



Preoperative Posturing of Patients with Macula-On Retinal Detachment Reduces Progression Toward the Fovea

Jan H. de Jong, MD,^{1,2} Juan P. Vigueras-Guillén, MSc,² Tiarah C. Simon, MD,¹ Reinier Timman, PhD,³ Tunde Peto, MD, PhD,⁴ Koenraad A. Vermeer, PhD,² Jan C. van Meurs, MD, PhD^{1,2,5}

Purpose: Traditionally, preoperative posturing consisting of bed rest and positioning is prescribed to patients with macula-on retinal detachment (RD) to prevent RD progression and detachment of the fovea. Execution of such advice can be cumbersome and expensive. This study aimed to investigate if preoperative posturing affects the progression of RD.

Design: Prospective cohort study.

Participants: Ninety-eight patients with macula-on RD were included. Inclusion criteria were volume optical coherence tomography (OCT) scans could be obtained with sufficient quality; and the smallest distance from the fovea to the detachment border was 1.25 mm or more.

Methods: Patients were admitted to the ward for bed rest in anticipation of surgery and were positioned on the side where the RD was mainly located. At baseline and before and after each interruption for meals or toilet visits, a 37°×45° OCT volume scan was performed using a wide-angle Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany). The distance between the nearest point of the RD border and fovea was measured using a custom-built measuring tool.

Main Outcome Measures: The RD border displacement and the average RD border displacement velocity moving toward (negative) or away (positive) from the fovea were determined for intervals of posturing and interruptions.

Results: The median duration of intervals of posturing was 3.0 hours (interquartile range [IQR], 1.8–14.0 hours; n = 202) and of interruptions 0.37 hours (IQR, 0.26–0.50 hours; n = 197). The median RD border displacement was 2 μm (IQR, –65 to +251 μm) during posturing and –61 μm (IQR, –140 to 0 μm) during interruptions, a statistically significant difference ($P < 0.001$, Mann–Whitney U test). The median RD border displacement velocity was +1 μm/hour (IQR, –21 to +49 μm/hour) during posturing and –149 μm/hour (IQR, –406 to +1 μm/hour) during interruptions, a statistically significant difference ($P < 0.001$).

Conclusions: By making use of usual interruptions of preoperative posturing we were able to show, in a prospective and ethically acceptable manner, that RD stabilizes during posturing and progresses during interruptions in patients with macula-on RD. Preoperative posturing is effective in reducing progression of RD. *Ophthalmology* 2017;■:1–13 © 2017 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Retinal detachment (RD) is a progressive and, if left untreated, blinding disease. The annual incidence of primary rhegmatogenous RD was reported to be 18 per 100 000 people in The Netherlands¹ and 12 per 100 000 people in the United States.² Surgery is successful in reattaching the retina in more than 95% of patients.^{3,4} The visual prognosis after successful RD surgery is determined primarily by the extent of the RD. When the macula is not yet involved, visual outcome is significantly better.^{5–8} Therefore, between diagnosis and surgical treatment, all efforts are aimed at keeping the macula attached.

Traditionally, preoperative posturing consisting of bed rest and positioning is prescribed to patients with macula-on RD. Bed rest aims to restrict forces related to head and eye movement that are believed to reduce the height and extent of

RD.^{9–15} Bed rest also allows positioning of patients to address the potentially unfavorable effect of the force of gravity. A supine position is advised for RD in the superior quadrants and a sitting position for RD in the inferior quadrants.^{16–18}

Despite the major burden of posturing for patients and, when combined with hospital admission, on nursing staff, ward facilities, and public health costs, little prospectively collected evidence for preoperative posturing has been presented as yet. We believe that the want of a sufficiently accurate measuring method for progression of RD toward the fovea is the reason for this lack of evidence. With optical coherence tomography (OCT), such a measuring tool has become available that allows accurate and precise measurements of changes in the distance between the edge of the RD and the fovea.¹⁸

Because it is generally accepted that RD patients interrupt their bed rest regimen for meals and other short breaks,¹⁸ such intervals offer an excellent opportunity to acquire prospective and comparative data. The aim of this study was to investigate in an ethically acceptable manner whether preoperative posturing affects the progression of macula-on RD. Secondary objectives were to identify risk factors for progressive RD and to determine the reproducibility of OCT measurements.

Methods

Study Design

This study was designed as a prospective cohort study with OCT recordings of distance between the RD and fovea during preoperative posturing and interruptions of posturing. The study was approved by the local internal review board of the Rotterdam Eye Hospital and the medical ethical committee of the Erasmus Medical Center, Rotterdam, The Netherlands (identifier, 2014-502; www.trialregister.nl identifier, NTR4884). This report is the first of 3 planned cohorts of a larger prospective trial and includes patients with detachments observed up to 48 hours. The first cohort is the baseline cohort. The interruption intervals will be prolonged in the second and third cohorts compared with the baseline interval, and we plan to include 50 patients per cohort. During the inclusion period of the 50 patients in the baseline cohort, we additionally included 48 patients with RD in the other retinal quadrants following the same eligibility criteria to explore the differences between RD locations and posturing advices. All patients were hospitalized and examined in the Rotterdam Eye Hospital, Rotterdam, The Netherlands. The study was conducted in accordance with the tenets of the Declaration of Helsinki.

Inclusion and Exclusion Criteria

Inclusion criteria were: age 18 years or older, written informed consent, nearest point of the RD border at 1250 μm or more from the foveola (safety measure) and within the range of the OCT system, sufficiently clear media to obtain an OCT scan, sufficiently accurate OCT scan, and ability to perform OCT within 1 hour after admission of the patient to the ward. No exclusion criteria were specified. The safety border of 1250 μm from the foveola was defined by the traditional size of the fovea centralis (with a radius of approximately 750 μm) and parafovea (ring of 500 μm around the fovea) combined.¹⁹

Surgery Planning and Posturing Advice

Patients diagnosed with macula-on RD were admitted to the ward for posturing while they were waiting for surgery the same day, the next day, or occasionally the day after. Surgery was planned as soon as possible, but no later than 48 hours from the start of hospitalization. Patients were admitted to the ward and planned for surgery independently from study eligibility. If patients were included in the study and progressed more than 250 μm , the OCT measurements continued, but surgery was rescheduled to an earlier time point if possible. We hypothesized that the risk of foveal involvement does not increase substantially with RD progression of less than 250 μm . Posturing consisted of 2 parts: bed rest and positioning. All patients were prescribed bed rest. Patients with RD mainly located in the superior quadrant were positioned supine, patients with RD in the temporal quadrant were positioned on the temporal side of the affected eye, patients with RD in the nasal quadrant were positioned on the nasal side, and patients with RD in

the inferior quadrant were instructed to sit upright. Patients were allowed to interrupt their posturing for meals, toilet visits, refreshment in the morning, and surgeon's examinations. Patients advised to sit upright interrupted their posturing by lying flat on the back for 20 minutes.

Optical Coherence Tomography Progression Measurements

Within 1 hour after arrival on the ward, a baseline volume OCT scan was performed and eligibility was determined. The volume scan was obtained with a Heidelberg Spectralis OCT system (Heidelberg Engineering, Heidelberg, Germany) using a wide-field lens (50°). The field of view of the volume scan was 37°×45°, the transverse resolution was 21 $\mu\text{m}/\text{pixel}$, 16 B-scans were averaged per retinal location, and the spacing of B-scans was 125 μm . If the scanning time was estimated to exceed 1 minute (because of unstable fixation or peripheral RD location), the number of B-scans per volume scan was decreased, but resolution and spacing were kept the same. Optical coherence tomography measurements were performed at the beginning and the end of each interruption as often as logistically possible. Patients were transported from their bed to the OCT using a wheelchair (10- to 50-m distance). If fewer than 3 OCT measurements could be obtained, the patient was withdrawn from the study and the data were excluded from analysis.

