Macular pigment and fixation after macular translocation surgery

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Keywords:

macular pigment, fixation, Scanning Laser Ophthalmoscope, macular translocation

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Abstract

Background: After full macular translocation (MT) surgery with 360 degrees retinotomy, the fovea is rarely identifiable. Our aim was to verify the position of the fovea, to determine how patients fixate after MT and to examine distribution and optical density of macular pigment (MP).

Methods: 9 patients after MT were investigated. The Utrecht Macular Pigment Reflectometer was used to quantify the MP optical density. A Scanning Laser Ophthalmoscope (SLO) was used to identify the fovea as the centre of MP distribution and determine the retinal locus of fixation.

Results: In all patients, we identified the fovea as the centre of MP distribution. The retinal areas used for fixation were displayed by SLO fixation analysis. Comparing their spatial relationship with the fovea, five patients fixated centrally and four eccentrically up to 7.5 degrees. In those patients, microperimetry showed that the atrophy caused by choroidal neovascularization (CNV) extraction prevented central fixation.

Conclusion: The combination of MP distribution and fixation analysis permits quantifying fixation behaviour even if the fovea morphologically cannot be localized. Our results suggest that the scotoma caused by spreading chorioretinal atrophy is the main cause for reduced visual acuity after MT and therefore the MT rotation angle is crucially important.

(200 words)

Introduction

Macular translocation (MT) with 360-degree retinotomy has been introduced in 1993 by Machemer and Steinhorst.[1] During the vitrectomy, the retina is completely detached from the retinal pigment epithelium (RPE) and the choroidal neovascularization is removed. The retina is turned around the optic nerve head in an angle of 30 to 40 degrees in order to place the fovea on a healthy-appearing RPE region. Following the translocation surgery, the eye is filled with silicone oil for several months and is counter-rotated by extraocular muscle surgery (Figure 1). Usually, the translocation surgery is preferred in the last eye if the fellow eye has a central disciform scar secondary to age-related macular degeneration (AMD) or in monocularly viewing patients. Although the indications for MT have been reduced since anti-VEGF therapy is available, it is still an important therapy option in cases of extensive subretinal hemorrhage, rupture of the RPE or if the anti-VEGF therapy fails.[2]

Since the MT technique was introduced, it was unclear whether patients used their original fovea or an eccentric preferred retinal locus (PRL) for fixation. In the majority of patients undergoing MT, it is not possible to identify and localize the original fovea after translocation because the morphology of the central retina has changed as due to macular disease, the vitrectomy and a spreading chorioretinal atrophy resulting from the surgical extraction of the chorioretinal neovascularisation. Therefore, it is not obvious whether patients fixate foveally or not after MT surgery.

We have recently introduced a new fixation quality index that allows precise quantification of the retinal locus of fixation and its stability in patients with macular diseases.[3] In this method, the position of the original fovea is estimated by using the optic nerve head position,

which is the best available measure in patients with severe morphologic changes in the macular region. However, in patients who have undergone MT surgery, this method is not suitable because the spatial relation between optic nerve head and original fovea can not be predicted anymore after surgical rotation of the retina and counter-rotation of the eye.

Therefore, we used the macular pigment, located in the retinal Henle fibre layer, as a physiological retinal marker for the original fovea. (The macular pigment should not be confused with the RPE and is, as an inner-retinal pigment, rotated together with the whole retina during MT surgery.) We measured the MP distribution and overlaid it with the retinal area that was used for fixation in patients having undergone MT surgery. Our main questions were whether the post-MT-surgery patients fixate with their original fovea. We further analyzed the influence of the fixation stability and the location of the PRL on visual acuity.

Materials and Methods

Patients

We investigated 9 patients (9 eyes) after MT with 360-degree-retinotomy. All had a subfoveal CNV; in 8 eyes the CNV as due to AMD and in the remaining 1 eye due to pathologic myopia (patient no. P1-02). 5 were males and 4 females, the age of the AMD patients was 74.8 ± 5.8 years (mean $\pm$ SD); the myopic patient was 39 years old. The mean time interval between the examination and the MT was 2.1 ± 0.9 years. Best corrected visual acuity before translocation ranged from 20/666 (0.03) to 20/80 (0.25) and after translocation from 20/666 (0.03) to 20/50 (0.4). All patient data are shown in Table 1. None of the subjects had received eccentric viewing training before. Patients gave their informed consent before recruitment. The study was approved by the ethics committee of the Tübingen University Hospital, and it conformed

to the tenets of the Declaration of Helsinki. The surgical technique was described elsewhere.[2]

Fixation monitoring

We used a Rodenstock SLO 101 (Rodenstock, Ottobrunn, Germany) to image the fundus and to measure the fixation behaviour and the distribution of the macular pigment. For fixation assessment, we projected a bright red fixation cross of 36 arcmin diameter and 3.6×10^4 trolands on a dark background (Michelson contrast 0.986) onto the patient's retina for 10 seconds. We asked the patient to look at the cross the way he/she sees it best. The SLO video recordings were digitized and processed by image analysis software [3] that tracks the retinal movements automatically and draws the fixation plot, onto the SLO image of the retina showing those retinal locations used to fixate the cross (Figure 3C). Temporal resolution was 50 per second by analyzing every video field (half frame). The position of the PRL was defined as the medians of the horizontal and vertical distributions of all retinal coordinates.

