Eccentric Fixation in Stargardt's Disease Assessed by Tübingen Perimetry

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Purpose. To measure eccentric fixation characteristics in visual fields of patients with Stargardt's disease.

Methods. The positions of fixation loci (FL) in the visual field were determined by Tübingen perimetry (TP), using the position of the blind spots in 173 patients. Altogether, 669 visual fields were measured at baseline and during follow-up. Twenty patients were also examined by scanning laser ophthalmoscope (SLO).

Results. Ninety-five of 173 patients showed a ring scotoma with central fixation in at least one test, which could persist for up to 18.8 years. The median age for a 50% chance of the development of eccentric fixation was 23.6 years. One hundred four patients (203 eyes) used eccentric fixation in at least one eye; in 154 eyes, the FL was placed below the scotoma and in 33 eyes to the left of it, in 11 to the right of it, and in 5 above it. Once the FL was chosen, it remained within the same visual field area at subsequent tests, varying on average by 1.76°. Compared with SLO results, the mean distance between FL and PRL was 1.90°.

Conclusions. It is possible to determine the position of the FL by perimetry with sufficient accuracy if the blind spot is well delimited. Stargardt patients can keep central fixation for different time intervals before changing to an eccentric FL. Most of them show an FL below the central scotoma, which is considered favorable for horizontal reading. (*Invest Ophthalmol Vis Sci.* 2007;48:5815–5822) DOI:10.1167/iovs.06-0367

Stargardt's macular dystrophy (SMD) is an autosomal recessive macular degeneration that is bilateral and symmetrical, with diminished central vision as the typical initial symptom.[1,2] It was first described by Stargardt[3] and is the most common hereditary macular dystrophy.[1]

A wide range of 6 to 65 years for the onset of symptoms and heterogeneous clinical presentations have been reported,[2,4] but in the end stage, these patients typically develop an absolute central scotoma[2,4,5] that makes them lose the ability to fixate targets and analyze images in detail.[6,7] Reading, driving, and recognizing faces are reported as the most difficult daily living activities,[8] and it is known that these visual performance difficulties may appear in patients before visual acuity loss.[6]

Patients with absolute central scotoma develop eccentric fixation, a gaze strategy of sensory and oculomotor adaptations for using a preferred retinal locus (PRL),[9–11] and this is their only chance to regain the ability to solve difficult visual tasks, such as reading.[12–15] Per the definition, "eccentric fixation" corresponds to the condition in which the patient looks at the target directly with the eccentric PRL—that is, the patient has adopted the new viewing direction as "straight ahead." In contrast, in "eccentric viewing" the physiological gaze direction is still preserved, and the patient has to look intentionally beside the target, which mostly occurs in the early stages of the disease. In this article, "eccentric fixation" will be used as the generic term for any extrafoveal fixation, independent of the patient's subjective gaze direction.

The PRL position can be determined by direct measurements on fundus images (for example, by scanning laser ophthalmoscopy; SLO) and is defined relative to the macular lesion[7,16] or anatomic reference marks, such as the position of the optic disc.[17] Aulhorn[18] showed that eccentric fixation can be demonstrated perimetrically by the shift of the blind spot and scotoma. Although Rohrschneider et al.[6] and Sunness et al.[7] described characteristics of fixation in SMD, questions about the development of eccentric fixation remained unanswered. SMD progression was investigated in two longitudinal studies,[19,20] but the development of eccentric fixation was not considered in either of them.

In a previous report, we demonstrated that the FL found by Tübingen perimetry (TP) and the PRL found by SLO show good correspondence.[14] In this study, we sought to describe the development of eccentric fixation in patients with SMD retrospectively by analyzing a large number of 30° visual fields.

Materials and Methods

Tübingen Perimetry

Manual TP (Oculus, Wetzlar, Germany) was performed in standard conditions,[21] using the central 30° of the visual field with a 3.2-cd/m^2 background luminance and a 30-arcmin light spot as a fixation mark of 320 cd/m^2. The test target was moved at a velocity of 1° to 2°/s, target diameter was 10 arcmin, and intensity was 320 cd/m^2 (repeated with at least three lower light intensities; Goldmann standard).

In automated TP (Oculus), a four-point, diamond-shaped fixation mark (320 cd/m^2) with a size of 4° or 2° was used. The background luminance was 3.2 cd/m^2. The test was performed using a threshold strategy to determine light sensitivity in 67 points in the central 30° visual field. Threshold determination begins when a stimulus is presented with the expected intensity adjusted for the patient's age and eccentricity in every point (expected threshold). If the patient does not see the stimulus, the intensity is increased in 10-dB steps until the subject reports seeing it. At this point, the intensity is recorded and is then reduced in 5-dB steps, until the subject cannot see the stimulus. The threshold is determined by averaging the reversal points.

Patients were instructed to look at the fixation mark and keep their gaze in this direction as stable as possible during the examination.

