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Retinal sensitivity and fixation changes 1 year after triamcinolone acetonide assisted internal limiting membrane peeling for macular hole surgery – a MP-1 microperimetric study

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ABSTRACT.

Purpose: **To evaluate microperimetric changes 1 year after macular hole surgery with triamcinolone acetonide assisted internal limiting membrane (ILM) peeling.**

Methods: **Twenty-two eyes of 22 patients with stage 3 and 4 idiopathic macular holes of < 6 months' duration underwent vitrectomy with triamcinolone acetonide assisted ILM peeling. Best corrected visual acuity (BCVA) (logarithm of the minimum angle of resolution), and central retinal sensitivity were documented before and 1, 3, 6, and 12 months after surgery. Macular sensitivity (mean sensitivity in decibels -dB), and stability and location of fixation (preferred retinal locus) were determined using MP-1 microperimetry (Nidek). The MP-1 microperimetry sensitivity map was overlaid onto infrared images recorded on a Heidelberg scanning laser ophthalmoscope using dedicated MP-1 software to evaluate the fixation location before surgery. Anatomical success was evaluated with optical coherence tomography (OCT). Optical coherence tomography scans were recorded on an OCT 3000 scanner.**

Results: **Anatomical success was achieved in all 22 eyes. All patients completed 1 year follow-up. No recurrence of macular hole was seen in any patients in the follow-up period. The mean BCVA improved from 0.75 ± 0.2 before surgery to 0.31 ± 0.1 logMAR at the last visit ($p < 0.001$). Mean sensitivity improved from 3.7 ± 0.6 to 5.3 ± 1.0 dB at the last visit ($p < 0.001$). Before surgery, the preferred retinal locus was located on the margin of the hole in all, in 18 eyes on its upper part and in four eyes to the side or on its lower part. Preoperatively, 12 eyes were stable and 10 were relatively unstable, but 12 month after surgery, fixation stability had improved, and 20 eyes were stable and two were relatively unstable.**

Conclusions: **MP-1 microperimetry sensitivity map overlaid onto an infrared image using dedicated MP-1 software can be used successfully to evaluate fixation location in patients with a macular hole before surgery. With microperimetry findings, we can also measure functional macular changes more precisely than using BCVA alone after macular hole surgery. Our results also showed that retinal sensitivity and fixation properties were improved after vitrectomy with triamcinolone acetonide assisted ILM peeling in patients with idiopathic macular hole.**

Key words: fixation location – fixation stability – macular hole surgery – microperimetry – MP-1 – retinal sensitivity

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Introduction

Pars plana vitrectomy with internal limiting membrane (ILM) peeling has become the standard procedure for the treatment of a full-thickness macular hole. Surgical success is measured by anatomical closure of the hole, which is obtained in more than 90% of cases. Removal of the ILM has been shown to lead to good best corrected visual acuity (BCVA) and anatomical results (Brooks 2000). Most studies have reported statistically significant improvements in BCVA (Brooks 2000; Karacorlu et al. 2005; Shinoda et al. 2008). It is well known that some patients with a macular hole do not show satisfactory improvement even if anatomical closure achieved and BCVA improved (Matsumoto et al. 1998; Richter-Mueksch et al. 2007; Wakabayashi et al. 2008). This means that despite the improvement in BCVA and amelioration of metamorphopsia, the central retinal function is not normal, and other types of test must be adopted for interpretation of retinal function (Matsumoto et al. 1998). This is especially important for the cases that triamcinolone acetonide is used to facilitate visualization of ILM. The effect of triamcinolone acetonide assisted ILM peeling on the functional results of macular hole surgery is controversial (Karacorlu et al. 2005; Kwon et al. 2009). Our study attempts to address this issue using microperimetry, which is used clinically for assessment of macular function.

