

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

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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

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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**

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47 of Health's NIHR Biomedical Research Centre for Ophthalmology at Moorfields Eye
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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 μ m (119 μ m) pre-treatment vs 333 μ m (95 μ 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 μm (119.4 μm) pre-treatment vs 332.7 μm (95.4 μm) 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

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

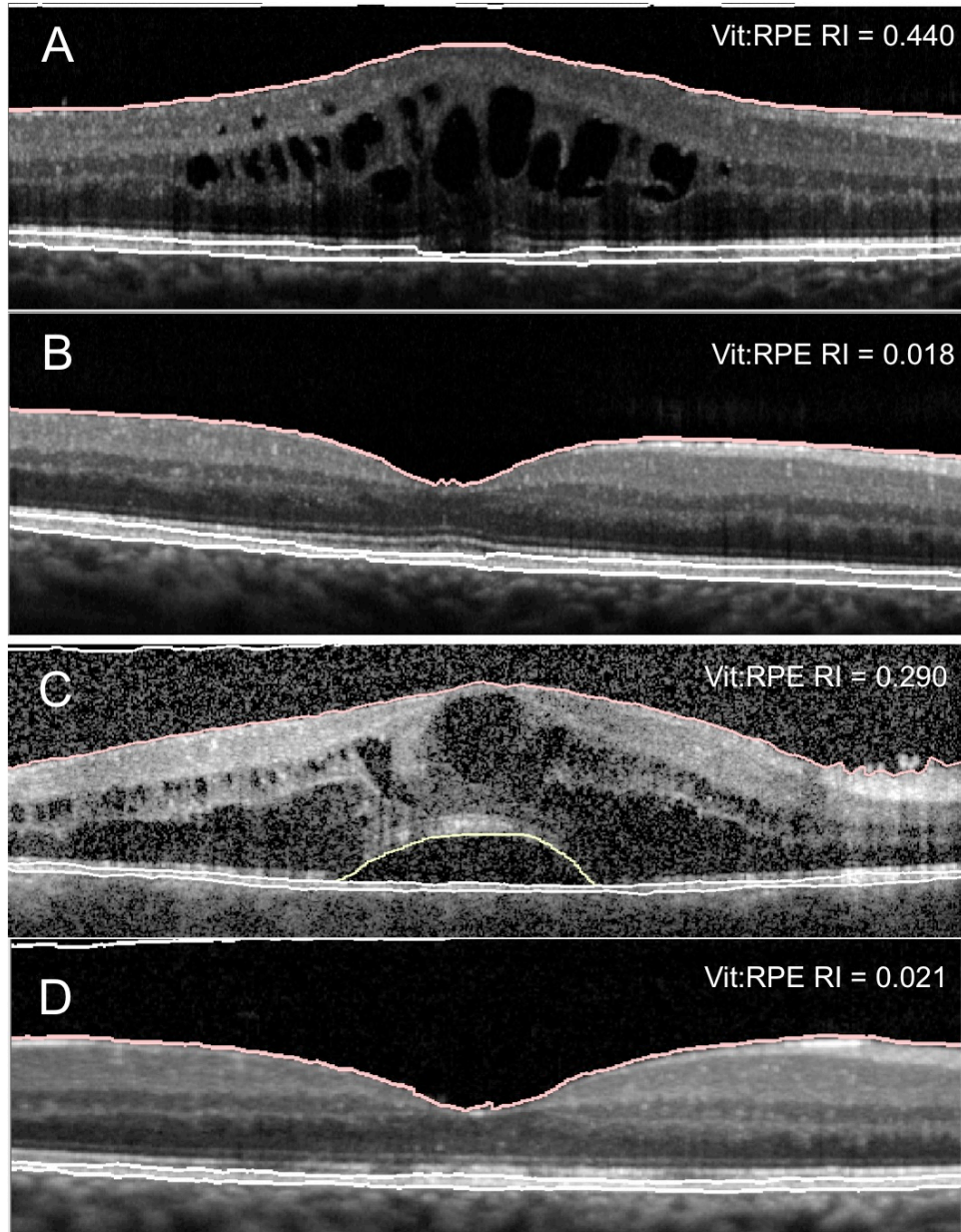
0	6
0.5+	6
1+	4
2+	4
3+	0
4+	0
Not available	2
AC Flare	
0	12 (54.54%)
0.5+	2 (9.09%)
1+	6 (27.27%)
2+	0
3+	0
4+	0
Not available	2 (9.09%)
Vitreous haze	
0	15 (68.18%)
0.5+	0
1+	2 (9.09%)
2+	1 (4.54%)
3+	0
4+	0
Not available	4 (18.18%)