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TABLE 1. Distribution of Patients Who Had One to Nine Visual Field Tests in a Period up to 24 Years of Follow-up*

		Number of visual fields									
		1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**sum**
Follow-up duration (years)	**0**	79									**79**
	1		8								**8**
	2		13	1							**14**
	3		12	4	1						**17**
	4		3	5	1						**9**
	5		10	2			1				**13**
	6		1	3					1		**5**
	7		4	1	2						**7**
	8		2	3		2					**7**
	10		2			1		1			**4**
	12			1					1		**2**
	14				1						**1**
	15					1					**1**
	16			1							**1**
	17			1					1		**2**
	19									1	**1**
	20					1					**1**
	24						1				**1**
	sum	**79**	**55**	**22**	**5**	**5**	**2**	**1**	**3**	**1**	**173**

* White background, <4 years follow-up; light gray background, ≥4-<8 years follow-up; gray background, ≥8 years follow-up.

Patients and Inclusion Criteria

All patients with a diagnosis of the classic form of SMD were included. To avoid discrepancies, we excluded patients classified as having fundus flavimaculatus, those with visual field loss in the periphery, and those with other eye diseases.

A preselection was performed from 783 visual fields of 184 patients in our archives, 114 visual fields were excluded due to poor demarcation of the blind spot (see criteria in the Analysis Procedure section). As a result, 669 visual fields (361 performed by manual and 308 by automated perimetry) of 173 patients represent the total sample. Patients' ages at the first test ranged from 7 to 55 years, and 53% were males. Refractive errors were never higher than ±5.0 D, and the best correction was routinely used during perimetry.

It would have been desirable to know the duration of the disease, but the onset could not be determined from the available data, so that only age at the first visual field measurement can be considered.

The research was conducted in accordance with the Declaration of Helsinki.

Number of Visual Fields and Follow-up

The 669 visual fields included were obtained in 352 visits (at 317 visits, both eyes were tested, in 35 only one eye). Table 1 lists the patients for whom we obtained one to nine visual field test results in a period of up to 24 years of follow-up.

In summary, 79 of 173 patients were examined only once and 94 had two visual field tests or more. Of these 94, 21 had a follow-up duration of 8 years or more and a mean of one visual field test every 2.3 years; 34 patients had a follow-up duration between 4 and 8 years, and mean of one visual field every 1.4 years; and 39 patients were followed up for 3 years or less and had, on average, one visual field result every 6.8 months.

Analysis Procedure

The FL measured in the visual fields corresponds to the preferred retinal locus (PRL). However, FL refers to visual field locations, whereas PRL denotes a location on the retina and is derived from fundus images. Thus, if the scotoma is shifted upward, the new visual field center (FL) is placed below the scotoma, which means that the patient uses a PRL above the foveal lesion. Figure 1I illustrates four possible FL locations.

Visual fields were scanned with a commercial scanner (CanoScan LiDE; Canon Europa NV, Amsterdam, The Netherlands) at 600 dpi. Blind spot location was performed with custom imaging software, a Windows-compatible application developed in a Delphi 5 environment (Fig. 1II).

Measurements were performed in two steps: First, the examiner calibrated a transparent image to be superimposed on the visual fields by clicking on the center of the chart and on a 30° mark along the horizontal axis. Second, a template (light blue frames in Fig. 1-II) containing the original position of the blind spot was adjusted.

The coordinates of the center of the template's blind spot were 15.5° nasal and 1.5° inferior to the visual field center, with a height of 7.2° and a width of 5.2°. These dimensions are based on normal values,[21] and the coordinates of the blind spot's center are in agreement with the estimated center of the optic disc head measured by SLO[17,22] and confirmed in a previous study by our group.[23]

The template could be shifted manually (in steps of 1°) to match its blind spot to the blind spot of the visual field; the program registered the distance between the original and the new visual frame center in Cartesian coordinates (Figs. 1, 2).

There are two main factors that account for the variability of this method: (1) the anatomic variations in the relation between fovea and optic disc position: the SE in vertical and horizontal is 0.9 to 1.1° and 0.8°-0.9°, respectively[17,22]; and (2) the quality of the patients' responses during the visual field measurement and the error attributed to the manual templates movements (blind spot delimitation and size).

In manual perimetry, we allowed the radius of the blind spot to be no larger than 1° vertically or horizontally compared to the template's blind spot (Fig. 2); this leads to a maximum blind spot area of 52 deg^2 which corresponds approximately with values found in normal subjects by using automated kinetic perimetry (maximum: 49 deg^2).[24] This