The initial distance measurements between fovea and the RD border were performed with the Heidelberg Spectralis OCT built-in measurement tool. After all OCT measurements were obtained, a selection of 21 B-scans was made around the location of the estimated nearest point of the RD for a more accurate and reproducible distance measurement. The order of the scans was randomized per patient to blind the primary grader (J.H.d.J.) during interpretation of the OCT scans. The location of the border of subretinal fluid was annotated in all B-scans using the annotation program ITK-SNAP (available at www.itksnap.org) (Fig 1).²⁰ The location of the fovea was identified in a separate volume scan with a transverse resolution of 21 $\mu\text{m}/\text{pixel}$ and a 32- μm spacing of B-scans.

To calculate the shortest distance between fovea and RD border, the scanning laser ophthalmoscopy (SLO) images corresponding to the OCT volume scans were registered using a custom-built registration tool. To align the SLO images, the primary grader annotated several points in each SLO image corresponding to common vessel crossings (Fig 1). Affine geometric transformation was applied involving translation, rotation, scale, and shear of the image to project all the annotations onto a single SLO image. Finally, by using simple geometric calculations, the shortest distances could be computed.

The distance measurements then were used to calculate the change in distance and the average RD border displacement velocity (change in distance per hour) during posturing and interruption intervals. The change in distance and average progression velocity from baseline at each time point was determined as well. The worst change from baseline was defined as the shortest distance measured in any of the OCT scans during follow-up. We calculated the average RD border displacement velocity to correct for the differences in interval duration and to enable a more valid comparison between posturing and interruptions.

Progression during interruptions was subdivided into progression of newly detached retina and previously detached retina (i.e., after reattachment). If the progression was partially of previously detached retina and partially of newly detached retina, the interval was assigned to the predominant type. To compare for the difference between RD locations, we divided the patients into a superior RD group with supine positioning, a temporal RD group with

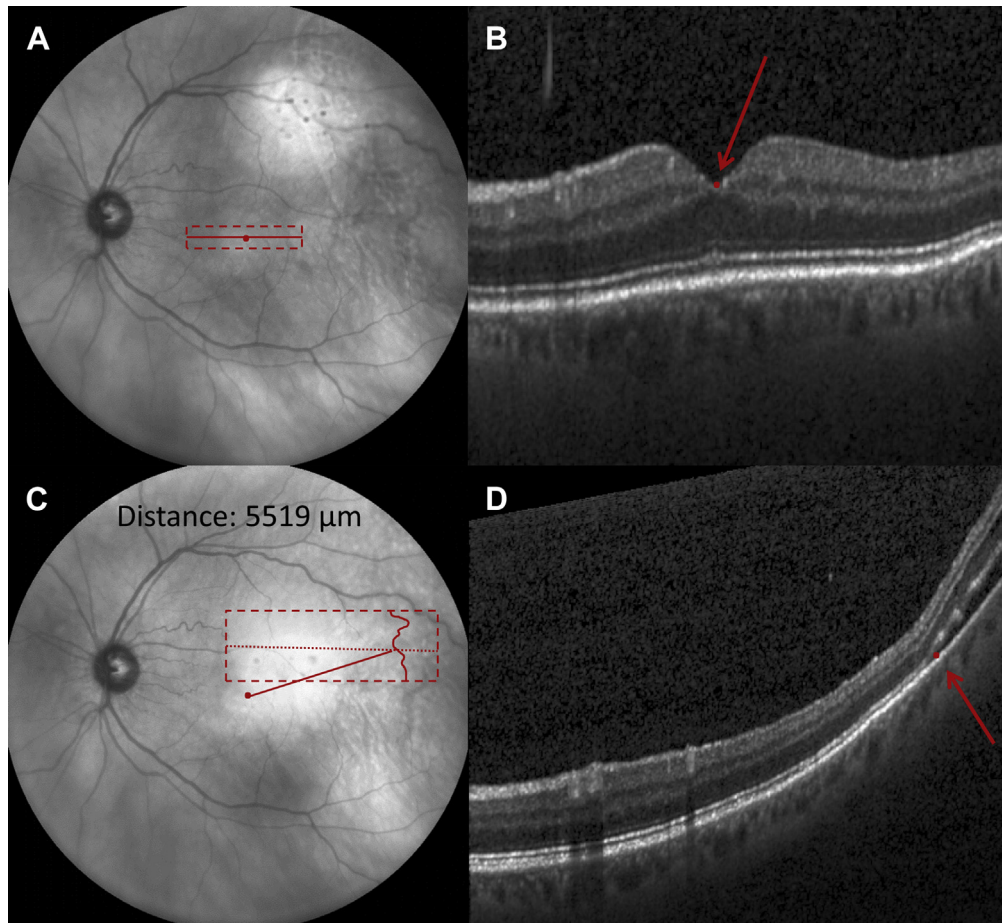


Figure 1. Measurement of the change in distance between (A, B) fovea and (C, D) retinal detachment (RD) border. A small volume scan was performed to image the fovea (red dashed rectangle in panel A) and (B) the central point of the fovea was identified. A second volume scan was aimed at the RD border around the estimated nearest point to the fovea (red dashed rectangle in panel C). The point of subretinal fluid closest to the attached part of the retina was annotated in all B-scans (see panel D). A custom-built software tool was used to merge the scanning laser ophthalmoscope images of (A) the foveal volume scan and (C) the RD volume scan. The shortest distance between RD border and fovea then was calculated to be 5519 μm .

temporal side positioning, a nasal RD group with nasal side positioning, and an inferior RD group with sitting upright positioning.

Secondary Outcome Measures

The following secondary outcome measures were recorded: age, gender, duration of visual field loss (days), duration of follow-up (hours), spherical equivalent refraction (diopters), baseline distance between RD border and fovea (micrometers), size of retinal breaks (clock hours), RD location (deviation from superior of the nearest point on the RD border at baseline, in degrees), extent of RD (degrees), and angle between retina and retinal pigment epithelium (RPE) at the RD edge (degrees). Patients were interviewed to determine the existence and duration of visual field loss using identical questions for all patients. If patients did not report visual field loss, they were excluded from analysis. The duration of follow-up was calculated between admission and the time point of the worst change from baseline and the last OCT. The size of retinal breaks was estimated by the operating surgeon. The baseline OCT and SLO were used to determine the extent of RD and the angle of the actual direction of closest point on the RD border as well as the change of this direction over time. The angle between the retina and RPE was measured with ImageJ software (<https://imagej.nih.gov/ij/>).

Reproducibility Analysis

To evaluate the intrarater variability of the RD–fovea distance measurements, 25 patients were selected randomly from the total of 98 patients. A total of 125 volume scans belonging to these 25 patients were annotated 3 times by the primary grader (J.H.d.J.). The order of scans was rerandomized among the 3 datasets to make them unidentifiable and the annotation was repeated at a different time point. This was performed to estimate the intrarater variability caused by the interpretation of the primary grader. Additionally, the baseline volume OCT scan of 6 patients judged to be representative of the entire population were repeated 4 times. This was carried out within the shortest possible timeframe, and the distance between fovea and RD border was measured. In between the repeated measurements, the patient removed his head from the chinrest to include the variation caused by the repeated acquisition of an OCT scan in our estimate of the intrarater variability.

To evaluate the interrater variability of the distance measurements, the same dataset used to evaluate the intrarater variability with a total of 125 volume scans was annotated by 5 graders of the Moorfields Reading Centre, London, United Kingdom. All graders were instructed to annotate the point of subretinal fluid closest to the attached part of the retina in all B-scans using ITK-SNAP²⁰ and were trained with 3 example volume scans before they started with

the dataset of 125 volume scans. The order of the scans was randomized per patient to blind the graders during interpretation of the OCT scans. The interrater variability of the change in distance of 100 intervals then was evaluated.

