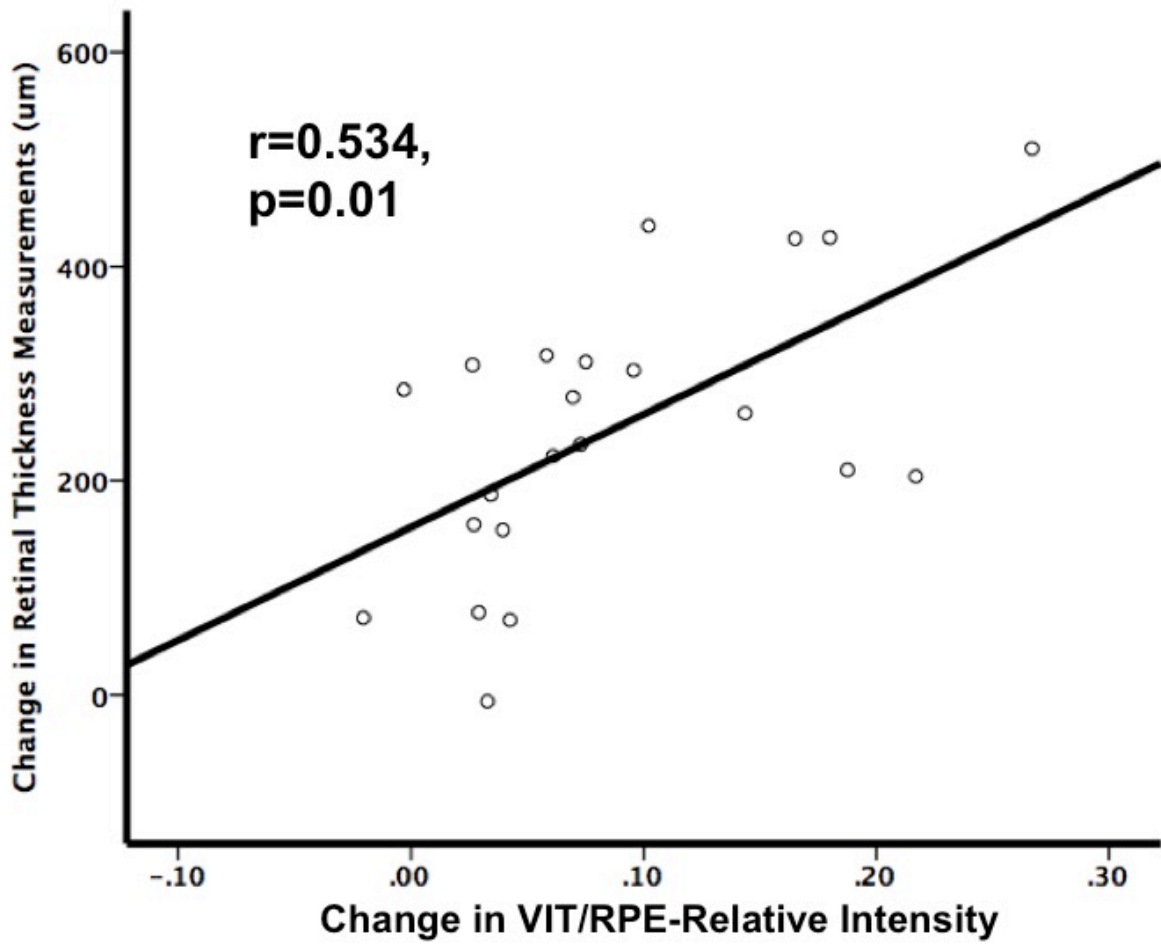


428

429 Figure 2. VIT/RPE–Relative Intensity before and after treatment with  
430 Sub-Tenon Triamcinolone Acetonide (STTA) for Uveitic Cystoid Macular  
431 Oedema (CMO).

---

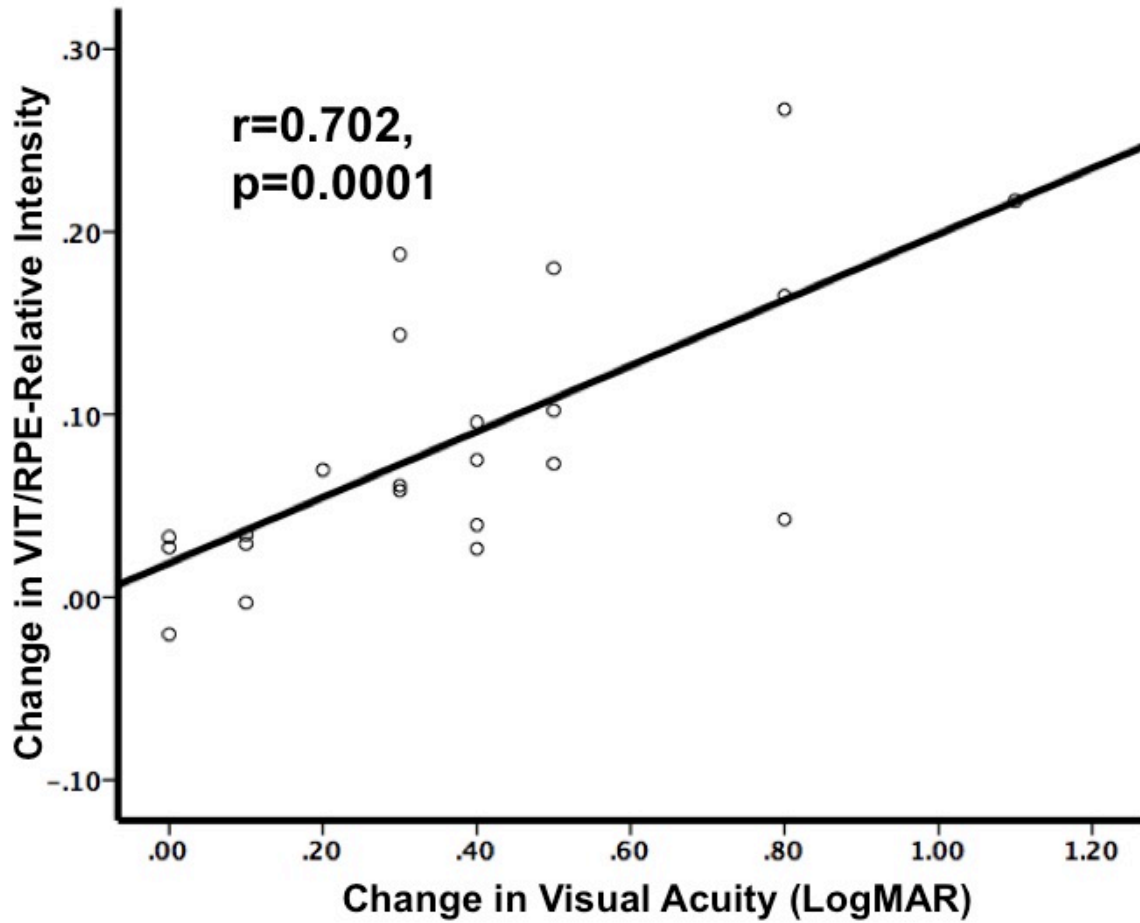
432



435 Figure 3. Correlation between change in VIT/RPE-Relative intensity and  
436 change in mean central retinal thickness.

437

438



439

440 Figure 4. Correlation between change in VIT/RPE–Relative intensity and  
441 change in visual acuity.

442