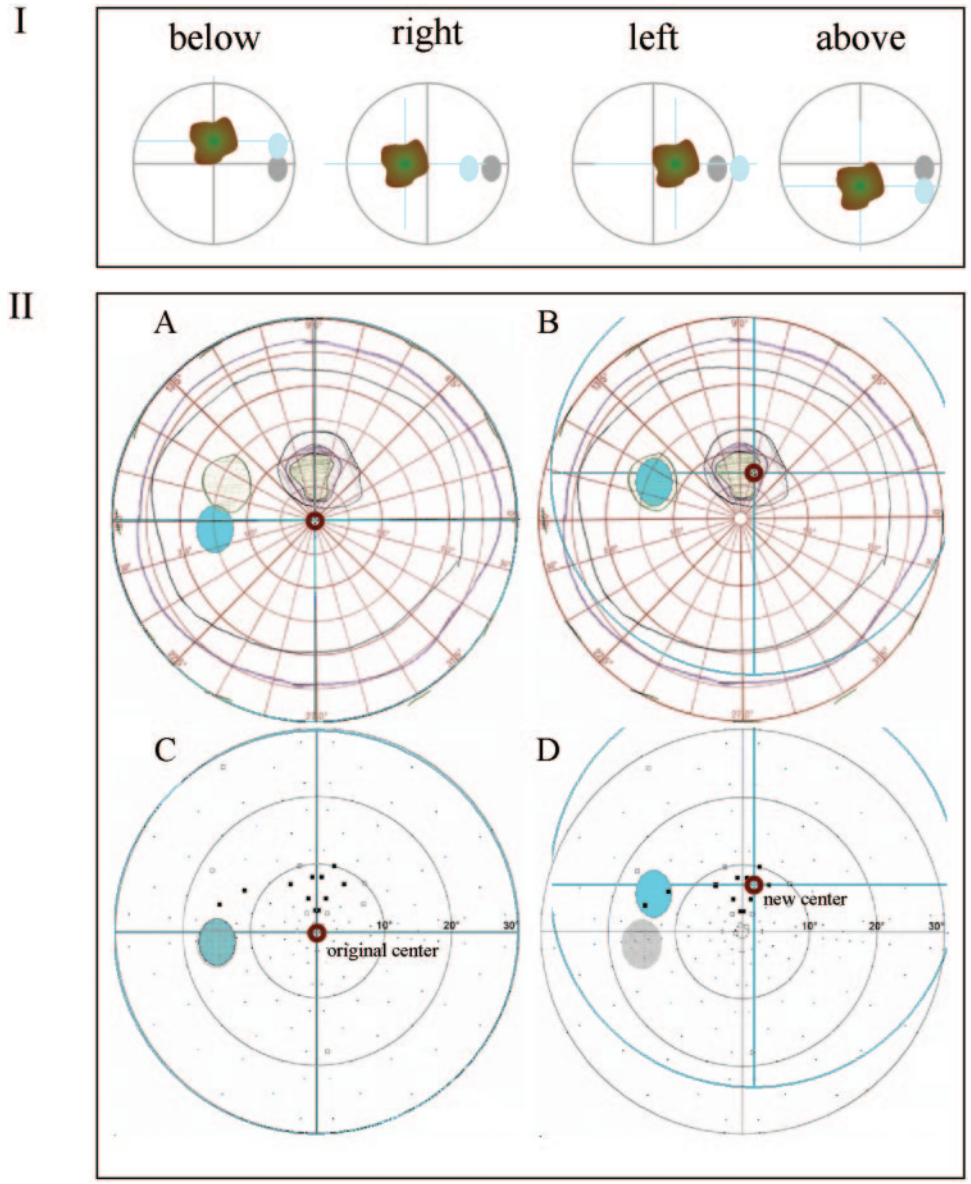

FIGURE 1. **(I)** The scheme illustrates the relationship between the blind spot, visual field center, and shifted scotoma for four different FL locations. First on the *left*: an example of a scotoma and blind spot shifted upward, with the FL placed below the scotoma. **(II)** The measurement procedure is shown in **(IIA)** and **(IIC)**: Visual fields superimposed by a calibrated transparent shape (*blue frames*) with the presumed foveal center and the original blind spot position (based on measurements in normal subjects.[21] **(IIB, IID)** The transparent shape is shifted to be aligned with the new blind spot position. *Red* points are placed on the center of the transparent shape. They represent the original visual field center in **(IIA)** and **(IIC)**, and the shifted center in **(IIB)** and **(IID)**.

dimension would add an uncertainty of ±1°, considering the optic disc position's standard deviation of 1.1° vertically and 0.9° horizontally (with SLO). Therefore, we can estimate that the FL determined with kinetic perimetry in this method would vary ±3.1° vertically and ±2.8° horizontally (two times SD +1°).

In automated perimetry, the template's blind spot was placed so that it intersected at least two test points with lowest sensitivity that could be isolated from the scotoma and considered as part of the blind spot. In examinations in which the template's blind spot fitted only two test points (example in Figs. 1, 2), the template could have been shifted 4.5° vertically and 1.5° horizontally and would have still kept the two points within the template's blind spot (Fig. 2). Therefore, we can estimate the "worst case" uncertainty by determining the fixation position with static perimetry at ±5.6° vertically and ±3.3° horizontally (two times SD +4.5° vertically and +1.5° horizontally). However, in these cases the examiner (AM) tried to place the two points in the center of the template's blind spot. We consider it reasonable to assume that in blind spots represented by only two points, these two points probably represent the center of the blind spot, because the points at the margin are more likely to be missed due to eye movements in fixation instability.

There are two main limitations of this method: (1) blind spot shifting smaller than 1° without a clear scotoma shifting could not be detected; and (2) a paracentral scotoma simulating a shifted central scotoma in association with ambiguous blind spot position would cause erroneous assumption of eccentric fixation. But we consider both to be very rare situations.

Scotoma Classification

The scotomas were divided into four categories:

ABSOLUTE: areas of no perception at maximum stimulus intensity (1000 apostilbs for manual perimetry and 20 dB below normal in automated perimetry).

RELATIVE: areas with lower sensitivity than normal but above ABSOLUTE.

RING: central island of normal or moderately reduced sensitivity surrounded by absolute scotoma in three or more visual field quadrants.

NO: absence of any scotoma.

