

Fundus autofluorescence and spectral domain optical coherence tomography as predictors for long-term functional outcome in rhegmatogenous retinal detachment

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1	Title:
2	Fundus autofluorescence and spectral domain optical coherence tomography as predictors for long-term functional
3	outcome in rhegmatogenous retinal detachment.
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32	

- 34 35 **Purpose:** 36 To detect pre- and postoperative retinal changes in fundus autofluorescence (AF) and spectral domain optical coherence 37 tomography (SD-OCT) and to correlate these with functional outcome in patients with primary rhegmatogenous retinal 38 detachment (RRD). 39 40 **Methods:** 41 A prospective, 30-month study of patients operated with 25-gauge vitrectomy for primary RRD. Patients were examined preoperatively and after 6 and 30 months, using ultrawide-field AF images (UWFI) (Optos 200Tx) and SD-42 43 OCT (Topcon 3D OCT-2000) imaging. 44 45 **Results:** 46 Of 84 patients (84 eyes) included at baseline, 100.0% and 86.9% were re-examined at month 6 and 30, respectively. 47 Preoperative findings such as macular attachment, detachment >750 µm from foveola, lack of intraretinal separation, 48 and subfoveal elevation ≤500 µm were all associated with better BCVA at month 6 and 30. Postoperative disruption of 49 the photoreceptor layer was associated with poor BCVA at month 6 (p<0.001) but not at month 30. 50 At baseline, AF-demarcation of RRD was demonstrated by a hyperfluorescent edge in 92.0% and was associated with 51 visual impairment at month 6 (p=0.003) and 30 (p=0.003). 52 Visual outcome at month 30 was good ($\leq 0.3 \log MAR$ ($\geq 20/40 Snellen$)), regardless of the preoperative, macular status. 53 However, with significantly better visual outcome in patients with macula attachments versus partly or totally macular 54 detachments (p<0.001). 55 56 **Conclusion:**
- 57 Fundus AF and SD-OCT is able to identify retinal reestablishment up to 30 months after primary RRD, with good
- 58 correlation to BCVA. These findings emphasize the importance of long-term studies for final visual recovery.
- 59

ABSTRACT:

60 Key words:

- 61 Fundus autofluorescence, Long-term outcome, Optical coherence tomography, Visual outcome Rhegmatogenous
- 62 retinal detachment, Vitrectomy
- 63

64 Introduction

65

- 66 Rhegmatogenous retinal detachment (RRD) is an acute ophthalmic condition, which may cause severe visual
- 67 impairment or blindness. Anatomical success rates have improved remarkably during the last decades and final
- anatomical success rates are now close to 100% [1-3]. However, despite anatomical success, functional outcome is still
- 69 variable [4-6]. Visual impairment after RRD have previously been associated with macular status [7,6], area of
- 70 detachment [6-9], duration of macular detachment [10,9], height of macular detachment [10], preoperative proliferative
- vitreoretinopathy (PVR) [7,8,10], cystic macular edema [10], retinal folds[10,11], subretinal fluid [10], epiretinal
- 72 membranes [10], and disruption of the inner segment/outer segment (IS/OS) junction [12].
- 73 Spectral domain optical coherence tomography (SD-OCT) provides high resolution images of the macular architecture.
- 74 This can be used to visualize and evaluate the microstructural changes before and after successful reattachment.
- 75 Likewise, fundus autofluorescence (AF) can be used to detect retinal changes due to hyperfluorescent, stress-induced
- 76 lipofuscin-accumulation in the retinal pigment epithelium (RPE) [13]. Studies have used fundus AF to detect macular
- displacement following RRD [14,15]. They found that macular displacement, following successful RRD-surgery, was
- associated with visual disturbance, as distortion of lines or objects appearing smaller or narrower.
- 79 Short-term prospective studies have identified important risk-factors for postsurgical failure [16] but long-term studies
- 80 of retinal markers for functional outcome are needed.
- 81 Hence, we aimed to evaluate whether results from SD-OCT and fundus AF images could serve as non-invasive
- 82 predictors for long-term visual acuity in RRD.