Methods

We identified 22 eyes of 22 consecutive patients with stage 3 and 4 idiopathic macular holes of < 6 months' duration, which were undergoing triamcinolone acetonide assisted ILM peeling for a macular hole. We defined the macular hole duration based on patients' history alone. We excluded patients with moderate to dense lens opacity, corneal opacity, a history of refractive surgery, glaucoma or ocular hypertension, a history of intraocular inflammation such as anterior or posterior uveitis, multifocal choroiditis, a history of retinal detachment, a history of ocular trauma, and optic neuropathy. None of the patients had any medical or ocular conditions that might have affected their retinal function or altered their microperimetry results. Written informed consent was obtained from all patients, and procedures were performed to conform to the tenets of the Declaration of Helsinki. The patients underwent complete ophthalmic examination, including BCVA measurement (with ETDRS chart), slit lamp biomicroscopy, indirect ophthalmoscopy, colour fundus photography, infrared and autofluorescence imaging, optical coherence tomography (OCT). Best corrected visual acuity expressed as logMAR was obtained at a distance of 4 m. Autofluorescence and infrared images were recorded on a Heidelberg scanning laser ophthalmoscope (Heidelberg Engineering, Heidelberg, Germany). Optical coherence tomography scans were recorded on an OCT 3000 scanner (Carl Zeiss Ophthalmic System, Humphrey Division, Dublin, CA, USA). All patients underwent analysis by OCT 3000 scanner (Carl Zeiss Ophthalmic System, Humphrey Division, Dublin, CA, USA) radial line OCT scan producing 6 × 6 mm scans the day prior to surgery. Optical coherence tomography scans were considered to be of good quality and used only if all six radial line images had a signal-to-noise ratio higher than 35 dB, more than 95% of accepted A-scans and signal strength of five or more as recommended by OCT scanner manufacturer. All six scans were examined by an ophthalmologist experienced in OCT interpretation. Macular hole size was measured using callipers in the 'retinal thickness analysis' mode, the scan with the largest distance between edges of the hole was taken to be the most accurate as this was more likely to represent the true diameter of the hole rather than an 'off centre' measurement. From the chosen scan, the shortest distance across the full-thickness defect was defined as the size of the hole as described in previous studies (Ip et al. 2002). Macular sensitivity was evaluated by MP-1 microperimetry (Nidek Technologies, Padova, Italy). The MP-1 provides a 45° nonmydriatic view of the fundus with automated correction for eye movements. We performed microperimetry under room dim light condition. Goldmann I stimuli and a 4-2 staircase strategy were used, and a circular test grid with 46 stimulus locations covering an area of 8° was applied. The white stimuli were projected on a white background with background luminance set to 1.27 cd/m^2 and a stimulus presentation time of 200 ms. The perimetric strategy of the current version of the MP-1 software starts at an initially defined threshold level for each stimulus. A 4-2 staircase strategy is then carried out, and the last seen threshold value is taken as the final threshold. The instrument tests the same luminance levels at all test locations before moving on to the next luminance level (i.e., for all locations one luminance level is projected after the other). Differential light threshold values were compared by calculating 46 points with in 8°, which were averaged automatically by the MP-1 microperimetry software program for mean sensitivity in a polygon. Absolute scotoma was defined as when there was no response to the brightest stimulus. It was categorized as a 'relative scotoma' when a circumscribed area of reduced differential light threshold could be found.

The microperimetry sensitivity map was also overlaid onto other images using dedicated MP-1 software. This software allows for the exact superimposition of sensitivity data to different images separately (infrared, autofluorescence, fluorescein angiography, indocyanine green). The superimposition is obtained by the semi-automatic detection of two identical anatomical landmarks on both images. This software has previously been tested for validity and repeatability (Midena et al. 2007). We superimposed sensitivity data on the infrared image of the Heidelberg scanning laser ophthalmoscope, because of it is one of the best for observing certain characteristics of macular holes.

For the assessment of fixation, the fundus movements were tracked during 46 points with in 8° examination while the patient gazed at the fixation target. The autotracking system calculated horizontal and vertical shifts relative to a reference frame and drew a map of the patient's eye movements during the examination. The recorded fixation points were classified into three categories for fixation stability analysis (stable, relatively unstable, unstable). Fixation was regarded as 'stable' if more than 75% of the fixation points were inside the 2° diameter circle, as 'relatively unstable' if < 75% were inside the 2° diameter circle but more than 75% inside the 4° diameter circle, and as 'unstable' if < 75% were inside the 4° diameter circle. We assessed fixation location before surgery by noting whether fixation was inside the hole or in the upper, lower, temporal, or nasal area of the macula, close to hole. The location of the spot on the retina was considered as the preferred retinal locus (PRL). After surgery, the definition of PRL is done subjectively and may be debatable; for that reason we could not precisely determine PRL after macular hole surgery.