Microperimetry

For the determination of spatial retinal function, we used custom developed SLO microperimetry software using gaze-contingent stimulus placement.[4] This method represents a further development of Rodenstock microperimetry and allows retinal function testing with automatic real-time correction for eye movements. The software detects retinal movements by tracking a vessel branching 25 times per second in every video frame and shifts the stimulus automatically if an eye movement occurred. If the eye moved during a stimulus presentation (120 ms), the patients' answer was automatically discarded. We used this method to detect the border of the absolute scotoma resulting from CNV extraction using a stimulus size corresponding to Goldmann III stimulus (0.43 degrees diameter).

Spatial distribution of the macular pigment and localization of the fovea

Fundus reflectance maps were recorded at 488 and 514 nm Argon laser wavelengths with the SLO that is equipped with an Argon laser (Figure 2). If the fundus was imaged with blue 488 nm Argon light, the pigment absorbed the light because of its specific absorbance spectrum and the macular region appeared black. The green Argon light (514 nm) causes only low absorption by the pigment. Peripheral retinal areas have approximately the same reflection characteristics for both wavelengths, apart from a small difference in the lens optical density. Since the lens and the macular pigment are the only absorbers in this wavelength region, digital subtraction at two wavelengths of log reflectance maps provided density maps of the sum of both absorbers, i.e. the spatial distribution of the pigment. Note that the reflectance images were first aligned, using anatomical landmarks such as retinal blood vessels. We fitted the observed density distribution with a Gaussian distribution on a constant background.[5,6] The retinal position with the highest MPOD was considered as the position of the fovea.

Retinal fixation locus and stability

The centre of the fixation plot, i.e. its x- and y-median, defines the preferred retinal locus used for fixation (PRL), as described previously.[3] We compared its position with the position of the fovea. A spatial distance between PRL and the fovea less than 1 degree was considered as a central fixation. To quantify the fixation, we used the fixation stability index [3] (FSI). In brief, this index does not depend on a normal distribution of the fixation data and quantifies the number of all ‘new’ locations on the retina that are used for fixation even if multiple PRL are present. Theoretically, ‘perfect’ fixation uses only one location and, thus, has an FSI of 100 %. Additionally, we calculated the conventional BCEA values of the fixation stability in order to allow easier comparison with previous work of other groups.

Optical density of the macular pigment

The recently developed Macular Pigment Reflectometer (MPR) has been used to quantify the MPOD at the retinal locus of fixation. The MPR has been described in detail by Van de Kraats et al.[7] In short, the clearly visible illumination beam was set in the subject's pupil a little above its centre, allowing room for the invisible detection beam. After calibration of the reflectance and focusing of the light beam on the retina, patients were asked to fixate a 1-degree white light spot (retinal illuminance 1.04×10^7 Troland, and retinal irradiance 4.6 mW/cm^2). At the pupil position with highest reflectance, 5 measurements were performed. For the safety of the patients, a UV-cutoff filter was used (GG395, Schott, Mainz, Germany). Calculated maximum safe exposure times are 26 min. for healthy eyes, and 20 min. for aphakics (Health Council of the Netherlands, committee on optical radiation. Health based exposure limits for electromagnetic radiation in the wavelength region from 100 nanometer to 1 mm“, Health Council of the Netherlands, The Hague, 1993). With a separation of 0.8 mm, the reflected light is caught by a detection pupil located underneath the illumination pupil. Finally, the reflected light is spectrally analyzed by a fibre spectrometer (Ocean Optics SD2000, Ocean Optics Inc, Dunedin, Florida). A wavelength range of 400–800 nm was used for MPOD analysis by using custom optical modelling software. Briefly, the model contains three reflectors, the inner-limiting membrane (ILM), the cone-photoreceptor discs in the outer segments, and the choroidal space. Anterior to the receptor layer, absorption takes place in the lens and in the macular pigment. Posterior to the receptor layer, absorption takes place in melanin and blood. The Levenberg-Marquardt routine [8] was used by the software to fit the measured data with the optical model by minimizing chi-square values.