83

84 Methods

85

86 Study design and patient population

87

We performed a clinical, prospective long-term follow-up study of patients who underwent surgery for primary RRD at
the Department of Ophthalmology, Odense University Hospital, Odense, Denmark. The inclusion period was between
1st of January 2013 and 12th of July 2013, and follow-up time was 30 months. At the time of the study, the department
was the only vitreoretinal unit in the Region of Southern Denmark, an area with approximately 1.2 million inhabitants.
Patients younger than 16 years were referred to other Danish hospitals according to Danish health care regulations.
This study was approved by the Research Ethics Committee of the Region of Southern Denmark and by the Danish
Data Protection Agency. All parts of the study were conducted in accordance with the criteria of Helsinki II

- 95 Declaration and in accordance with good epidemiological and clinical practice. Written informed consent was obtained96 from all patients.
- 97

98 Baseline examinations

99

100 The attending ophthalmologist at the department performed standard eye examination, including best corrected visual

- 101 acuity (BCVA) as measured by Snellen at six meters with subjective refraction and custom clip-on trial frame with
- 102 glasses, intraocular pressure (IOP) (Goldmann applanation tonometry) and slit-lamp biomicroscopy using the 90 diopter

- and three-mirror lens. The presumed duration of macular detachment (partial/total) was defined as self-reported time
- 104 from significant loss of vision to primary RRD surgery. All examinations were performed as close to primary operation
- as possible. Images were captured after mydriatic eye drops (one drop of tropicamide 1%, and one drop of epinephrine
- 106 10%) in each eye.
- 107 Patient baseline examinations were performed by the study investigator (CP). Examination included auto refraction
- 108 (Canon RK-F2, Full Auto Ref-Keratometer, Amstelveen, The Netherlands), SD-OCT (3D OCT-2000, Topcon, Tokyo,
- Japan) and ultra-widefield imaging (Optos 200Tx, Optos plc, Dunfermline, Scotland, United Kingdom). The macular
- 110 status (attached/partly detached/detached) was determined by SD-OCT. In cases where macula could not be detected by
- 111 SD-OCT, surgical descriptions were used. Intraretinal separation was graded in patients with macula detached or partly
- detached. It was defined/graded as: separation of the intraretinal microstructures and layers (yes/no). Patients with no
- intraretinal separation had near normal appearance of the macula.
- 114 SD–OCT images were graded by the same trained grader (MPP). Fifteen percent of SD-OCT images were re-graded by
- another trained grader (CP) to test for agreement. Intraclass correlation coefficient (ICC) was very high for subfoveal
- and central retinal thickness measurements (>0.99 for both), and kappa values were fair (subfoveal bleb: 0.33),
- moderate (intraretinal separation: 0.46), good (cystic macular edema: 0.75) and very good (macular status: 1.00,
- detachment distance from fovea: 1.00), respectively. Color and AF images were graded by the same trained grader (CP)
- by a standardized protocol. PVR was graded by the classification system defined by Machemer et al [17] in grades A,
- 120 B and C. Retinal area (clock hours) and type of detachment (bullous, shallow or combined) were graded using color
- 121 ultra-widefield images.
- 122

123 Surgical information

124

Patients were allocated for operation as soon as possible with respect to established guidelines. Patients with macula