All surgery was performed by the same surgeon (MK). Following core vitrectomy with 23 gauge instruments 0,1 ml (4 mg) commercially available suspension of triamcinolone acetonide (Kenakort-A; 40 mg/ml, Bristol-Myers Squibb Co, Princeton, NJ, USA) was injected over posterior pole. The posterior hyaloid was clearly observed. After separation of hyaloid from the optic nerve head and macular area, a subtotal vitrectomy was performed. Triamcinolone acetonide suspension, 0.1 ml (4 mg), was injected again over the posterior pole and the ILM was directly grasped with an end gripping intraocular forceps and peeled in a circumferential manner around the macular hole. The peeled area was clearly observed as an area lacking of the white specks of triamcinolone acetonide particle on the retina. In all patients, at the end of surgery 12% C_3F_8 gas was used to provide tamponade. The patients were instructed to use a face-down posture for 80% of the time for a 1-week period.

Changes in functional (BCVA and MP-1 microperimetry) parameters observed in eyes with macular hole after surgery with triamcinolone acetonide–assisted ILM peeling were compared with baseline value (1, 3, 6, and 12 month versus base) by Repeated anova test. The spss software for Windows version 12.0 (SPSS Inc, Chicago, IL, USA) was used for the statistical analysis. A $p < 0.05$ was considered statistically significant.

Results

Twenty-two eyes of 22 patients with an idiopathic macular hole were included in this study. Seventeen were women, and five were men; the mean age of the patients was 61 ± 6 years (range, 46–70 years). There were 17 eyes with stage 3 and 5 with stage 4 macular hole. Preoperative BCVA ranged from 0.3 to 1.0 (logMAR, mean 0.75). All patients completed 1 year follow-up.

The ILM was successfully peeled in all eyes without intraoperative complication. After surgery, complete closure of the macular holes in all eyes was confirmed by OCT. Recurrence was not seen in any patients. We did not observe any intraocular pressure elevation or any residual triamcinolone in macular region after surgery. Eleven patients were already pseudophakic before macular hole surgery. Some phakic patients showed progression of nuclear sclerosis with increase in myopia (< 1.00 diopter). However, these patients had no decrease in BCVA. Cataract surgery was performed in these patient as lenticular changes could effect the microperimetry results. Eight of 11 patients (73%) developed nuclear cataract during the postoperative course and underwent cataract surgery with intraocular lens implantation later. Mean cataract operation time is 8 ± 4 months. Preoperative and postoperative BCVA, mean retinal sensitivity, and fixation stability in eyes with macular hole are shown in Table 1. Fig. 1, which shows the mean BCVA during the follow-up period. It improved from 0.75 ± 0.2 to 0.31 ± 0.1 logMAR at the last visit ($p < 0.001$). Best corrected visual acuity at the last visit had improved at least one line in all 22 eyes (Table 1). Before surgery, the PRL was located on the margin of the hole in all eyes, 18 eyes on its upper part and four eyes on side or lower part (Fig. 2). In Fig. 3, retinal sensitivity improvement shown with MP-1 microperimetry images and macular hole closure shown with OCT images before and 12 month after surgery of patient number 8.

Preoperatively, 12 eyes had stable and 10 had relatively unstable fixation.

Table 1. Clinical characteristics of patients with macular hole before and 12 months after surgery.