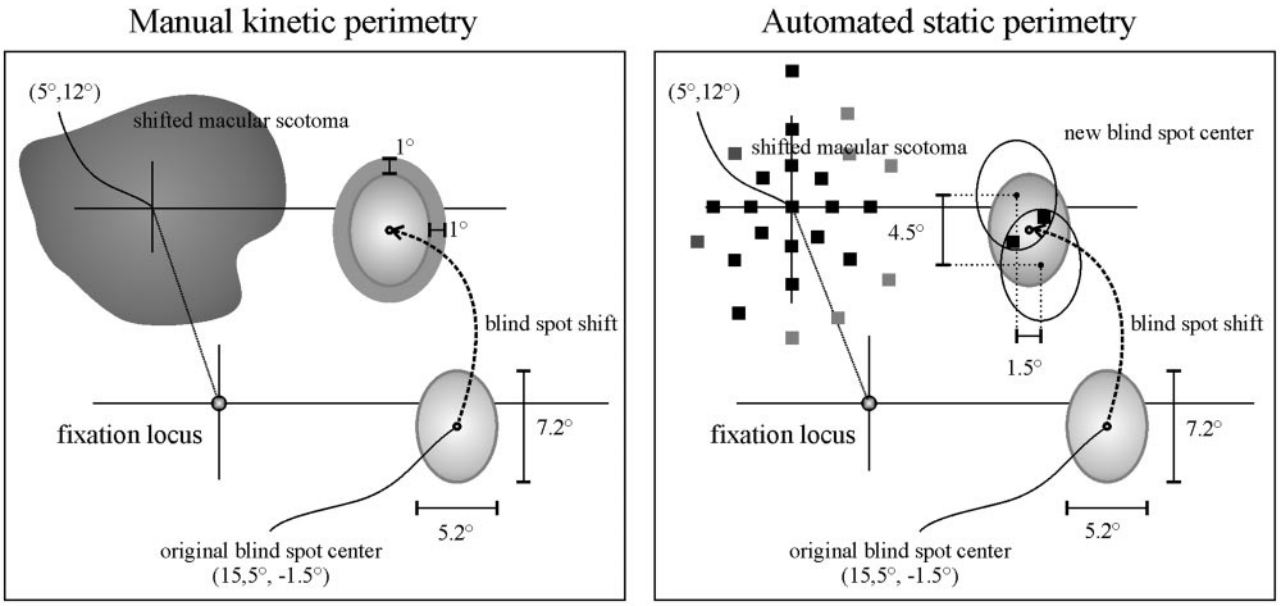

FIGURE 2. Size and position of the template's blind spot (*gray*) and determination of the FL aligning the template's blind spot and the visual field's blind spot. In kinetic TP (*left*) the visual field's blind spot (*dark gray*) was allowed to be 1° larger than the template's blind spot along the vertical and/or horizontal axis. Consequently, in the "worst case" the examiner could have placed the template's blind spot with ±1° additional error (horizontally and/or vertically), although we tried to align both centers. In static perimetry (*right*), the alignment of the template's blind spot was performed to a minimum of two test points with lowest sensitivity that could be isolated from the scotoma and considered as a central part of the blind spot (*squares* within the shifted template's blind spot). In this case, an attempt was made to place the two points in the center of the template's blind spot. However, although unlikely, these two points could in the worst case be from any part of the blind spot, so that an error of 4.5° vertically and 1.5° horizontally could have occurred (worst case). Therefore, in visual fields with only two points delimiting the blind spot the FL must be 4.5° or more apart from the visual field center.

Scanning Laser Ophthalmology

Fixation tests (SLO 101; Rodenstock Instruments, Munich, Germany) were performed in 38 eyes. The fixation mark was a black cross of 36 arcmin width on a bright red background. Custom software (developed in our laboratory) was used to track the position of a user-defined landmark automatically on every video field (50 Hz; PAL), and the PRL was determined using the relation between the coordinates of the tracked landmark, the coordinates of the fixation mark and the coordinates of the estimated foveal position, taking the horizontal (x) and vertical (y) median of the fixation centroid as coordinates of the PRL, as previously described.[23]

RESULTS

Blind-Spot Matching in Central Fixation

Central fixation was found in 319/669 visual fields (250 of them by automated perimetry). The superimposed transparent template always matched the original blind spot, showing that there were no relevant influences from variability in eye size (higher refractive errors were excluded) and/or eye rotations during perimetry.

Symmetry at Baseline

Restricting ourselves to patients for whom we had information from both eyes at baseline (166/173 patients), we observed 98 with central fixation bilaterally, 48 with eccentric fixation bilaterally and 20 with eccentric fixation unilaterally. This finding shows a high degree of association of the two eyes (κ = 74%).

Scotoma Type at Baseline

Table 2 shows the distribution of scotoma type and fixation behavior at baseline. RELATIVE scotoma is the only scotoma type that occurred in central fixation and in eccentric fixation; RING scotoma was always associated with central fixation and ABSOLUTE scotoma with eccentric fixation. As expected, eyes with NO scotoma always showed central fixation.