- 126 attached were admitted to bed rest, with allowance to restroom visits and to sit while eating. If patients were admitted
- 127 Friday, Saturday or during holidays they were operated the next following weekday. Patients with macula detached
- were sent home with information of minimal physical exertion until the time of operation. This was performed within aweek and preferably as soon as possible.
- 130 Patients were treated with pars plana vitrectomy (PPV), using a standard 25-gauge three-port system (Constellation,
- 131 Alcon, Fort Worth, TX, USA). Peeling of the internal limiting membrane (ILM) was, at the time of study, a standard
- combination to PPV. Silicon oil (1000 centistokes) or sulfur hexafluoride gas was used for tamponade. Gas was the
- 133 preference but oil was used in eyes with inferior tears, severe or complicated cases or at the discretion of the surgeon.
- 134 During the study the vitreoretinal unit consisted of one experienced and four highly experienced vitreoretinal surgeons.
- 135 Intraoperative data were collected using the surgical descriptions.
- 136
- 137 Follow-up examinations
- 138
- 139 Follow-ups were performed by the study investigator (CP) at month 6 and 30. Examinations included a complete
- 140 ophthalmologic examination including auto refraction, BCVA measured by the Early Treatment Diabetic Retinopathy
- 141 Study (ETDRS) scale, IOP, slit-lamp biomicroscopy, SD-OCT, and ultra-widefield imaging.

143 Data and statistical analyses

- 144
- 145 For statistical analysis, Snellen and ETDRS values were converted to logarithm of minimal angle of resolution
- 146 (logMAR) using the base of the reciprocal of the Snellen fraction and a 0.02 logMAR-unit for each letter correctly read
- 147 on the ETDRS-chart. We allocated logMAR values for counting fingers (logMAR=2.5), hand movements
- $148 \qquad (logMAR=2.7) \text{ and light perception (logMAR=3.0)}. \text{ Good BCVA was defined as } \le 0.3 \text{ logMAR (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and } \ge 0.3 \text{ logMAR} \text{ (} \ge 20/40 \text{ Snellen)} \text{ and }$
- 149 poor BCVA as $>0.3 \log$ MAR (<20/40 Snellen).
- 150 Descriptive statistics were used for distribution of demographic and clinical characteristics. Non-parametric data was
- 151 expressed in median (with range). Differences in categorical data were analyzed using the Chi-square test or Fisher's
- 152 exact test for small samples. Differences in continuous data were analyzed using Mann-Whitney U-test, and Kruskal-
- 153 Wallis was used for three-way comparisons. For OCT-grading, inter-rater agreement was determined by kappa
- 154 (categorical variables) and ICC (continuous variables).
- 155 Due to small subsample sizes, regression analysis was not performed. P-values < 0.05 were considered as statistically
- 156 significant. All statistics was performed by Stata 13.0 (StataCorp, College Station, TX, USA).

157 158

159	Results:
160	
161	A total of 110 patients with primary RRD were seen during inclusion. We excluded patients who were not operated for
162	social or medical reasons (n=3), patients with pre-existing retinal or macular pathology and reduced vision before RRD
163	$(\leq 20/40$ Snellen, n=9), patients with previous eye trauma (n=2) and patients with no follow-up data (n=5). Eighty-four
164	patients (84 eyes) were included in the study (Figure 1). Mean age of included patients was 63.3 (SD 9.9) years. Table 1
165	presents baseline demographics and characteristics for included patients.
166	
167	Figure 1
168	
169	Table 1
170	
171	-Gradable images
172	
173	Baseline SD-OCT and fundus AF images were obtained in 82 (97.6%) and 80 (95.2%) patients. Of these 11 (12.3%)
174	and two (2.5%) were non-gradable due to poor image quality. Patients with gradable images at baseline and follow-up
175	were included for long-term analysis of median BCVA in according to structural finding in SD-OCT and AF images at
176	baseline and follow-up. Three patients could only attend follow-up after two months. We included these patients in
177	month 6 evaluations as the results didn't significantly change when including them.
178	
179	Inclusions versus exclusions
180	
181	Baseline characteristics for included (n=84) and excluded patients (n=26) as well as for attendees at month 30 (n=73)
182	and patients who dropped out during follow-up (n=11), were analyzed. Excluded patients and patients who dropped out
183	were more likely to have macula detached at the time of operation (p=0.005 and p=0.02). In addition, non-attendees at
184	month 30 were more likely to be older (p=0.004) and to be pseudophakic (p=0.06) as compared to attendees at month
185	30.
186	
187	Surgery
188	
189	Patients with PVR Grade B or C were more likely to be treated with PPV and silicon oil (n=25, 43.1%) as compared to
190	those without PVR or with Grade A PVR (n=7, 26.9%, p=0.16). Peeling of the internal limiting membrane was
191	performed in most eyes (n=78, 92.9%). Nearly all patients who were phakic at baseline had cataract surgery prior to
192	month 30 (42 of 43 patients). Six patients (7.1%) were operated for retinal re-detachment within three months from the
193	primary operation. All re-detachments were surgically re-attached. However, one patient still had silicon oil in the eye
194	at month 30. The rate of anatomical success for attendees at month 30 was 98.6% (72 of 73 patients). Patients with re-
195	detachment were included in the evaluation. The inclusion did not significantly change the results.
196	
197	