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

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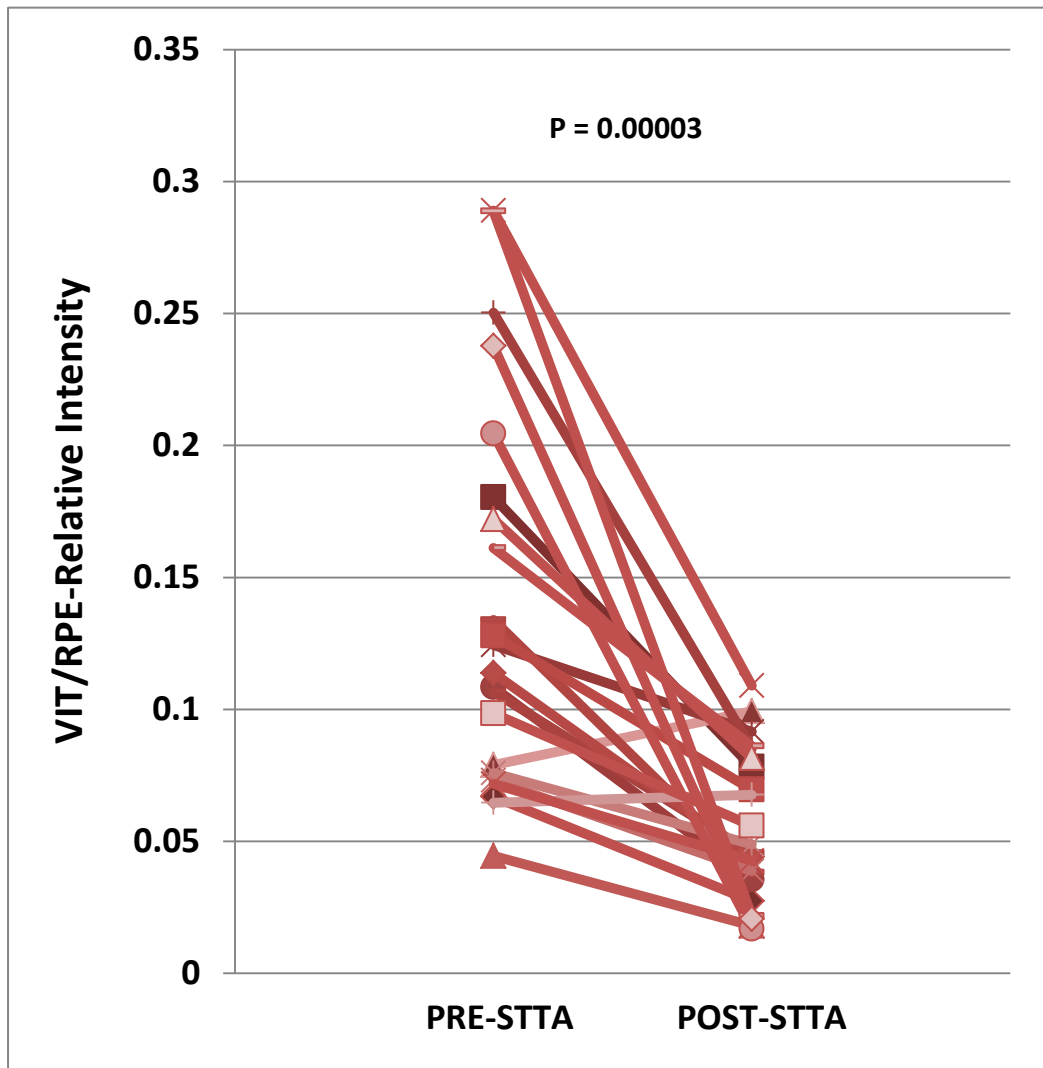
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419