TABLE 2. Distribution of Scotoma Type and Fixation Behavior at Baseline in Central and Eccentric Fixation

	Total				Central Fixation				Eccentric Fixation			
			Age (y)				Visual Acuity				Visual Acuity	
Scotoma	Eyes (n)	%	Min	Max	Eyes (n)	%	(logMAR)	Decimal	Eyes (n)	%	(logMAR)	Decimal
ABSOLUTE	95	28.0	8	63	0	0	—	—	95	28.0	0.86 ± 0.02	0.14
RELATIVE	40	11.8	12	56	15	4.4	0.62 ± 0.08	0.24	25	7.4	0.90 ± 0.06	0.12
RING	161	47.5	7	60	161	47.5	0.45 ± 0.02	0.35	0	0	—	—
NO	43	12.7	8	30	43	12.7	0.49 ± 0.09	0.33	0	0	—	—

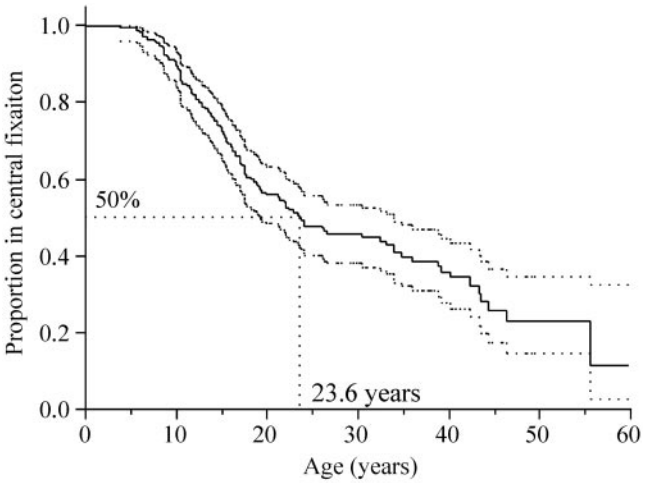

FIGURE 3. Proportion of the patients who keep central fixation in both eyes as a function of age. Curves are the result of product-limit survival estimation (Kaplan-Meier): *Solid curve*: survival estimate; *dashed curves*: upper and lower limits of the 95% confidence interval. The median age when patients began to display eccentric fixation was 23.6 years.

Of the 339 eyes evaluated at baseline, 161 (47.5%) showed a ring scotoma, which occurred in patients aged from 7 to 59 years, and the maximum time that a patient continued showing a ring scotoma in successive visual fields was 18.8 years (median = 1.7 years). An absolute scotoma was found in 95 eyes (28.0%), all of which showed eccentric fixation.

Visual Acuity at Baseline

Visual acuity (VA) ranged from −0.08 to 2 logMAR (20/15–20/2000; upper 90% quantile = 1 logMAR or 20/200) and was better in eyes with central fixation than in eyes with eccentric fixation at baseline. Taking only the worse eye per patient that presented central or eccentric fixation bilaterally, mean VA ± SE in eyes with central fixation was 0.47 ± 0.02 logMAR (20/60) and with eccentric fixation, 0.87 ± 0.03 logMAR (20/150; $P < 0.01$).

Eccentric Fixation and Age

To estimate the rate of eccentric fixation as a function of age, we included all patients: those who kept central fixation, those who showed the transition, and those who presented with eccentric fixation since the first visual field.

After the maximum-likelihood principle, there are three possible assumptions: (1) For eyes that kept central fixation until the last test, the patients' age at the last test were censored (according to Kaplan Meier analysis); (2) if a transition from central to eccentric fixation was observed, it was estimated to have occurred between the last observation with central fixation and the first observation with eccentric fixation; and (3) if the transition had occurred before the first test, the contribution to the likelihood is given by the half of the age at the first test.

Kaplan-Meier analysis was performed to determine the relationship between probability of eccentric fixation and age. A total of 104 patients adopted eccentric fixation either at baseline (70 patients) or during follow-up (34 patients), and 69 patients kept central fixation during follow-up (censored) (Fig. 3). The estimated median age for development of eccentric fixation was 23.6 years. There was considerable variability concerning probability of eccentric fixation depending on age. Considering the first and last quartile, there is a 25% chance of the development of eccentric fixation before the age of 14.6 years and a 25% chance of having eccentric fixation after the age of 46.5 years.

There was a statistically significant cohort effect, showing that in patients with early birth dates eccentric fixation developed later in life than in patients with late birth dates. For example, patients who were born before 1970 changed from central fixation to eccentric fixation, on average, at age 39 years, whereas patients born in 1970 or later changed from central fixation to eccentric fixation at age 15 years (log-rank test $P < 0.0001$) (see the Discussion section).

FL Placement in Eccentric Fixation

For this analysis we considered only one visual field per eye that showed eccentric fixation. If there was more than one visual field showing eccentric fixation for the same eye, we selected one examination with the best demarcated blind spot.

Of 104 patients (203 eyes) who used eccentric fixation in at least one eye during the entire follow-up period, in 154 (75.9%) eyes the FL was placed below the scotoma (scotoma shifted upward; PRL above the foveal lesion); in 33 (16.3%) eyes, it was placed to the left of it, in 11 (5.4%) to the right of it, and in 5 (2.5%) above it (Fig. 4).