B Pre- and postoperative changes detected by SD-OCT

199

Median foveal thickness at month 6 in patients with macula attached and detached/partly detached was 261µm (range 132-543µm) and 226µm (range 87-310µm), respectively (p=0.08). At month 30 median foveal thickness was increased to 269µm (range 173-1112µm) and 245µm (range 158-571µm), respectively (p=0.13). These changes were not statistically significant, as compared to month 6 (p=0.28 and p=0.052 for patients with macula attached and

- 204 detached/partly detached, respectively), but indicate regeneration. Figure 2 illustrates different structural changes in
- 205 UWFI, AF and SD-OCT images.
- 206
- 207 Figure 2

208

- 209 Structural pre- and postoperative changes in OCT are presented in Table 2. Patients with preoperative macula
- attachment had better visual outcome at month 6 and 30 as compared to patients with macula partly or totally detached.
- 211 For those groups, median BCVA was 0.02 (20/21), 0.20 (20/32) and 0.37 logMAR (20/47 Snellen) at month 6
- 212 (p<0.001) and 0.02 (20/21), 0.10 (20/25) and 0.26 logMAR (20/36 Snellen) at month 30 (p<0.001), respectively.
- 213 Likewise, preoperative RRD >750 μm from foveola (p=0.009 and p=0.01), lack of intraretinal layer separation
- 214 (p=0.004 and p=0.006) and subfoveal elevation $\leq 500 \mu m$ (p=0.02 and p=0.04) were all associated with a better outcome
- at month 6 and 30. At month 6 disruption of IS/OS junction was demonstrated in 50.0% and associated with a decreased
- 216 BCVA (0.34 vs 0.06 (20/44 vs 20/23 Snellen), p<0.001). However, at month 30, IS/OS junction disruption was only
- 217 present in 25.0% and there was no association with decreased BCVA (p=0.19). Postoperative changes like subfoveal
- bleb (p=0.83 and p=0.76), cystic macular edema (p=0.47 and p=0.17) or retinal folds (p=0.40 and p=0.58) were not
 associated with BCVA at month 6 and 30, respectively.
- 220

221 Table 2

- 222
- 223 *Pre- and postoperative changes detected by AF*
- 224

225 Structural pre- and postoperative changes in fundus AF are presented in Table 3, and illustrated in Figure 2. Notably, 69

patients (92.0%) had a hyperfluorescent edge (HFE, Figure 2, V) of RRD prior to surgery. The HFE correlated with the

- area, judged by OCT, with impression of extent of fluid. As compared to patients without HFE, the HFE group had a
- 228 decreased median BCVA at month 6 (0.22 vs. -0.10 logMAR (20/33 vs. 20/16 Snellen), p=0.003) and month 30 (0.14
- 229 vs. -0.05 logMAR (20/28 vs. 20/18 Snellen), p=0.003), respectively.
- 230 Other preoperative AF-findings like hypo- or hyperfluorescence of the area of RRD or PVR were not associated with
- postoperative BCVA. However, the presentation of bullous RRD's and severe PVR (grade B and C) was highly
- 232 hypofluorescent with well-defined borders.
- 233 Ghost vessels have previously been described [14,15,11] as hyperfluorescent lines in RPE parallel to retinal blood
- 234 vessels localized in previously areas of detachment. Neither postoperatively detected ghost vessels nor HFE correlated
- with BCVA. Figure 3 illustrates ghost vessels in a patient with macula off at time of surgery.
- 236