Statistical Analysis

Linear mixed modelling was used to describe the intrarater and interrater variability. The patient, image, and grader effects were included as random effects. An univariate *F* test and a pairwise comparison with Bonferroni correction were performed to test for differences between the graders. The intraclass correlation coefficient (ICC) and the 95% limits of agreement were determined, as well ($\pm 1.96 \times$ standard deviation [SD]).

Because of the apparent skewed distribution of RD–fovea distance and velocity measurements, nonparametric testing (Mann–Whitney *U* test) was used to compare between posturing and interruptions intervals. The Mann–Whitney *U* test also was performed to compare between progression of newly detached retina and previously detached retina, between posturing at night and posturing during the day, and between patients with a follow-up duration of 16 hours or less and more than 16 hours to relate our study outcome to the findings of Hajari et al.¹⁸ The Kruskal–Wallis test and pairwise comparison of the Mann–Whitney *U* test with Bonferroni correction were used to test for differences between the RD location groups (superior, temporal, nasal, and inferior RD).

Spearman's ρ was used to test for correlations between the worst progression from baseline and the following supposed risk factors: duration of visual field loss, duration of follow-up, spherical equivalent refraction, baseline distance between RD border and fovea, size of retinal breaks, RD location, extent of RD, and angle between retina and RPE. Statistical analyses were performed with SPSS software version 21 (IBM Corporation, Armonk, NY). Two-sided *P* values less than 0.05 were considered significant.

Results

Patients

Between February 24, 2015, and January 26, 2016, 391 macula-on RD patients were hospitalized before surgery in the Rotterdam Eye Hospital, 181 of whom were screened for eligibility. Of this screening pool, 71 patients were not eligible for this study. In 36, the distance between the fovea and RD was smaller than 1250 μm ; in 16 patients, the border of the RD could not be determined because of a peripheral RD location beyond the limits of the OCT system, a bullous RD overhanging the RD border, or poor OCT quality; in 7 patients, even a narrowed volume scan protocol took more than 2 minutes because of poor fixation of the patient or a peripheral RD location; 11 patients declined to participate; 1 patient demonstrated suspected methicillin-resistant *Staphylococcus aureus* and remained in a quarantine room. Of 110 included patients, 12 patients were sent to the operation room before 3 OCT measurements could be conducted and were withdrawn from this study and further analysis. In the remaining 98 included patients, a total of 497 OCT scans were obtained (range, 3–13 OCT scans per patient), and these are presented in this report. All patients with 2 or more OCT scans provided written informed consent.

Patient characteristics are summarized in Table 1. Of 98 patients, 24 were instructed to lie supine, 42 were instructed to lie on the temporal side, 22 were instructed to lie on the nasal side, and 10 were instructed to lie to sit upright. With the 497 OCT scans, 399 intervals were recorded comprising 202

Table 1. Patient Characteristics

Characteristic	Data
No. of patients in the study	98
Age (yrs)	
Mean \pm SD	59 \pm 8
Gender (male:female; no.)	66:32
Phakic:pseudophakic (no.)	65:33
Snellen visual acuity	
Mean	20/25
Range	20/400–20/17
Refraction spherical equivalent (diopters)*	
Median (IQR)	−3.00 (−4.50 to 0.00)
Range	−10.00 to 5.75
Mean \pm SD	−3.20 \pm 3.78
Moderate myopia (≤ 6.0 and ≥ 3.0)	28/98
High myopia (≥ 6.0)	23/98
Duration of visual field loss (days)	
Median (IQR)	4 (2–8)
Range	0.5–120
Mean \pm SD	8 \pm 16
No reports of visual field loss (no.)	24/98
Primary/recurrent RD	92/6
History of vitrectomy	3
History of scleral buckling	3
Posterior vitreous detachment (yes/no)	98/0
Extent of RD (°)	
Median (IQR)	105 (90–135)
Range	45–300
Mean \pm SD	114 \pm 45
Size of retinal tear (no.)	
Single small (≤ 0.50 clock hours)	27
Multiple/large (> 0.50 clock hours)	63
No breaks found	8
Angle between retina and RPE	
Median (IQR)	8 (4–13)
Range	1–40
Mean \pm SD	10 \pm 8
Posturing advice (no.)	
Supine	24
Temporal side	42
Nasal side	22
Sitting upright	10

IQR = interquartile range; RD = retinal detachment; RPE = retinal pigment epithelium; SD = standard deviation.

*In patients with pseudophakic lens status, the spherical equivalent refraction before cataract surgery was used.

posturing intervals and 197 interruptions. A description of the duration of hospitalization and measured intervals is given in Table 2. The course of RD progression differed extensively between patients as presented in Figure 2. The median change in direction from the fovea to the nearest point of the RD border was 4° (interquartile range, 2°–7°; range, 0°–69°) during follow-up.

Reproducibility

The intrarater variability caused by the interpretation of the primary grader was 23 μm (standard deviation [SD]) and the 95% limits of agreement of the intrarater variability were ± 45 μm . The intrarater variability caused by both the interpretation of the primary grader and the OCT acquisition was 29 μm (SD), and the 95% limits of agreement of the intrarater variability were ± 58 μm . The ICC for repeated measurements was 0.999 (ICC type 3, 1; 95% confidence interval [CI], 0.998–1.000).

Table 2. Hospitalization and Timing of Optical Coherence Tomography Examinations

Characteristic	Data
Time between baseline OCT and surgery (hours)	
Median (IQR)	21.5 (18.5–23.8)
Range	1.2–48.0
Mean \pm SD	20.9 \pm 10.0
Time between baseline OCT and last OCT (hours)	
Median (IQR)	16.5 (3.9–20.2)
Range	0.8–39.9
Mean \pm SD	14.8 \pm 9.5
No. of posturing intervals	202
Duration of posturing intervals (hours)	
Median (IQR)	3.0 (1.8–14.0)
Range	0.3–23.1
Mean \pm SD	6.8 \pm 6.1
No. of interruptions	197
Duration of interruptions (hours)	
Median (IQR)	0.37 (0.26–0.50)
Range	0.15–1.91
Mean \pm SD	0.42 \pm 0.24

IQR = interquartile range; OCT = optical coherence tomography; SD = standard deviation.

The interrater variability of distances was 47 μ m (SD), and the residual variation in the model was 80 μ m (SD). The 95% limits of agreement of the combined grader and residual effects were \pm 182 μ m. The interrater ICC for distances was 1.000 (ICC type 3, k; 95% CI, 1.000–1.000). The mean \pm SD difference per grader with the mean of the 6 grader measurements was -25 ± 69 μ m for grader 1, -9 ± 49 μ m for grader 2, 97 ± 115 μ m for grader 3, -23 ± 80 μ m for grader 4, -22 ± 47 μ m for grader 5, and -17 ± 53 μ m for grader 6 (a positive difference indicates a systematically larger distance to the fovea). A univariate *F* test showed a significant difference among the graders ($P < 0.001$). Pairwise comparison showed that the annotations of grader 3 were statistically significantly different from those of the other graders ($P < 0.001$).

Figure 3 shows 3 examples of the 3 patients with the poorest agreement between grader 3 and the other graders. The presence of a low-reflective photoreceptor outer segment layer hanging under the detached and highly reflective ellipsoid zone seems to be the reason for the different interpretation of grader 3 (Fig 3A–C). The arbitrary discrimination between photoreceptor outer segments and subretinal fluid also is demonstrated by the different interpretation of grader 1 in Figure 3B.

The interrater variability of change in distance per interval was redundant and set to 0 by the model, but the residual variability was of 89 μ m (SD) and the 95% limits of agreement of the interrater variability were \pm 175 μ m. The interrater ICC for change per interval was 0.996 (ICC type 3, k; 95% CI, 0.995–0.997). The mean \pm SD difference per grader with the mean of the 6 grader measurements was 5 ± 79 μ m for grader 1, -5 ± 64 μ m for grader 2, 4 ± 130 μ m for grader 3, 4 ± 74 μ m for grader 4, -1 ± 69 μ m for grader 5, and -6 ± 52 μ m for grader 6. Although the mean differences between the graders were much smaller for change for intervals than for distances, the SDs are in the same order of magnitude.