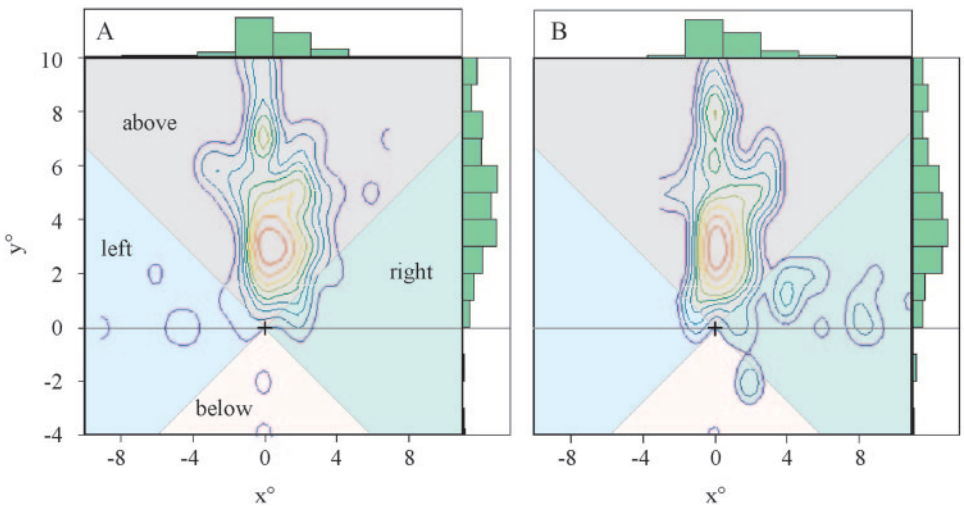

FIGURE 4. Distribution of the blind spot and scotoma shifting direction of *left* (**A**) and *right* (**B**) eyes that experienced eccentric fixation. The data are summarized taking one visual field per eye. The quantile density estimation is used to divide the visual field into contours that represent quantile areas of 10%. *Centered black cross*: the new visual field center, thus the new FL. The histograms on *top* and at the *left* of the graphs' borders show the distribution of the coordinates x and y separately and show a clear preference for scotoma shift to the upper visual field (85.9%), which means fixation below the scotoma.

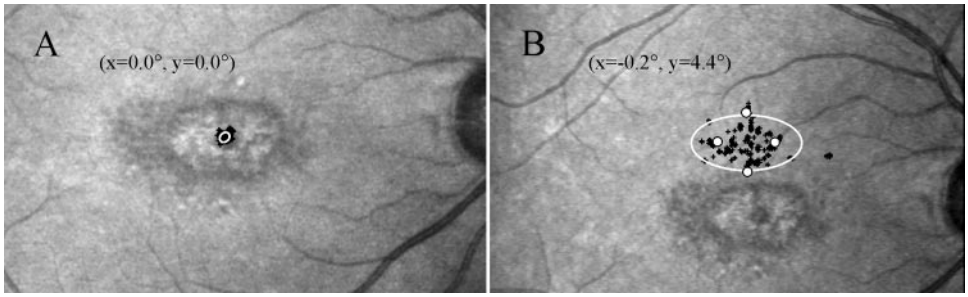

FIGURE 5. SLO images of one patient's fundus showing different fixation behavior with different fixation targets—a typical feature in a ring scotoma. *Crosses*: fixation points during examination; *white ellipse*: 90% bivariate ellipse which represents the PRL centroid. (**A**) Central fixation was used with a 36 minarc cross as fixation target, but eccentric fixation (**B**) was used when the target was a 4° diameter diamond (represented by the four *white dots*).

Symmetry of FL Placement

As all visual fields were monocular, we investigated the symmetry of the FL location in patients with eccentric fixation in both eyes at the same day ($n = 79$). Of these, 58 (73%) placed the FL in the same visual field sector in both eyes (56 below, 1 above, and 1 to the left of the scotoma).

Comparison with SLO

Of the 38 eyes examined by SLO, 11 showed central fixation in both measurements, 25 showed eccentric fixation with both methods, and 2 showed central fixation in the SLO when the fixation mark was a cross of 36 arcmin and eccentric fixation in TP. However, eccentric fixation was also found in these eyes when performing the SLO test using a 4° diamond-shaped fixation mark (see example in Fig. 5).

Figure 6 shows an example of eccentric fixation found by both methods, with the PRL at coordinates $x = 0.1$; $y = 6.4$ and the FL at $x = 0$; $y = 7$. Of interest, in this example, the PRL was placed distant from the lesion border, but in perimetry, this FL was placed within the relative scotoma area, which shows that the scotoma can be larger than the visible lesion.

Considering eyes that showed eccentric fixation in both methods ($n = 25$), the mean distance ± SE between FL determined by TP and PRL determined by SLO was 1.90 ± 0.20°. Up to 10° eccentricity there was no correlation between eccentricity and the difference between the FL and PRL ($r = 0.08$; $P = 0.1132$).

Variation of the FL Position over Time

Eyes that fixated eccentrically never fixated centrally again in subsequent tests.

In eccentric fixation, there was a tendency to keep the new FL in the same visual field area in subsequent tests. To determine the variability of FL position after development of eccentric fixation in eyes that showed eccentric fixation in at least 2 visual fields (53 patients, 92 eyes), we calculated the distance of subsequent eccentric FLs and their mean position. The mean of the maximum distances found per eye was 1.76 ± 1.05°, after an average follow-up duration of 6.23 years, which shows the small variation of FL position over time. Figure 7 shows an example of scotoma shift directions measured at five different times in one eye.