- 237 Figure 3
- 238
- 239 Table 3
- 240

241 Discussion

242 To the best of our knowledge, this is the first prospective study of substantial duration to evaluate the pre-and

- postoperative retinal changes by SD-OCT and AF UWFI in relation to long-term visual outcome, in patients operated
 with 25-gauge vitrectomy for primary RRD.
- 245 Macular detachment has been identified as the primary structural reason for visual impairment in RRD [18,19].
- However, retinal imaging technology has gone through a rapid development during the last 50 years, especially the
- 247 developments of scanning laser ophthalmoscopy, AF, and SD-OCT. These techniques have made it possible to study
- 248 microstructural changes which may be associated to visual impairment in patients with RRD
- 249 In our study SD-OCT showed to be a valuable imaging tool for the assessment of postoperative visual-loss. We found a
- 250 worse BCVA at month 6 and 30 in patients with; preoperative macular detachment/partly detachment, retinal
- 251 detachment \leq 750µm from foveola, a high subfoveal amplitude of retinal detachment (>500 µm) and in patients with the
- presence of intraretinal layer separation in the detached macula. These findings are consistent with previous reports [6-10,12,20].
- 254 The preoperative presence of intraretinal separation in the detached macula has previously been found to correlate with
- higher incidence of postoperative disruption in the photoreceptor IS/OS junction and the ELM [20]. This study was not
- designed to investigate this correlation. However, we found that disruption of the IS/OS-junction was present in half of
- the patients at month 6, compared to only one in four patients at month 30. Disruption of the IS/OS-junction was only
- associated with visual impairment at month 6, indicating retinal repair and reestablishment of the photoreceptors and
- cone function between month 6 and 30. Disruption of the IS/OS-junction has been associated with cone dysfunction inother retinal diseases [21].
- Like previous studies, we found a high anatomical success-rate of RRD [1-3], Surprisingly, final functional outcome
- 262 was good (≤0.3 logMAR (≥20/40 Snellen)) regardless of the preoperative, macular status, but patients with macula
- 263 attached had significantly better final visual outcome, as compared to patients with partly or total macular detachment
- (p<0.001). These findings were in accordance to findings in previously studies [6,7,10].
- 265

266

- Fundus AF UWFI was a reliable method to demark RRD and to identify areas of advanced PVR (grade B and C). These
 findings may be explained by the fact that lipofucin-accumulates due to stress and that RPE cell damage leads to loss of
- 269 lipofuscin, respectively [13]. In addition, the preoperative presence of a hyperfluorescent edge was demonstrated in
- 270 more than ninety percent of patients. A previous study found that the presence of HLE corresponded with the presence
- of shallow detachment with subretinal fluid in OCT [22], However they did not correlate preoperative HLE to visual
- outcome. In our study, preoperative HLE was associated with visual impairment at month 6 and at month 30. As far as
- 273 we know, this has not been examined in other studies of RRD. However, in non-exudative age related macular

- degeneration focal hyper-autofluorescence has been identified in the junctional zone surrounding patches of atrophy
- [23] and has been given as an indicator of upcoming atrophy and visual dysfunction[24] The association between HLE
- and worse visual outcome is an interesting finding that warrants upcoming studies with larger subsamples .
- 277

278 The key strength of this study is the long follow-up period and the high attendance at included patients throughout the

study (86.9% at month 30). Other strengths are the same grader/examiner for all images, and the re-grading of SD-OCT

images, followed by a test for agreement between graders (ICC and kappa). This was done in order to obtain a high

reliability, and to validate the grading. The inter-rater agreement showed reasonable results, but also implied that some

282 grading was biased by the grader

The study was limited by the non-randomized design and the relatively small sample size. These limitations induce therisk of bias and the possibility of not detecting small differences, respectively.