Given the small mean difference of -6 μ m and smallest SD of 52 μ m, the interpretation of the primary grader (J.H.d.J., grader 6) provided accurate and precise results for the change per interval. The 95% limits of agreement between the measurements of grader

6 and the average of all graders were \pm 102 μ m. The interpretation of the primary grader also was used for the other 73 patients presented in this study, of which the order of scans per patient was randomized as well.

Example Patient

An example of the change in distance between RD border and fovea of a patient with a superior temporal RD is shown in Figure 4. This patient regressed during nighttime posturing and progressed during interruptions. The last OCT 39.6 hours from admission revealed regression of 992 μ m from baseline (see the first and the last measurement point in Fig 4). On the right, 3 example OCT scans are displayed, indicated by the red 1, 2, and 3 in the graph. During the posturing interval between OCT 1 and 2, 2085 μ m of regression was found, and during the interruption between OCT 2 and 3, progression of 519 μ m was found.

Comparison of Posturing and Interruptions

To elucidate whether preoperative posturing influences RD progression, we compared displacement of the RD border during posturing intervals and interruptions. The median RD border displacement during posturing was 2 μ m (interquartile range [IQR], -65 to 251 μ m; $n = 202$) and the mean \pm SD displacement was 265 ± 919 μ m. The median RD border displacement during interruptions was -61 μ m (IQR, -140 to 0 μ m; $n = 197$), and the mean \pm SD displacement was -94 ± 193 μ m. The difference between posturing and interruptions was statistically significant ($P < 0.001$; Fig 5). As reported in Table 2, the interval during interruptions was much shorter than during posturing intervals. The median interval during posturing was 3.0 hours (IQR, 1.8–14.0 hours), and that during interruptions was 22 minutes (IQR, 15–30 minutes).

The median RD border displacement velocity during posturing was $+1$ μ m/hour (IQR, -21 to 49 μ m/hour), and the mean \pm SD velocity was 19 ± 122 μ m/hour. The median RD border displacement velocity during interruptions was -149 μ m/hour (IQR, -406 to 1 μ m/hour), and the mean \pm SD velocity was -259 ± 535 μ m/hour. The difference between posturing and interruptions was statistically significant ($P < 0.001$; Fig 6).

We further compared posturing intervals during the day and during the night. The median RD border displacement velocity during daytime posturing intervals was -4 μ m/hour (IQR, -51 to 47 μ m/hour; $n = 128$) and at night was $+13$ μ m/hour (IQR, -1 to 59 μ m/hour; $n = 74$); these differed statistically significantly from each other ($P < 0.001$). The median duration of posturing intervals during the day was 2.1 hours and that during the night was 14.5 hours.

We also compared progression during interruptions in previously detached retina (i.e., after reattachment) and in newly detached retina. The median progression velocity during interruptions in an area of previously detached retina was -312 μ m/hour (IQR, -633 to -162 μ m/hour; $n = 86$) and in an area of newly detached retina was -160 μ m/hour (IQR, -358 to -78 μ m/hour; $n = 62$). The RD progression during interruptions in previously detached retina was significantly faster ($P < 0.001$) compared with RD progression of newly detached retina.

We further analyzed the effect of posturing on RD progression in different groups of patients based on the RD location and positioning advice. We found statistically significant differences for the change in distance toward the fovea between posturing and interruptions for the temporal and nasal RD group ($P < 0.001$; Fig 5), but not for the superior and inferior RD group. The difference in RD border displacement velocity between posturing

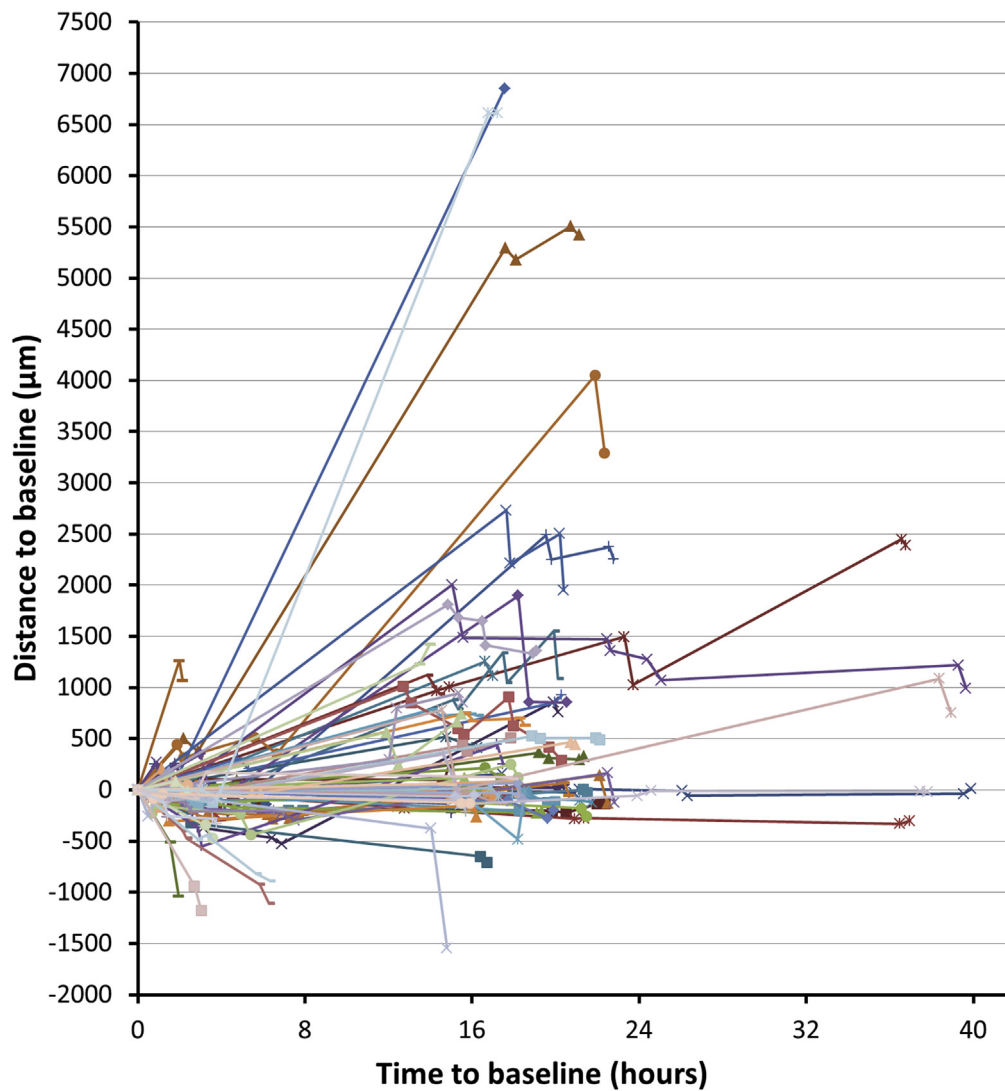


Figure 2. Graph showing the course of the change in distance between the retinal detachment (RD) border and fovea compared with baseline during the study follow-up period. Individual patients are represented by different colors. The markers on the lines represent the time points on which the optical coherence tomography (OCT) measurements were performed. The change in distance from baseline differed extensively between patients.