Visual Acuity and Follow-up

Testing the effect of follow-up duration on VA, an analysis of variance showed that VA became worse with time at a rate of 0.02 logMAR per year. This rate was higher after development of eccentric fixation: 0.23 logMAR per year ($P < 0.01$).

Considering the 34 patients who could be measured before and after adopting eccentric fixation, with a median of three visual fields per eye and a median time interval between two consecutive tests of 2.3 years, they showed a median interval between the last test with central fixation in both eyes and the first test with eccentric fixation in at least one eye of 2.1 years. For this subset, visual acuity measured in the last test with central fixation did not show statistically significant correlation with the time interval until eccentric fixation was adopted ($r = 0.01$; $P = 0.964$). This shows that worse VA with central fixation did not lead to a faster development of eccentric fixation (Fig. 8).

DISCUSSION

The course of Stargardt's disease is marked by central vision loss and development of eccentric fixation. In this study, we showed that perimetry can be a reliable method for assessment of fixation behavior. Its advantage is that it is a standardized method that it is available in most ophthalmology clinics.

However, it is not always possible to determine the FL in visual fields. In this cohort, 114 of 783 tests could not be analyzed due to absence or poor delineation of the blind spot. Moreover, if a patient develops a paracentral scotoma simulating a shifted central scotoma, in association with an ambiguous blind spot position, this could be erroneously interpreted as

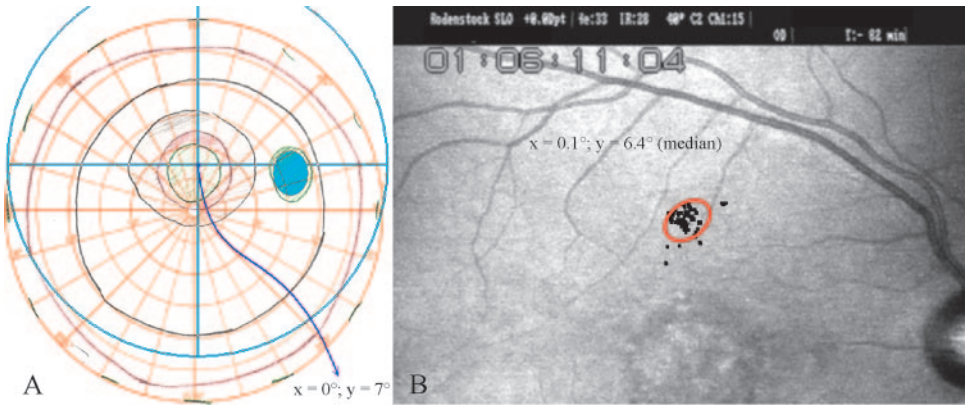

FIGURE 6. Example of FL assessed by Tübingen perimetry (**A**) and SLO (**B**). (**A**) The *solid blue area* is superimposed on the visual field, matching with the blind spot position. (**B**) *Black points* placed above the damaged macula represent the fixation points and the *red* ellipse is the 90% bivariate ellipse that represents the PRL centroid. In both methods the eccentric fixation was identified: coordinates measured in the visual field are x, 0°; y, 7° (corresponding to the direction of the scotoma/blind spot shift), whereas x, 0.1; y, 6.4° recorded by SLO refers to the PRL coordinates (medians of the points' coordinates).

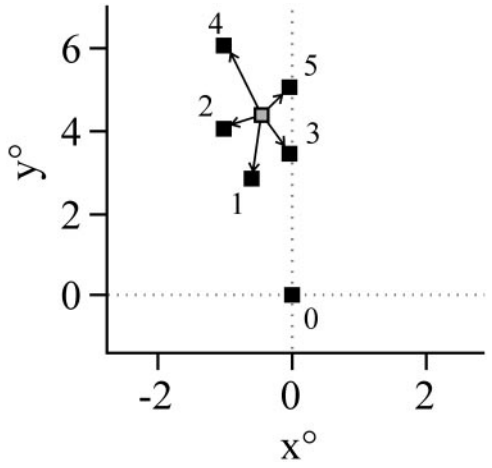

FIGURE 7. Example of blind spot and scotoma shift directions measured at five different times in one eye. *Black squares*: position of the shifted visual field center; *gray square:* the mean between the eccentric points; *arrows:* the distances between eccentric points and their mean. This patient's baseline visual field was recorded in 1982 when he still used central fixation (0). The first visual field test that showed eccentric fixation was performed in 1984 (1), the second in 1986 (2), the third in 1987 (3), the fourth in 1988 (4), and the fifth in 1989 (5). In all of them, the scotoma was shifted roughly into the same visual field area. This example shows that patients do not change the sector of the visual field used for placing the eccentric FL.

eccentric fixation. Nevertheless, if the blind spot is clearly delimited, visual fields can be used as an alternative, especially in retrospective evaluations or if fixation cannot be determined by direct fundus controlled devices (e.g., SLO). In doing so, the determined coordinates must be interpreted carefully and in association with other information about the fixation behavior, such as scotoma size and position, and funduscopic examination.