Blood samples

Relations between lutein blood concentration and optical density have been described in the literature.[9–11] Plasma concentration of lutein was measured in order to correlate it with the optical density of the pigment. Fasting blood samples were drawn into Monovettes (Sarstedt, Germany) containing EDTA. Plasma was collected after centrifugation at 3000 g for 10 min under light protection. The samples were stored at -80°C until analysis. The analysis of lutein was performed at BioTeSys GmbH, (Esslingen, Germany) using an isocratic reversed phase HPLC method consisting of a pumpsystem (1525 Waters, Eschborn, Germany). In brief, lutein was extracted from plasma, proteins were precipitated and supernatant was used for analysis. Separation was performed with a C18-column and the peak detection occurred with UV-Vis detector at 445 nm.

Results

Preferred retinal locus, fixation stability and microperimetry

In all 9 patients, the fovea position was clearly identified by calculating the centre of the pigment density distribution. Comparing its location with the position of the PRL, we found that 5 patients fixated centrally, i.e. their PRL was less than 1 degree apart from the fovea (i.e. the maximum of the MP density). By this definition, 4 patients fixated eccentrically. The latter group had a PRL that was 3.4 to 7.5 degrees away from the fovea. In two of the eccentrically fixating patients, the PRL was shifted nasally (towards the optic disc), in one patient upwards, and in one patient temporally. In none of these patients, the PRL was shifted downwards (towards the atrophic lesion). All fixation graphs and the pigment distribution are shown in Figure 4.

Fixation stability ranged from 59.6% to 89.8% (mean in the centrally fixating patients 85.8% and in the eccentrically fixating 71.4%, which was not found as a statistical significant difference). Furthermore, the stability showed no significant correlation with the eccentricity of the PRL, with visual acuity or with time since macular translocation. The clinical data of all patients are shown in Table 1.

All patients who fixated eccentrically used a PRL at the border of the absolute scotoma in the region of the CNV extraction zone.[12]

Visual acuity

The patients' visual acuity before and after MT is graphically shown in Figure 5. Visual acuity after translocation was significantly correlated with the eccentricity of the PRL ($r^2=0.52$; $p=0.04$), but not significantly with the fixation stability. Visual acuity after MT (logMAR) was significantly better in the centrally fixating patients than in the eccentrically fixating ones.

Macular pigment density and lutein serum concentration

The optical density of the pigment varied between 0.11 and 0.59 (mean: 0.23). The lutein plasma concentrations varied between 0.1 and 0.56 $\mu\text{mol/l}$ (mean: 0.29 $\mu\text{mol/l}$). Both parameters were significantly correlated ($r^2=0.64$, $p<0.01$).

Discussion

Extensive chorioretinal and pigment epithelium atrophy following MT has been described before. In a long-term study of patients after MT [13], it was seen in 44 of 90 patients. Cahill et al.[14] compared the occurrence of RPE atrophy between neovascular AMD patients and geographic atrophy patients after MT and found a significantly higher prevalence in the latter. The reason may be that, in both studies, the fovea was not accurately localized and the extent of the atrophic zone was estimated from fundus photographs and/or fluorescein angiographic recordings. In an SLO study [15] on MT patients, microperimetry was performed and the scotoma resulting from the RPE atrophy was determined. It was not reported whether the extent of the scotoma and the morphological atrophy were corresponding.

In eyes after MT with 360 degree retinotomy, the whole retina is turned around the optic nerve head and is tilted in an irregularly way. Thus, it becomes impossible to estimate the foveal position by its spatial relationship to the optic nerve head. By ophthalmoscopy it is difficult to detect the exact position of the fovea in these patients. From the pathophysiological point of view, macular translocation creates an interesting situation: patients with severe submacular changes (in their better eye) are treated in order to restore foveal vision by connecting the central retina with an intact RPE and choroidal substrate.

Therefore, it is interesting whether the patients indeed use their former fovea for fixation. By detecting the fovea through the macular pigment distribution and overlaying it with the fixation curve, the spatial relationship between the morphological fovea and the functional area of fixation can be measured.

We found that more than the half of the patients after translocation fixates centrally. These patients had a significant better visual acuity than the patients who fixate eccentrically. In a recent study [16] about quality of life and reading performance after MT, we showed that reading after MT is still possible. Those patients who fixated eccentrically, showed chorioretinal and pigment epithelium atrophy, which caused an absolute scotoma that involved the foveal region. In the current study, we have shown that the extent of the scotoma was bigger than the morphologic atrophy (Figure 3). The fixation stability of our patients was comparable to those of the MT patients in a recent study on MT versus patch graft in neovascular AMD. [17]

It can be concluded that the expansion of the subretinal RPE atrophy is one crucial point for the postoperative outcome of visual acuity. The bigger the angle of rotation around the optic nerve head and the smaller the extent of the subretinal CNV are, the higher is the probability that the subretinal scar does not involve the fovea.