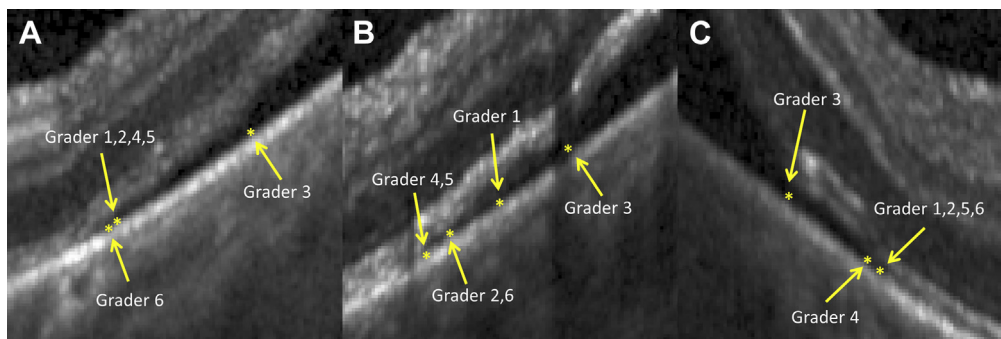


Figure 3. Examples of optical coherence tomography images for which poor agreement on the border of subretinal fluid was found between grader 3 and the other graders. The annotation of the different graders is indication with yellow asterisks. The graders were instructed to annotate the point of subretinal fluid closest to the attached part of the retina. The presence of a low-reflective photoreceptor outer segment layer hanging under the detached and highly reflective ellipsoid zone seems to be the reason for the different interpretation of grader 3 (A, B, C), but also for the different interpretation of grader 1 in (B).

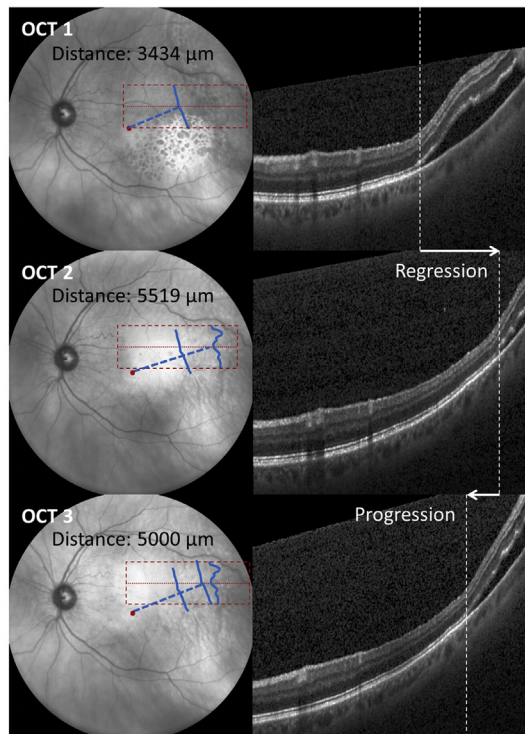
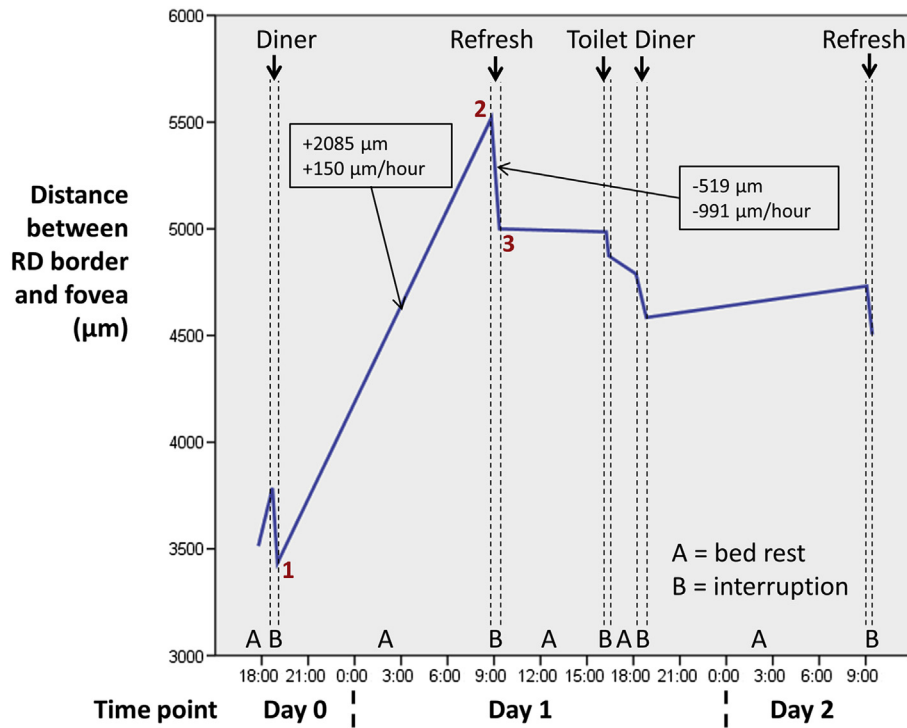


Figure 4. Example of the change in distance between retinal detachment (RD) border and fovea during the hospitalization of a patient with superior temporal RD in the left eye. On the graph on the left, the full course of hospitalization is shown and the reason for interrupting posturing is indicated. On the right, 3 example optical coherence tomography (OCT) scans are displayed, indicated by red numerals 1, 2, and 3 in the graph. The red dashed rectangle indicates the location and size of the volume scan, and the red line indicates the location of the B-scan. The fovea is indicated with a red dot, the RD border is indicated with a blue line, and the blue dashed line indicates the shortest distance to the fovea. The baseline OCT measurement provided a distance of 3434 μm (see OCT 1). During the posturing intervals in the night, the RD regressed (see OCT 2), and during interruptions, the RD progressed (see OCT 3). Between OCT 1 and 2, a regression of 2085 μm was found (+150 $\mu\text{m}/\text{hour}$) and between OCT 2 and 3, a progression of 519 μm was found (−991 $\mu\text{m}/\text{hour}$).