		MP-1 microperimetry sensitivity(dB)		MP-1 microperimetry fixation stability		Visual acuity (logMAR)		
Patient No.	Age (years)	Before surgery	12 m after surgery	Before surgery	12 m after surgery	Before surgery	12 m after surgery	Hole size (μ)
1	60	3.6	5.7	RU	S	0.7	0.4	300
2	60	4	5.2	RU	S	0.3	0.1	400
3	69	5.4	7.5	RU	RU	0.5	0.1	370
4	55	3.4	5	S	S	1	0.4	500*
5	66	3.2	4.5	RU	S	0.5	0.3	360
6	56	3.3	5.1	S	S	0.7	0.5	510*
7	66	5.1	5.3	S	S	1	0.4	490
8	46	3.9	6.9	S	S	0.7	0	350
9	70	3.1	5.4	S	S	0.7	0.3	410
10	63	4.1	4.4	S	S	1	0.3	330
11	62	5	6.6	RU	S	0.5	0.2	310
12	70	3.3	4.8	S	S	1	0.4	480
13	58	3.1	5.5	S	S	0.6	0.2	390
14	60	3.4	7.2	S	S	0.7	0.2	410
15	50	4.2	5.4	RU	S	0.4	0.2	370
16	65	2.9	6.6	RU	S	0.5	0.1	380
17	69	3.8	3.9	RU	RU	1	0.5	470
18	68	3.5	4	RU	S	1	0.6	570*
19	60	4	5.1	S	S	1	0.6	510*
20	62	3	5.2	RU	S	1	0.6	560*
21	60	3.1	4.1	S	S	0.7	0.2	370
22	54	3.4	4.9	S	S	1	0.3	450

S = stable; RU = relatively unstable; m = month.
* Stage IV macular hole.

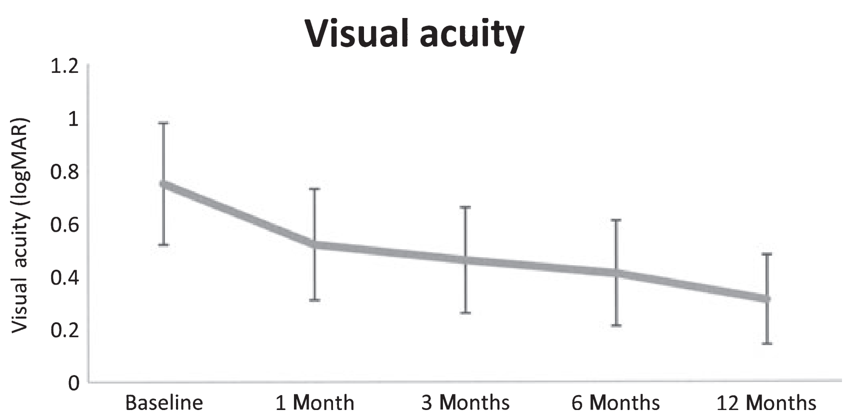

Fig. 1. Mean best corrected visual acuity (BCVA) (logarithm of the minimum angle of resolution units) before and after macular hole surgery. Best corrected visual acuity improved significantly 1,3,6 and 12 months after surgery ($p < 0.001$).