The PRL can be defined as the median of all fixation points recorded by SLO, whereas the FL is determined by the position of the blind spot. Despite discrepancies between methods (different stimulus contrast and pattern; as well as the fixation target) and uncertainties in the determination of the psychophysical blind spot, their good agreement shows that in cases with a well-established PRL (for details about SLO examination see Reinhard et al.[23]) visual fields can allow a correct determination of the FL.

For the patient, knowledge about the FL is essential for rehabilitation, especially for reading, as one of the most important tasks in everyday life. We found that SMD patients often go through an intermediate phase before an absolute scotoma develops, showing a ring scotoma that can persist for up to 18.8 years. This phase can be critical for the patients in dealing with everyday tasks. The fovea maintains good visual acuity, but the central island may be too small for reading.[14] This phenomenon is evident in Figure 5, where a small cross is fixated centrally, but a 4° diameter diamond is fixated eccentrically.

In agreement with a previous report,[20] our data show that most of the SMD patients ultimately reached a visual acuity of 1 logMAR (20/200). Furthermore, visual acuity at the last test before eccentric fixation was adopted was not a predictive factor for the time needed for the development of eccentric fixation. This finding can be explained by the presence of the central ring scotoma, which can be associated with good or reduced visual acuity (e.g., the remaining fovea inside the ring scotoma may not be sensitive enough for recognizing an optotype), but can still be used to fixate the target in perimetry.

We estimated a median age for development of eccentric fixation of approximately 23 years. However, there was considerable variability concerning age and eccentric fixation, and this may reflect the different disease phenotypes, and the reported wide age ranges for the onset of symptoms.[2,4] Unaccountably, there was a statistically significant cohort effect showing that patients with early birth date developed eccentric fixation later in life compared with patients with late birth date. We believe that this is a bias in our data, provoked mainly by two factors: (1) once eccentric fixation has been adopted, visual field control testing was no longer performed on a regular basis and possibly therefore fewer older patients with early birth date who showed longstanding eccentric fixation were included in the study; and (2) the awareness and knowledge of eccentric fixation has been much higher in later decades, which may have provided the patients with more information about the benefits of using of an eccentric FL.

Most SMD patients in this study placed their eccentric FL below the scotoma (i.e., the PRL above the lesion on the retina; Fig. 4). This is in accordance with our former study that also showed a clear predominance of the new FL to be placed on the lower visual field.[14] The preference for the upper retina (i.e., the lower visual field) cannot be explained by the spatial resolution in this area, since the cone and ganglion cells ratio distribution is radially asymmetrical, with the horizontal meridian having a higher density than the vertical.[25] However, placing the new FL between central scotoma and blind spot or in the temporal side of the scotoma would constrict lateral eye movements during reading, which requires a minimal horizontal visual field area.[15,26–29]

In a review, Trauzettel-Klosinski[28] discussed the questions related to the preferential directions that patients with macular scotomas use to find the new FL in the visual field and concluded that placing the FL below the scotoma (upper retina) is considered favorable for horizontal reading, because it does not cover any part of the current line to be read. Accordingly, in reading tasks not involving eye movements, Petre et al.[30] showed that the fixation area plays an important role in reading performance.

Furthermore, it has been shown that a favorable FL can be trained to achieve better conditions for reading.[31] However, it has been shown in several studies that patients with macular scotomas and different diagnoses without goal-directed training establish the PRL in the upper retina much less frequently.[16,32]

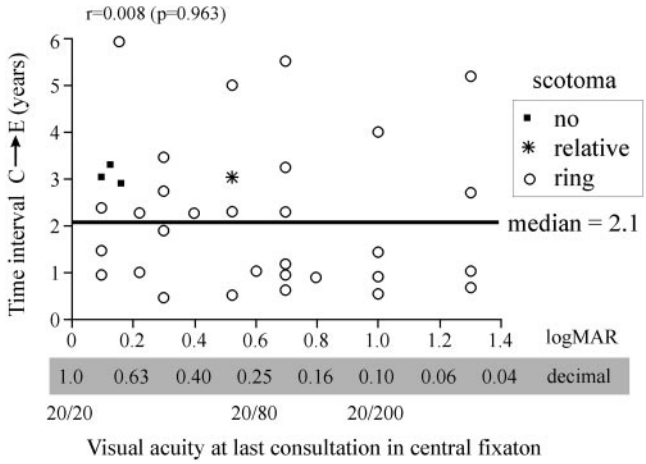

FIGURE 8. Relationship between interval from the last test with central fixation and the first test with eccentric fixation and the visual acuity at last test with central fixation. VA at last test with central fixation was not a predictor of the time necessary for development of eccentric fixation.

After an eccentric FL is developed, patients with SMD tend to keep the FL in the same area of the visual field in subsequent tests, which indicates a preference for a certain FL location that can be influenced by preexisting individual features. For instance, Altpeter et al.[33] presented evidence that focal visual attention mechanisms can influence the preference by demonstrating that areas with high attentional capabilities are candidates for a future FL.

In conclusion, patients with SMD experience development of a central scotoma, and they frequently choose one eccentric FL. However, this development is often delayed by the presence of a ring scotoma, which may persist for different periods. Once fixation is eccentric, SMD patients tend to keep the same FL over time, and there is a preference for placing the FL below the scotoma.

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