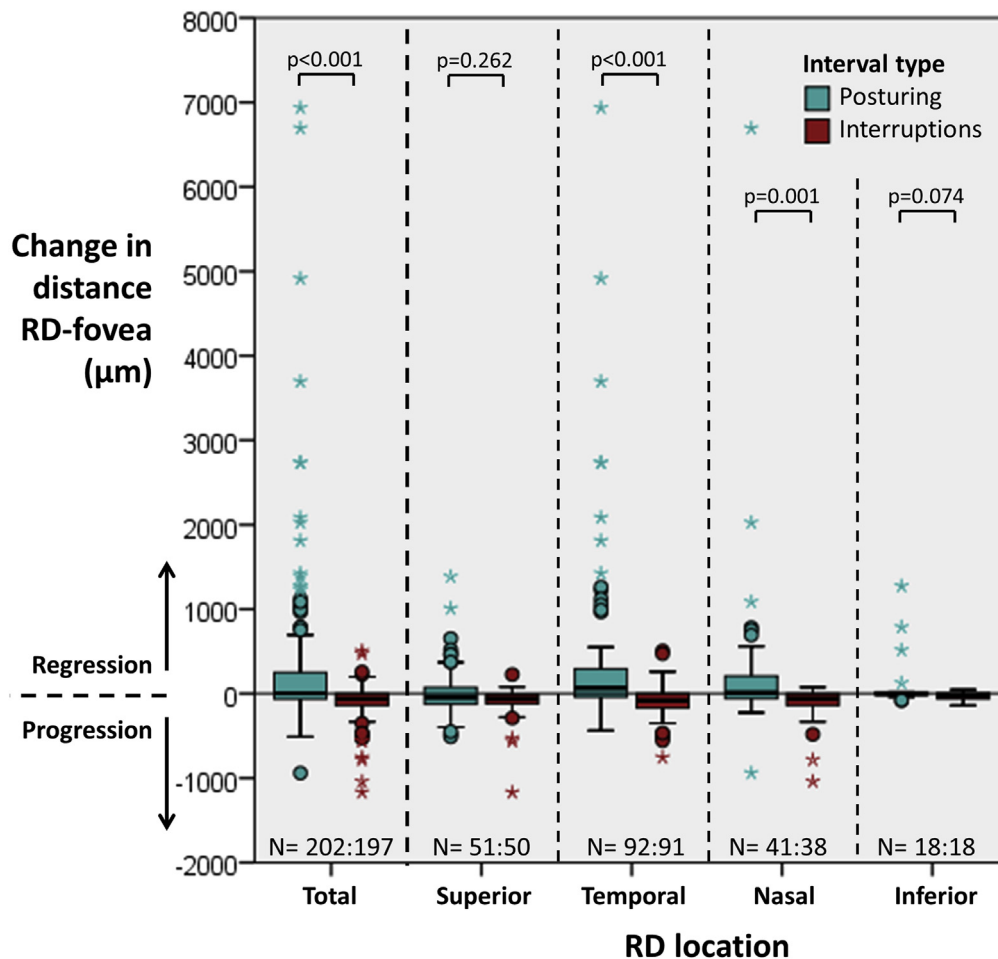


Figure 5. Retinal detachment (RD) border displacement (in micrometers) showing progression (negative change) or regression (positive change). The change during posturing and interruptions is shown for all patients (total) and is subdivided according to RD location and positioning advice. The difference between posturing and interruptions were statistically significantly different for the temporal and nasal RD group, but not for the superior or inferior RD group (see *P* values in figure, Mann–Whitney *U* test). *N* = *a*:*b* indicates the number of intervals of posturing (*a*) and interruptions (*b*).

and interruptions was significantly different for all RD location groups (Fig 6).

Change from Baseline

Although posturing reduces progression compared with interruptions, some patients do progress from baseline. Table 3 shows 3 time points: baseline OCT, worst change from baseline (smallest distance during follow-up), and the last OCT. At the worst change from baseline, a median change of $-84 \mu\text{m}$ (IQR, -221 to $-25 \mu\text{m}$; range, -1544 to $1948 \mu\text{m}$) was found, 21 of 98 patients showed more than $250 \mu\text{m}$ of progression, and 4 of 98 showed more than $1000 \mu\text{m}$ of progression. The median duration from baseline to the point of worst change from baseline for the 21 patients with more than $250 \mu\text{m}$ of progression was 6.3 hours (IQR, 3.3–15.7 hours; range, 1.5–36.5 hours), and the average velocity was $-87 \mu\text{m}/\text{hour}$ (IQR, -179 to $-41 \mu\text{m}/\text{hour}$; range, -535 to $-9 \mu\text{m}/\text{hour}$). The 4 patients with more than $1000 \mu\text{m}$ of progression from baseline all had primary, superior RD with multiple or large retinal tears and were phakic. Three of these 4 patients maintained supine positioning, and 1 of 4 patients was instructed to lie on the nasal side. One of 4 patients had myopia of more than 6.0 diopters. The extent of RD varied between 90° and 110° .

In 14 of 21 patients with more than $250 \mu\text{m}$ of progression, surgery was already planned for the first available time on the operation room program. In 6 of 21 patients, we were able to reschedule the patients a few hours earlier. In 1 of 21 patients, the patient underwent surgery after normal working hours and surgery was not postponed to the next day owing to the apparent progressive nature of the RD.

After the worst change from baseline, some patients showed regression, especially during the night, and the median change from baseline to the last OCT was $-3 \mu\text{m}$ (IQR, -127 to $457 \mu\text{m}$). The maximum progression from baseline was $1544 \mu\text{m}$ and the maximum regression from baseline was $6850 \mu\text{m}$. None of our patients progressed to macula-off RD during follow-up. Only 1 patient progressed within $1000 \mu\text{m}$ of the fovea. This patient showed a baseline distance between the RD border and fovea of $1256 \mu\text{m}$ and progressed to $707 \mu\text{m}$ in 3 hours. The next morning, after 14 hours of posturing, the patient had regressed to an RD–fovea distance of $1698 \mu\text{m}$. The patient with the maximum regression of $6850 \mu\text{m}$ regressed so extensively that at the last OCT before surgery, only a small amount of subretinal fluid was seen around the retinal hole at 12.4 mm from the fovea after regressing in 18 hours from a baseline distance of 5.5 mm .

Figure 7 displays progression from baseline for at-worst change from baseline for all patients (total) and subdivided by RD

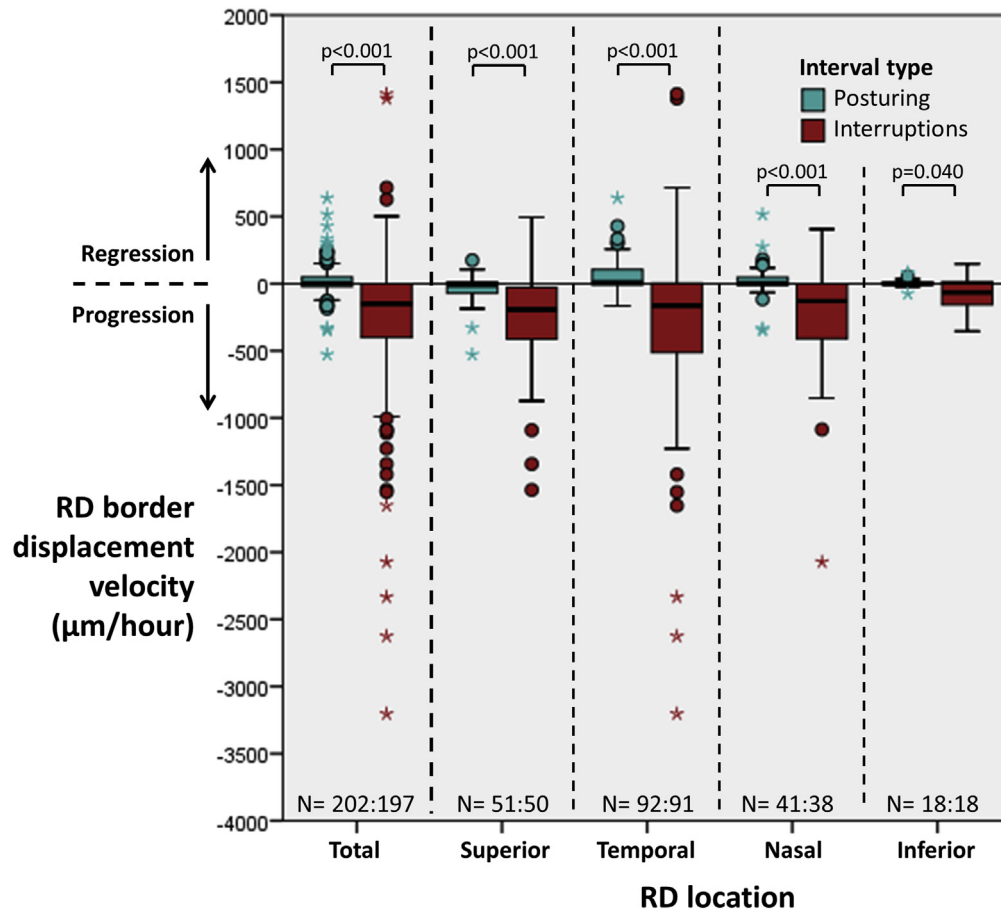


Figure 6. Retinal detachment border displacement velocity (in micrometers per hour) showing progression (negative velocity) or regression (positive velocity). The average velocity during posturing and interruptions is shown for all patients (total) and subdivided according retinal detachment (RD) location. The difference between posturing and interruptions was statistically significantly different for all groups (see *P* values in figure, Mann–Whitney *U* test). *N* = *a*:*b* indicates the number of intervals of posturing (*a*) and interruptions (*b*).