For the baseline values the most important limitation lies in the fact that some patients had to wait more than 24 hours

from baseline measurements to primary operation. This delay induces the risk of incorrect baseline data, as the RRD

- 287 may have progressed with a risk of macula involvement and thereby the risk of worse baseline BCVA. It was not
- 288 practically possible to reduce the time delay. However, in order to address the risk of macular progression, we cross-
- 289 matched the macular status in baseline SD-OCT images, with the surgical description. This cross-match did not detect 290 any changes in the macular status from baseline to the time of surgery.
- 291 The baseline BCVA was measured by the attending ophthalmologist in Snellen. At follow-ups the BCVA was measured
- by the same examiner (CP) using the ETDRS-scale. To ensure comparable values, we converted Snellen and ETDRS
- values to logMAR. This change in measurements induces the risk of inaccurate and incorrect values.
- 294 Spectral domain-OCT and AF UWFI showed to be reliable methods that demonstrate retinal repair and reestablishment
- of functional outcome up until 30 months after primary surgery for RRD. Furthermore, findings strengthen the idea that
- a detached macula with near normal appearance has more visual potential as compared to the detached macula with a
- disrupted intraretinal appearance. Taken together, these findings suggest a role for preoperative SD-OCT and UWFI,
- especially in the selection of patients who might benefit from early surgery, despite macula off. Furthermore, retinal
- images may also help surgeon in preoperative preparations and in counselling patients when informed about their RRD.
- 300 Upcoming randomized studies should test SD-OCT and AF methods as non-invasive markers of long-term functional301 outcome in RRD.
- 302

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- 310 Denmark.
- 311
- 312 The included data has not been presented before.
- 313

314 Disclosure:

- 315 The authors declare no conflicts of interest and no proprietary interest.
- 316 CDP, JG, TP and AG contributed to the concept and design of the study. CDP contributed to the acquisition of data.
- 317 MPP contributed to the grading of SD-OCT images.
- 318 Data analyses were performed by CDP, who also wrote the initial draft of the paper. AG, TP and JG revised the paper
- critically for intellectual content. All authors approved the final version of the paper.

320 Ethical approval:

- 321 This study was approved by the Danish Data Protection Agency and the Research Ethics Committee of the Region of
- 322 Southern Denmark. All parts of the study were conducted in accordance with the Helsinki declaration II and in
- accordance with good clinical practice.
- 324

325 Informed consent:

- 326 Informed consent was obtained from all individual participants included in the study.
- 327
- 328

329 REFERENCES:

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Figure legends

Figure 1: Flow-chart of patients included.

AF: autofluorescence

OCT: optical coherence tomography

Figure 2: Ultra-widefield color, AF and SD-OCT images of patients with macular detachment.

Figure 3: Autofluorescence image that illustrates ghost vessels (RPE ghost vessels and corresponding displaced retinal vessels are highlighted with blue and white arrows, respectively).

Figure 1: Flow-chart of patients included.



AF: autofluorescence

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Figure 2: Ultra-widefield color, AF and SD-OCT images of patients with macular detachment.



Figure 3: Autofluorescence image that illustrates ghost vessels (RPE ghost vessels and corresponding displaced retinal vessels are highlighted with blue and white arrows, respectively).



 Table 1: Patient demographics and baseline characteristics.

Sex (n, %)				
Male	55 (65.5)			
Female	29 (34.5)			
Age (mean ±SD)	63.3 (9.9)			
Best corrected visual acuity* (n, %)				
Good	32 (38.1)			
Poor	52 (61.9)			
Macular status				
Attached	30 (35.7%)			
Partly detached	26 (31.0 %)			
Detached	28 (33.3 %)			
Pre-operative lens status, (n, %)				
Phakic	48 (57.1)			
Pseudophakic	36 (42.9)			
Area of retinal detachment				
> 6 clock hours	28 (33.3)			
≤ 6 clock hours	56 (66.7)			
Excessive myopia* (n, %)	22 (26.3)			
Type of tamponade (n, %)				
Gas	52 (61.9)			
Silicone oil	32 (38.1)			
Peeling of internal limiting membrane (n, %)	78 (92.9)			
Proliferative vitreoretinopathy (n, %)				
Non or grade A	26 (31.0)			
Grade B or grade C	58 (69.0)			

*Best corrected visual acuity categorized as good ($\leq 0.3 \log MAR$, $\geq 20/40 Snellen$) or poor (>0.3 logMAR, <20/40 Snellen). Excessive myopia defined as \geq -5 diopters.