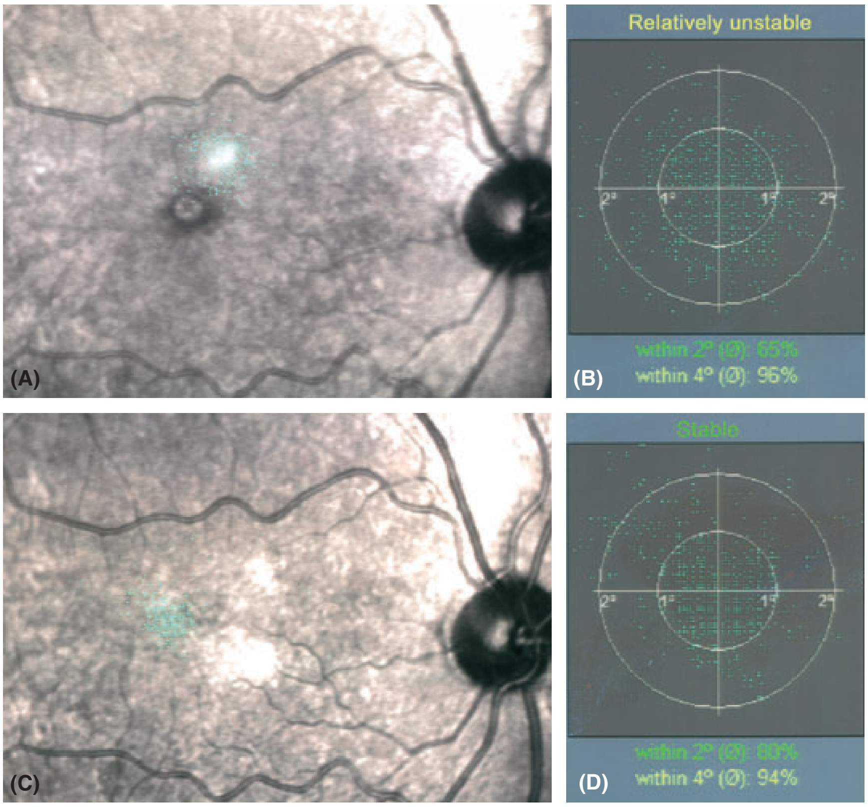

Fig. 2. To evaluate relationship with macular hole and microperimetric parameters, we superimposed sensitivity data onto an infrared image on the Heidelberg scanning laser ophthalmoscope. (Patient 11) Before surgery, the preferred retinal locus was located on the margin of the hole (A) and fixation was relatively unstable (B). Twelve months after surgery, fixation stability was improved and become stable (C, D).

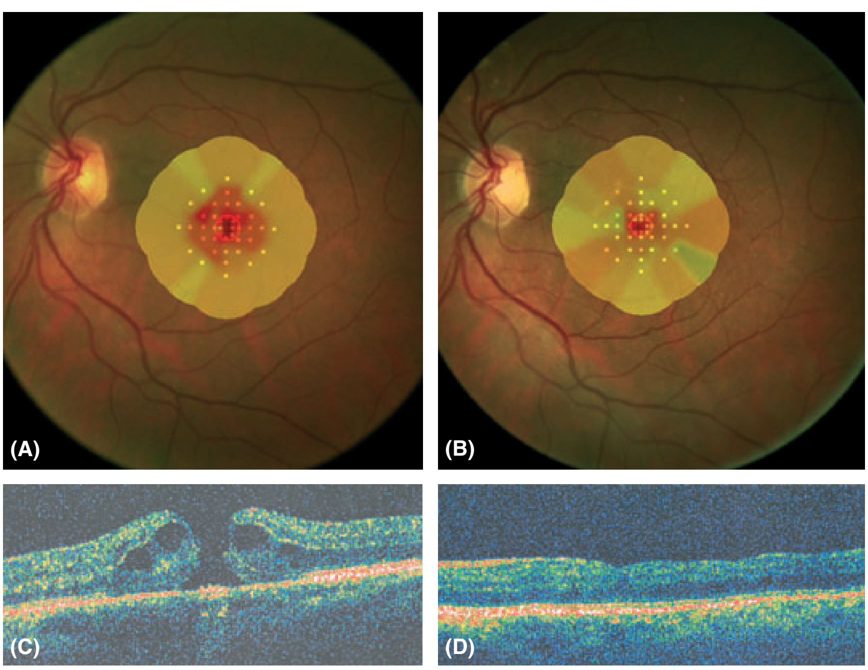

Fig. 3. Retinal sensitivity improvement shown of patient 8, before (A) and 12 months after surgery (B), and same patient's hole closure shown with optical coherence tomography images before (C) and 12 months after surgery (D).

Twelve months after surgery, fixation stability had improved, and 20 eyes had stable and two had relatively unstable fixation (Table 2). Relative scotomas become better and some absolute scotomas disappeared, and mean sensitivity improved from 3.7 ± 0.6 to 5.3 ± 1.0 dB at the last visit ($p < 0.001$), (Table 2).

Discussion

The positive effects of ILM peeling on anatomical and functional outcomes in macular hole surgery have been reported (Brooks 2000). Several authors have reported on advantages of dyes such as indocyanine green, trypan blue or triamcinolone acetonide for ILM peeling (Haritoglou et al. 2002a; Perrier & Sebag 2003; Karacorlu et al. 2005; Shinoda et al. 2008). Controversies exist, however, regarding the application and possible toxic effects of dye or triamcinolone acetonide used to facilitate the surgical procedure. Most studies have reported statistically significant improvements in BCVA (Brooks 2000; Karacorlu et al. 2005; Shinoda et al. 2008).