Table 3. The Distance and Change in Distance between the Retinal Detachment Border and the Fovea

	Distance Retinal Detachment Border and Fovea (μm)	Change from Baseline Distance (μm)	Change from Baseline Time (hours)	Change from Baseline Average Velocity (μm/hour)
Baseline OCT				
Median (95% CI)	4050 (3740–4837)	NA	NA	NA
Interquartile range	2741–6132			
Range	1256–14122			
Mean ± SD	4982±2872			
Smallest distance during follow-up				
Median (95% CI)	4294 (3765–5090)	–84 (–122 to –58)	5.9 (3.6–12.5)	–11 (–21 to 6)
Interquartile range	2782–5854	–221 to 25	2.4–16.0	–48 to 3
Range	707–13819	–1544 to 1948	0.5–36.5	–535 to 499
Mean ± SD	4926±2803	–54±472	9.2±7.7	–25±105
Last OCT				
Median (95% CI)	4674 (4017–5374)	–3 (–53 to 49)	16.5 (15.5–17.6)	0 (–4 to 6)
Interquartile range	3077–6284	–127 to 457	3.9–20.2	–11 to 27
Range	1358–13857	–1544 to 6850	0.8–39.9	–535 to 637
Mean ± SD	5336±3019	356±1272	14.8±9.5	7±116

CI = confidence interval; OCT = optical coherence tomography; SD = standard deviation.

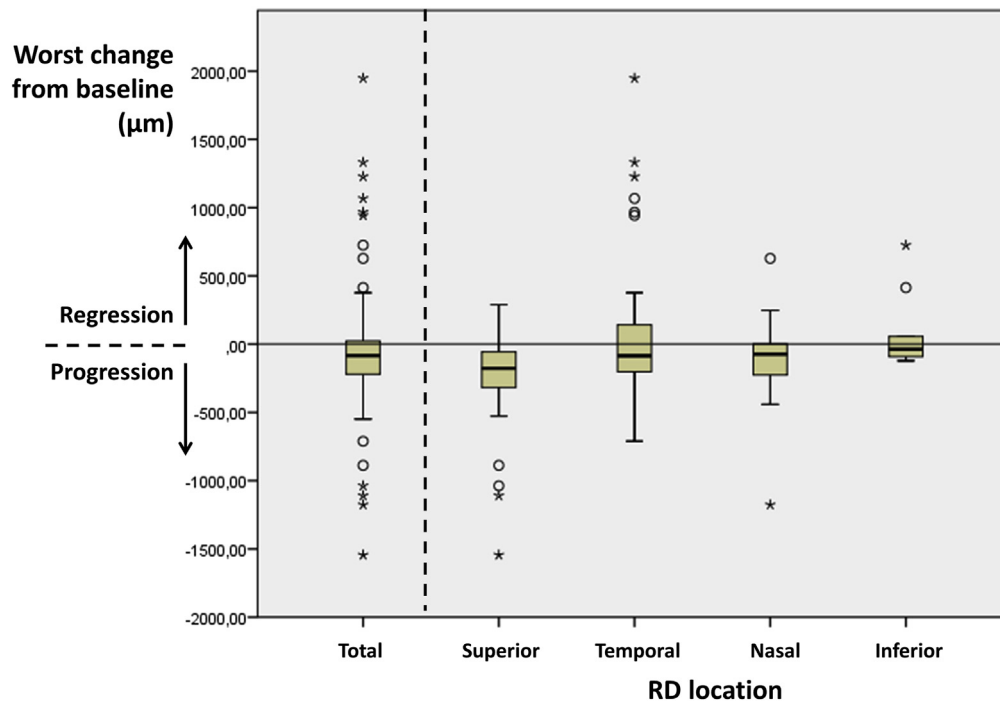


Figure 7. Graph showing the worst change from baseline in micrometers for the total of patients and a stratification according to retinal detachment (RD) location. The progression from baseline seemed to be larger in the superior RD group, although pairwise comparison did not reveal significant differences between the RD groups.

location. The Kruskal-Wallis test resulted in a significant difference among the RD location groups ($P = 0.026$). There seemed to be more progression from baseline in the superior RD group, but pairwise comparison did not result in significant differences between the groups.

Risk Factors for Progression

Statistically significant correlations were found between the worst progression from baseline and a larger baseline distance between RD border and fovea, a shorter duration of visual field loss, an RD location with a smaller deviation from superior, and a smaller extent of RD (Table 4). No significant correlations were found between progression and the duration of follow-up, spherical equivalent refraction, the angle between retina and RPE, and the

size of retinal breaks. Of the 2 patients with the largest tears of 4 clock hours, 1 progressed and 1 did not.

Patients with a duration of follow-up of 16 hours or fewer showed a median change from baseline to the last OCT of $-26 \mu\text{m}$ (IQR, -211 to $53 \mu\text{m}$; $n = 44$) and patients with more than 16 hours of follow-up showed a median change from baseline to the last OCT of $79 \mu\text{m}$ (IQR, -79 to $792 \mu\text{m}$; $n = 54$), which was statistically significant different ($P = 0.005$). After exclusion of the 7 patients who were rescheduled to an earlier surgery time because of more than $250 \mu\text{m}$ of progression, the difference was still statistically significant ($P = 0.008$), with a median change from baseline in the group with a follow-up of 16 hours or fewer of $-18 \mu\text{m}$ (IQR, -142 to $56 \mu\text{m}$; $n = 41$), and a median change from baseline in the group with a follow-up of more than 16 hours of $114 \mu\text{m}$ (IQR, -69 to $873 \mu\text{m}$; $n = 50$).

Table 4. Risk Factors for Progression from Baseline

Risk Factor	Spearman's Correlation Coefficient with Worst Progression from Baseline, ρ (95% Confidence Interval)*	P Value
Baseline RD–fovea distance (mm)	-0.321 (-0.114 to -0.499)	0.001
Extent of RD (clock hours)	0.262 (0.068 – 0.438)	0.009
Duration of visual field loss (days)	0.240 (0.009 – 0.485)	0.039
Deviation from superior ($^{\circ}$)	0.229 (0.031 – 0.400)	0.023
Duration of follow-up (hours)	-0.036 (-0.230 to 0.161)	0.725
Spherical equivalent refraction (diopters)	-0.144 (-0.344 to 0.065)	0.158
Angle between retina and RPE ($^{\circ}$)	-0.156 (-0.341 to 0.032)	0.125
Size of retinal breaks (clock hours)	0.065 (-0.115 to 0.242)	0.523

RD = retinal detachment; RPE = retinal pigment epithelium.

*A negative correlation means that a larger value for the risk factor results in more progression. A positive correlation means that a smaller value for the risk factor results in more progression.

Discussion

Preoperative posturing advice has been given to patients with macula-on RD for decades all around the world, in some countries combined with hospital admission.^{9–18,21} The first study performed using OCT to elucidate the progression rate of RD showed that delay of surgery beyond 16 hours was associated with a greater risk of progression.¹⁸ Moreover and most importantly, this study highlighted the use of OCT as a precise research tool and allowed us to study the relationship between posturing and RD progression in an ethical manner. We could record progression safely with an OCT device located on the ward by using the accepted reasons for interrupting posturing, like toilet visits and meals. We were able to demonstrate that the median RD border displacement velocity during posturing was $+1 \mu\text{m}/\text{hour}$ (IQR, -21 to $49 \mu\text{m}/\text{hour}$) and $-149 \mu\text{m}/\text{hour}$ (IQR, -406 to $1 \mu\text{m}/\text{hour}$) during interruptions that was statistically significantly different ($P < 0.001$). Therefore, we conclude that preoperative posturing significantly reduces progression of RD.

Retinal detachment progression is likely to be affected by several forces of different importance. Gravity is involved in specific positioning, with the detached retina in the lower-most position. However, it is considered unlikely that gravity will much affect intraocular fluid dynamics because the density differences between retina and vitreous are rather small.²² Shear forces on the retina by eye and head movements are expected to affect RD progression as well.^{23,24} Bed rest not only allows for specific positioning, but also helps to reduce eye and head movements. Although there is no evidence available, posturing at home may increase the risk of RD progression because of the traveling time, the lack of nurse surveillance, and the need to perform domestic duties. Therefore, while patients are awaiting surgery in some European hospitals, patients are admitted to the hospital instead of being sent home to improve their compliance with the posturing regimen.