	Month 6 (n=70)			Month 30 (n=64)			
	n (%)	Median (range) BCVA (logMAR)	р	n (%)	Median (range) BCVA (logMAR)	р	
<u>Preoperative</u>							
Macular status			<0.001*			<0.001*	
Attached	25 (35.7)	0.02 (-0.14 – 1.26)		25 (39.1)	0.02 (-0.20 - 1.66)		
Partly detached	25 (35.7)	0.20 (-0.20 – 0.64)		23 (35.9)	0.10 (-0.10 – 0.52)		
Totally detached	20 (28.6)	0.37 (0.14 - 0.88)		16 (25.0)	0.26 (0.08 - 0.66)		
Detachment from foveola**			0.009*			0.01*	
>750µm	7 (15.9)	0.04 (-0.20 -0.38)		7 (18.4)	0.06 (-0.06 - 0.18)		
≤750 μm	37 (84.1)	0.32 (-0.06 - 0.88)		31 (81.6)	0.20 (-0.10 - 0.66)		
Highest point of RRD***			0.10			0.06	
≤500µm	15 (35.7)	0.20 (-0.20 – 0.56)		14 (38.9)	0.10 (-0.10 – 0.52)		
>500 µm	27 (64.3)	0.30 (-0.02 - 0.88)		22 (61.1)	0.20 (-0.06 - 0.66)		
Intraretinal separation****			0.004*			0.006*	
Yes	20 (47.6)	0.39 (0.02 - 0.88)		15 (41.7)	0.24 (0.02 - 0.52)		
No	22 (52.4)	0.20 (-0.20 – 0.70)		21 (58.3)	0.10 (-0.10 – 0.66)		
Subfoveal elevation			0.02*			0.04*	
≤500µm	25 (50.0)	0.22 (-0.20 - 0.60)		22 (56.4)	0.13 (-0.10 – 0.60)		
>500 µm	20 (50.0)	0.35 (0.02 - 0.88)		17 (43.6)	0.24 (-0.06 - 0.66)		
Postoperative****							
Disruption of IS/OS junction			<0.001*			0.19	
Yes	35 (50.0)	0.34 (0 - 1.26)		16 (25.0)	0.17 (-0.12 – 1.66)		
No	35 (50.0)	0.06 (-0.20 - 0.6		48 (75.0)	0.10 (-0.20 - 1.18)		
Sub-foveal bleb			0.83			0.76	
Yes	10 (14.3)	0.20(0-0.56)		13 (20.3)	0.08 (-0.06 - 0.60)		
No	60 (85.7)	0.21 (-0.20 – 1.26)		51 (79.7)	0.14 (-0.20 - 1.66)		
Cystic macular edema			0.47			0.17	
Yes	11 (15.7)	0.18 (0-0.98)		13 (20.3)	0.16 (-0.08 - 1.18)		
No	59 (84.3)	0.22 (-0.20 – 1.26)		51 (79.7)	0.10 (-0.20 – 1.66)		
Folds or retinal layers			0.40			0.58	
Yes	9 (12.9)	0.14 (-0.20 – 0.56)		12(18.8)	0.11 (-0.10 – 0.52)		
No	61 (87.1)	0.22 (-0.14 - 1.26)		52 (81.2)	0.10 (-0.20 - 1.66)		

Table 2: Median best corrected visual acuity (BCVA) in patients with rhegmatogenous retinal detachment(RRD) according to macular appearance at baseline and at month 6 and 30.