In our study, triamcinolone-assisted ILM removal achieved a primary anatomical closure in all cases. Best corrected visual acuity improved from 0.75 ± 0.2 to 0.31 ± 0.1 logMAR at the last visit ($p < 0.001$).Triamcinolone assisted ILM peeling has been described as an effective surgical technique with regard to the anatomical closure and visual outcome in macular surgery (Karacorlu et al. 2005; Kumagai et al. 2007; Tewari et al. 2008). Kumagai et al. (2007) reported that all macular hole closed after primary surgery in 96 eyes of 94 patients who underwent macular hole surgery with triamcinolone acetonide ILM peeling. Ninety eyes (94%) having improvement of BCVA after surgery. They found as postoperative complications in mean 17-month follow-up period; retinal detachment in one eye and transient intraocular pressure elevation in five patients. Tewari et al. (2008) also reported anatomical hole closure rate in 36 eyes(97%) of 37 eyes after triamcinolone acetonide–assisted ILM peeling macular hole surgery. They found that preoperative BCVA was improved from 20/150 to 20/63 after surgery. They reported

Table 2. Fixation stability and retinal sensitivity evaluated by MP-1 microperimetry in patients with macular hole.

Macular hole parameter	Before surgery	1 month	3 months	6 months	12 months
Fixation (*n*)					
Stable	12	19	20	20	20
Relative unstable	10	3	2	2	2
Unstable	0	0	0	0	0
Retinal sensitivity (dB)	3.7 ± 0.6	3.6 ± 0.6*	4.3 ± 0.6**	4.7 ± 0.7**	5.3 ± 1.0**

dB = decibel.
* $p < 0.01$, ** $p < 0.001$.

any retinal detachment but transient intraocular pressure elevation in five eyes after surgery. There have been case reports that have described persistence of triamcinolone in macular hole after surgery (Yamauchi et al. 2006). Contrary, in this study, we did not observe retinal detachment, any intraocular pressure elevation or any residual triamcinolone in macular region 12 month follow-up after surgery. Our patients showed progression of nuclear sclerosis with increase in myopia (< 1.00 diopter). However, these patients had no decrease in BCVA. Cataract surgery was performed in these patients as lenticular changes could effect microperimetry results. There were 19 (86%) pseudophakic eyes of 22 eyes at last follow-up examination in this study. Phakic three eyes (14%) have no cataract progression at last 12-month follow-up examination. Our anatomical and BCVA results are similar with that of others (Kumagai et al. 2007; Tewari et al. 2008).

Our results also compare favourably with other studies involving various techniques of ILM peeling using other stains (Haritoglou et al. 2002a; Perrier & Sebag 2003; Tewari et al. 2009; Cappello et al. 2009). But, some patients with macular hole do not show satisfactory improvement after surgery even if anatomical closure is achieved and BCVA improved. This means that despite the improvement in visual acuity and amelioration of metamorphopsia, the central retinal function is not normal, and other types of visual function test must be adopted for interpretation of retinal function (Matsumoto et al. 1998). One of those tests, microperimetry, allows automated functional analysis of the macula associated with real-time correction of eye movements. MP-1 microperimetry provides exact localization of the tested region on the retina, even in patients with unstable fixation.

Microperimetry can be performed with a differently sized point stimulus, ranging from Goldmann I to Goldmann IV (from 6.5 to 103 min/arc). In literature, there is no standard procedure and different Goldmann I, II or III sized point stimulus was used in different macular hole studies, and according to simulus size, mean retinal sensitivity was different in several studies (Haritoglou et al. 2002b; Mitamura & Othsuka 2005; Richter-Mueksch et al. 2007). There is only slight difference in delimitation of the blind spot between Goldmann stimulus size I or II. This is probably because of the small diameter of these stimuli. For Goldmann III size, however, smoothing of the borders of the blind spot occurs. Goldmann I size might be used in detecting and delineating small scotoma, such as because of macular holes (Bek & Lund Andersen 1989).