In this study, superior and inferior RD patients seem to be less affected by the posturing advice than the temporal or nasal RD groups (Fig 5). Although the comparison of RD displacement velocity during posturing and interruptions showed that superior RD patients also benefitted from posturing (Fig 6), the progression from baseline seemed to be larger in these patients (Fig 7). A supine posturing advice may be suboptimal for superior RD, because the force of gravity is not directed from the fovea to the RD area and the tear.²⁴ Trendelenburg positioning would achieve that better, but is highly inconvenient to patients and impractical without hospital admission. Patients with inferior RD and sitting in an upright position interrupted their posturing by lying supine while maintaining bed rest, instead of interrupting bed rest, as did patients with RD in the superior quadrants. The smaller effect of posturing and the smaller progression rate from baseline in these patients may point out that head- and eye movement-related forces are responsible for the development of RD more than gravity alone.^{24,25}

The progression velocity seemed to be twice as fast in previously detached areas of the retina compared with newly

detached retina. This is in accordance with the retinal adhesion experiments of Yoon and Marmor,²⁶ who showed that the retinal adhesion strength gradually increases after spontaneous reattachment, but is still only 75% of the normal adhesion strength after 4 weeks. The median progression velocity in newly detached retina of $160 \mu\text{m}/\text{hour}$ during interruptions is clinically meaningful. If patients do not follow posturing advice and their activity level is comparable with the light daily activities during bed rest interruptions of the patients in this study, then they are estimated to have on average 2.6 mm of progression in a 16-hour period. This extrapolation suggests that patients who the clinician believes may not comply with preoperative posturing may benefit from earlier surgical intervention. The higher regression rate during nighttime posturing compared with daytime posturing may be explained by better compliance with the posturing advice or fewer eye movements during the night.

Despite preoperative posturing, 21 of 98 patients progressed by more than $250 \mu\text{m}$ from baseline and 4 of 98 patients progressed by more than $1000 \mu\text{m}$ from baseline. The median worst change from baseline was $-84 \mu\text{m}$ (IQR, -221 to $25 \mu\text{m}$), whereas the median change from baseline to the last OCT was $+3 \mu\text{m}$ (IQR, -127 to $457 \mu\text{m}$). This demonstrates that regression may follow earlier progression during the first days of posturing. Only one of the patients progressed within $1000 \mu\text{m}$ from the fovea during follow-up. This seems to indicate that the current policy of preoperative posturing and surgery within 48 hours is sufficient to prevent macula-off RD. It is also in accordance with the low rate of progression to macula-off status of patients awaiting surgery as reported by Ho et al¹⁶ (3%), Ehrlich et al¹⁷ (2%), Wykoff et al²⁷ (0.5%), and Hajari et al¹⁸ (1%).

Patients with a superior RD location are slightly more at risk for progression than when the other quadrants are affected (Table 4; Fig 7).²⁸ We also found a slightly increased risk of progression from baseline of patients with a short duration of visual field loss, a larger baseline RD–fovea distance, and a smaller extent of RD. The relationship between duration of visual field loss and progression may be explained by symptomatic patients who may be more inclined to seek medical attention than patients whose detachments are progressing slowly, resulting in minimal or no symptoms.²⁹ The increased risk of progression in case of a larger baseline RD–fovea distance and smaller extent of RD both may be explained by a weaker retinal adhesion in the periphery, allowing faster progression. When creating an RD for macular rotation or RPE graft, it is a common observation among surgeons that the peripheral retina detaches much more easily than the posterior retina, suggesting a difference in adhesion. This phenomenon may be related to the greater photoreceptor density in the posterior pole.³⁰

We did not find an increased risk for progression if surgery was postponed beyond 16 hours from admission, like Hajari et al.¹⁸ On the contrary, a longer admission time significantly facilitated regression ($P < 0.001$) during the short follow-up of this study. In 1 patient, the RD almost

completely disappeared after only 18 hours of posturing, which shows that in rare cases, surgery no longer may be required after preoperative posturing. Even if we excluded the 7 patients who were rescheduled to an earlier surgery time because of more than 250 μm of progression, we found a significant difference between short (≤ 16 hours) and long (> 16 hours) admission times. The reason for this different outcome may be that we observed the patients also during the first hours of admission, whereas Hajari et al repeated the OCT only every morning. When performing OCTs in the morning, the progression during the previous day likely was concealed by reattachment during the night. However, the follow-up time of our study was limited, with a median of 16.5 hours (IQR, 3.9–20.2 hours). Delaying surgery beyond the follow-up duration of our study still may result in more progression because of a potentially poorer compliance with the posturing advice.

The 95% limits of agreement of the intrarater variability of the OCT distance measurements were $\pm 58 \mu\text{m}$, which was comparable with the 84- μm precision of the OCT measurements of Hajari et al.¹⁸ The 95% limits of agreement of the combined intrarater and interrater variability of the change in distance were $\pm 175 \mu\text{m}$, which describes the maximum variability of our scan protocol if multiple graders are used to interpret the OCT measurements. The accuracy of the primary grader in the determining the change in distance was $-6 \mu\text{m}$ and the 95% limits of agreement were $\pm 102 \mu\text{m}$. To obtain this precision, an elaborate training of graders is necessary. If measurements of the RD–fovea distance change with a precision of more than $\pm 102 \mu\text{m}$ are required, applying a higher scan resolution or larger number repeated B-scans per retinal location should be considered to improve the contrast between the photoreceptor outer segment layer and subretinal fluid.

The strengths of this study are the number of patients, the prospective nature of this study, the use of OCT on the ward allowing a safe and detailed analysis of the course of progression, and the reproducibility analysis. Limitations of this study are the logistic constraints (no measurements were performed at night, surgery ended the follow-up period) and the shorter hospitalizations of patients who showed progression. One patient with a giant retinal tear was given a higher priority in operation time planning and had to be withdrawn from the study, which might have introduced a small selection bias and might have affected the rate of progression from baseline we found. Nevertheless, we could not find a relationship between the size of the retinal tear and progression from baseline in the 98 included patients (Table 4).

In conclusion, we showed that preoperative posturing reduces the progression of macula-on RD. Despite posturing, 21 of 98 patients progressed by more than 250 μm from baseline. For future studies, prolongation of interruptions may reveal whether traveling home increases patient risk of progression. Monitoring compliance with the posturing advice using positioning sensors may illuminate whether a restriction of head movements rather than gravity is related with RD progression. Further analysis of putative risk factors is required to be able to design a model that can predict progression of macula-on RD.

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¹ The Rotterdam Eye Hospital, Rotterdam, The Netherlands.

² Rotterdam Ophthalmic Institute, Rotterdam, The Netherlands.

³ Section of Medical Psychology and Psychotherapy, Department of Psychiatry, Erasmus University Medical Center Rotterdam, Rotterdam, The Netherlands.

⁴ School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, Belfast, United Kingdom.

⁵ Department of Ophthalmology, Erasmus University Rotterdam, Rotterdam, The Netherlands.

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Conception and design: de Jong, Timman, Vermeer, van Meurs

Analysis and interpretation: de Jong, Viguera-Guillén, Peto, Vermeer, van Meurs

Data collection: de Jong, Simon, Vermeer, van Meurs

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Abbreviations and Acronyms:

CI = confidence interval; **ICC** = intraclass correlation coefficient; **IQR** = interquartile range; **OCT** = optical coherence tomography; **RD** = retinal detachment; **RPE** = retinal pigment epithelium; **SD** = standard deviation; **SLO** = scanning laser ophthalmoscopy.

Correspondence:

Jan H. de Jong, MD, Rotterdam Ophthalmic Institute, Schiedamse Vest 160, 3011BH Rotterdam, The Netherlands. E-mail: h.dejong@eyehospital.nl.