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)..

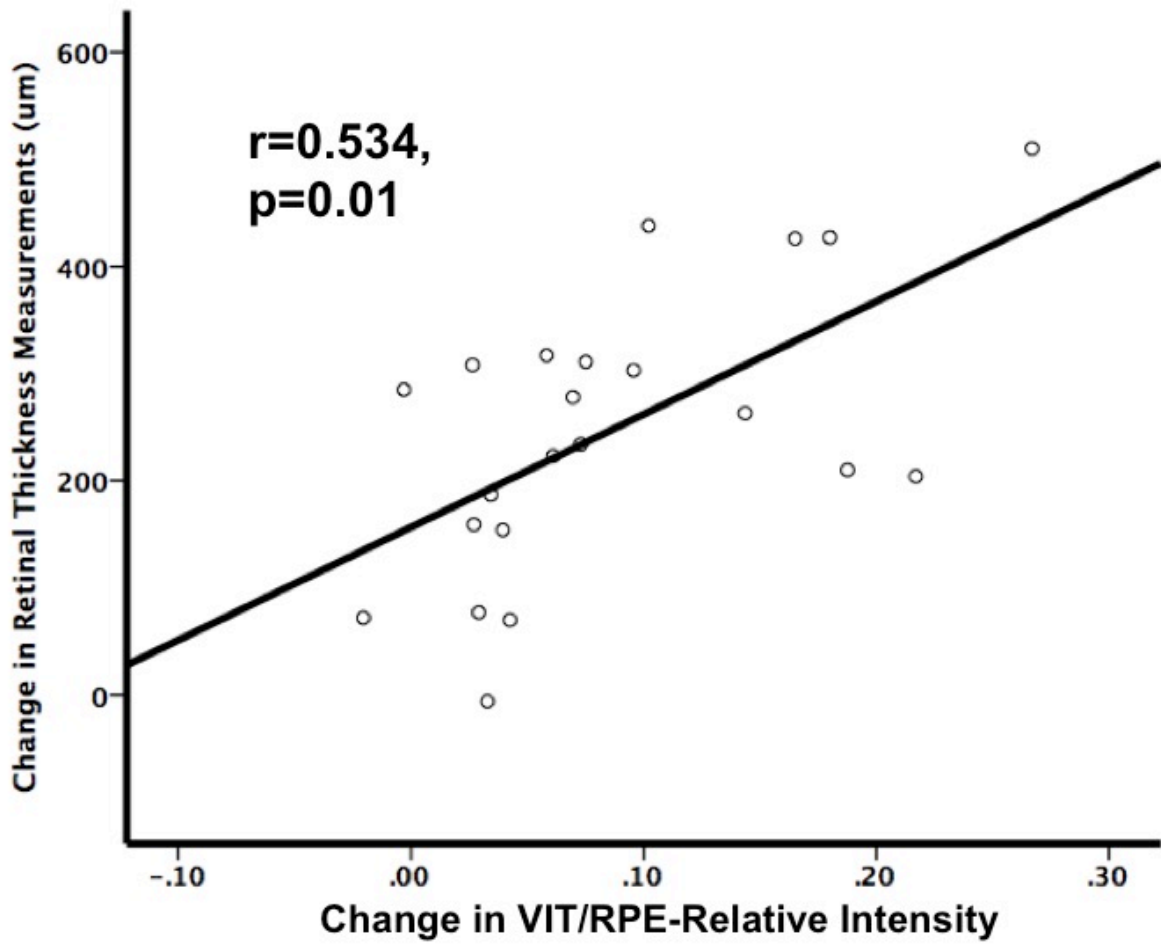
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428

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).