The measurements of the optical pigment density in our study show that the macular pigment is not destroyed by the MT procedure. After MT, its optical density (mean: 0.23) is reduced compared to normal persons (0.53 ± 0.13) [18], but it is still present and the centre of its distribution can still be determined.

278

279 **Acknowledgment**

280 The authors wish to thank Barbara Wilhelm, MD, University Eye Hospital Tübingen,
281 Germany and Wolfgang Schalch, PhD, DSM Nutritional Products, Basel, Switzerland, for
282 helpful comments on the planning of this study, and Manfred MacKeben, PhD, The Smith
283 Kettlewell Eye Research Institute, San Francisco, for valuable comments on the manuscript.

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294 **Competing interests**

295 There are no competing interests.

296

297

298 **Funding**

299 This study was supported by the Ministry of Science, Research and Arts,
300 Baden-Württemberg (Germany).

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Legends

Figure 1:

Principle of the macular translocation surgery with 360 degree retinotomy. Usually, this procedure is done in extensive submacular haemorrhage (A). The retina is rotated around the optic nerve with an angle of 30 to 40 degrees, i.e. the fovea is shifted upwards (B). The CNV is extracted; this leaves an atrophic choroidal and RPE lesion (white dot). The eye is filled with silicone oil. After a certain period (i.e. half a year), an extraocular muscle surgery is performed and the eye globe is rotated the other way around (C). The atrophic lesion is now located below the fovea. Our principle question was whether the patients use their original fovea for fixating (D).

Figure 2:

SLO visualization of the macular pigment. The relative optical density of the human macular pigment is shown versus the wavelength (white curve in A). Using the infrared diode laser for fundus imaging, the pigment does not absorb IR (B). The green wavelength of the SLO's Argon laser is absorbed moderately by the pigment; using this wavelength for fundus imaging, the fovea appears dark (C). The blue Argon wavelength is absorbed more, the fovea appears very dark (D). Digital subtraction of log reflectance maps of C and D provided density maps of the sum of both absorbers, i.e. the spatial distribution of the pigments.

Figure 3:

A: Fundus photograph of patient P1-15 (2.5 years after macular translocation). The position of the fovea is not recognizable. Around the optic disc, the retinal torsion is visible. B: SLO fundus image of the same patient. C: With our tracking software, the areas on the fundus that

‘touch’ the fixation cross within 10 seconds of fixation recording can be visualized and displayed on the fundus. The small yellow point represents the medians of the distribution, i.e. the preferred retinal locus (PRL). Thus, it is not clear if the patient fixates centrally or not. D: Digital overlay of fixation curve and macular pigment distribution – only now the fovea becomes visible as the centre of the pigment distribution and it is obvious that the patients fixates eccentrically (the PRL is located 3.6 degrees above the fovea). E: The results of microperimetry show that the patient has an absolute scotoma (black dots) with larger extent than the morphologic atrophic zone caused by the CNV extraction. The patient fixates at the scotoma border as near as possible.

Figure 4:

Synopsis of all patients including the fixation curve (red) and the macular pigment distribution (yellow). Left column: Patients who fixated centrally; right column: patients who fixated eccentrically.

Figure 5:

A: Visual acuity of the patients before and after macular translocation (logMAR). Black dots represent the centrally fixating patients, black rectangles the eccentrically fixating ones. The majority of the patients had a better acuity after translocation. B: Visual acuity (logMAR) and eccentricity of the PRL, which were statistically correlated ($r^2=0.52$; $p=0.04$), whereas acuity and fixation stability were not statistically correlated (C).

Table 1

Patient ID	age	eye	fixation	Eccentricity of PRL (degrees)	FSI (%)	BCEA (arcmin ²)	visual acuity (logMAR) before MT	visual acuity (logMAR) after MT	duration since MT (years)	Optical density of macular pigment	Lutein plasma concentration (μmol/l)
P1-02	39	right	central	0.6	89.8	222	0.7	0.7	0.6	0.59	0.56
P1-04	73	right	central	0.6	85.8	267	1.0	0.7	2.7	0.27	0.17
P1-05	69	right	central	0.8	75.2	884	0.6	0.4	2.8	0.11	0.10
P1-08	74	left	eccentric	3.4	67.9	1991	1.0	1.3	0.7	0.31	0.52
P1-10	75	right	central	0.9	85.9	374	1.5	0.7	2.2	0.16	0.10
P1-14	86	right	central	0.7	59.6	3235	1.0	0.9	3.1	0.23	0.36
P1-15	76	right	eccentric	3.6	74.6	1230	1.5	1.0	2.5	0.11	0.20
P1-17	78	left	eccentric	5.9	68.2	8777	0.7	1.0	2.2	0.14	0.21
P1-18	67	right	eccentric	7.5	74.9	1387	1.0	1.1	2.1	0.21	0.35

Table 1: Clinical data of all the patients after macular translocation (MT).