BCVA given with ranges. IS/OS: Inner segment/outer segment. * P-values < 0.05 were considered statically significant. ** The length from the retinal detachment to foveola was non-measurable in one patient. *** The highest point of retinal detachment was non-measurable in three patients with macula detached. **** Intraretinal separation was non-gradable in three patients with macula detached. **** Post-operative changes given for month 6 and 30, respectively.

	Month 6 (n=75)			Month 30 (n=68)		
	n (%)	Median (range) BCVA (logMAR)	р	n (%)	Median (range) BCVA (logMAR)	р
<u>Preoperative</u>						
Macula attached			0.59			0.48
Normal	11 (50.0)	0.04 (-0.10 -1.26)		13 (52.0)	0.02 (-0.20 - 1.18)	
Hypofluorescence	2 (9.1)	0.06 (0.02 - 0.10)		2 (8.0)	0.15 (0.00 - 0.30)	
Hyperfluorescence	8 (36.4)	0.09 (-0.08 - 0.98)		9 (36.0)	0.02 (-0.12 – 1.66)	
Hypo- and hyperfluorescence	1 (4.5)	0.54 (0.54 - 0.54)		1 (4.0)	0.60(0.60-0.60)	
Macula detached**			0.20			0.20
Normal	10 (18.9)	0.15 (-0.20 - 0.50)		9 (20.9)	0.06 (-0.06 - 0.40)	
Hypofluorescence	13 (24.5)	0.22 (-0.02 - 0.52)		9 (20.9)	0.18 (-0.08 - 0.60)	
Hyperfluorescence	24 (45.3)	0.35 (-0.06 - 0.88)		21 (48.9)	0.20 (-0.10 - 0.66)	
Hypo- and hyperfluorescence	6 (11.3)	0.24 (0.02 - 0.60)		4 (9.3)	0.14 (-0.06 - 0.28)	
PVR grade A			0.29			0.71
Normal	9 (47.6)	0.12 (-0.08 - 0.60)		10 (50.0)	0.04 (-0.20 - 1.18)	
Hypofluorescence	11 (52.4)	0.26 (-0.10 - 0.60)		10 (50.0)	0.09 (-0.20 - 0.52)	
PVR grade B and C			0.97			0.48
Hypofluorescence	48 (87.5)	0.22 (-0.20 - 0.98)		43 (89.6)	0.16 (-0.12 – 1.66)	
Hyperfluorescence	2 (3.6)	0.26 (0.02 - 0.50)		1 (2.1)	$0.00\ (0.00 - 0.00)$	
Hypo- and hyperfluorescence	5 (8.9)	0.18 (-0.08 - 0.64)		4 (8.3)	0.05 (-0.08 - 0.48)	
Hyperfluorescent edge of RRD			0.003*			0.003*
Yes	69 (92.0)	0.22 (-0.2 – 1.26)		62 (91.2)	0.14 (-0.2 – 1.66)	
No	6 (8.0)	-0.10 (-0.08 - 0.20)		6 (8.2)	-0.05 (-0.20 - 0.02)	
Postoperative***						
Ghost vessels present			0.11			0.28
Yes	10 (13.3)	0.40 (0.02 - 0.70)		11 (16.2)	0.10 (-0.02 – 1.66)	
No	65 (86.7)	0.20 (-0.20 – 1.26)		57 (83.8)	0.10 (-0.20 - 1.18)	
Hyperfluorescent demarcation			0.52			0.74
Yes	41 (46.2)	0.20 (-0.20 - 0.98)		32 (43.9)	0.11 (-0.12 – 1.66)	
No	34 (53.8)	0.22 (-0.08 - 1.26)		36 (53.1)	0.10 (-0.20 - 1.18)	

Table 3: Median best corrected visual acuity (BCVA) in patients with rhegmatogenous retinal detachment(RRD) according to macular appearance at baseline and at month 6 and 30.

BCVA given with ranges. PVR: Proliferative vitreoretinopathy. *A P-value < 0.05 was considered statically significant (marked). ** One patient was excluded from this evaluation as he had bullous retinal detachment that covered macula area.*** Post-operative changes given for month 6 and 30, respectively.