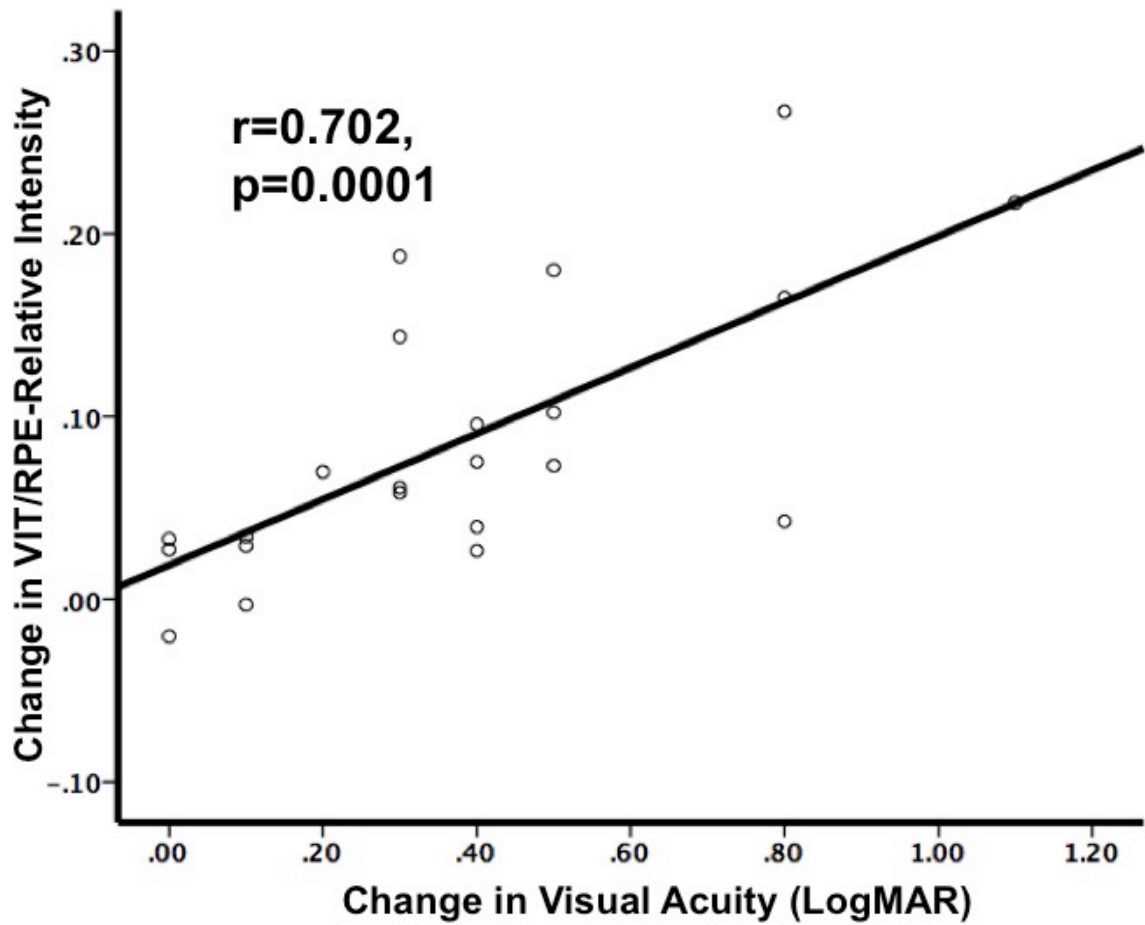
432



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

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

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