The microperimeter 1 allows real-time colour fundus image acquisition, and an overlay of the perimetric findings on to the image is also possible. But a major disadvantage of the MP-1 is the image quality of the first acquired black-and-white infrared image used for eye tracking during the examination. To achieve a satisfying contrast between retinal vessels and the fundus, which is necessary for the auto-tracking system, a high level of infrared illumination has to be used. This often results in artefacts in the centre of the infrared image, which makes a reliable detection of retinal pathology and test pattern placement very difficult. The option of the MP-1 to overlap the microperimetric results with a digital real-time colour fundus image has not provided reliable detection of macular defects of some patients (Rohrschneider et al. 2005). Recently, a microperimetry sensitivity map was overlaid onto images from other devices using dedicated MP-1 software. This software allows for the exact superimposition of sensitivity data to different images separately (infrared, autofluorescence, fluorescein angiography, indocyanine green). The superimposition is obtained by the semi-automatic detection of two identical anatomical landmarks on both images. This software has previously been tested for validity and repeatability (Midena et al. 2007). This method gives a more contrasted image of the macula than do MP-1 colour fundus photographs, making it easier to observe certain characteristics of macular holes before and after surgery. To evaluate the relationship between macular holes and microperimetric parameters, we superimposed sensitivity data onto infrared images on the Heidelberg scanning laser ophthalmoscope, because it is one of the best for observing certain characteristic of macular hole for PRL.

There are some studies that investigated microperimetric changes in patients with a macular hole before and after surgery. Guez et al. (1998) examined 40 eyes of 40 patients with full-thickness macular holes with a scanning laser ophthalmoscope and reported that, before surgery, the PRL was usually located on the upper part of the macular hole. After surgery, the PRL became central. Nakabayashi et al. (2000) used scanning laser ophthalmoscope microperimetry to identify fixation points in 13 patients with idiopathic macular holes before and after vitreous surgery and also measured the distance between preoperative and postoperative fixation points and the direction of movement. In this study, preoperatively, fixation was found to be at or near the margin of the macular hole in all eyes and was located above the horizontal meridian in most (84.6%) eyes. Postoperatively, there was a shift in the position of the fixation points. The distance between preoperative and postoperative fixation correlated with the degree of visual improvement, but the direction of movement was variable. We also found that before surgery the PRL was located on the margin of the hole in all, 81% on its upper part and 19% to the side or on its lower part.

Sunness et al. (1996) studied the fixation patterns in eyes with central scotoma from advanced atrophic age-related macular degeneration and Stargardt's disease. They found that the PRL was, in the vast majority, located in upper section of central atrophy. They surmised that fixation with the scotoma above the PRL would be preferred because this would move the scotoma out of the field used for reading, face recognition, and other tasks. Macular hole patients, who have even smaller central defects than patients with advanced atrophic age-related macular degeneration and Stargardt's disease, show the same behaviour for fixation location. The preference for fixation with the scotoma to the right rather than to the left is expected: a study of readers of languages read from right to left showed a preference in the opposite direction. This preference might reflect the necessity in reading to anchor oneself to the beginning of the word or of the line (Guez et al. 1995). But fixation with the scotoma below was very rare and unexplained (Sunness et al. 1996).

Richter-Mueksch et al. (2007) investigated MP-1 microperimetric changes in 19 patients with a macular hole before and after surgery. They found that improvement in fixation stability was a most striking feature: the number of patients with stable fixation doubled from 8 to 16 in the macular hole group. All patients who had unstable fixation before surgery recovered to a more stable fixation. Our findings are similar to those of this study. In our study, we did not find any unstable fixation before or after surgery, but 45% were relative unstable and 55% were stable before surgery. Fixation stability improved, and 12 months after surgery, 91% were stable and 9% were relatively unstable. Richter-Mueksch et al. (2007) did not mention fixation location pattern, but we showed the fixation location pattern in patients with macular hole before surgery. Improvement in fixation stability is important and it is shown that there is close relationship between reading skill and fixation stability (Deruaz et al. 2004; Cappello et al. 2009).

In a recent study, Cappello et al. (2009) also using MP-1 microperimetry after surgery for macular hole and pucker has suggested that a BCVA, retinal sensitivity and fixation stability and reading ability improvement was maintained up to 1 year of follow-up after macular hole surgery. They also found that macular holes did not have central fixation at baseline but this was recorded in all patients achieving hole closure after surgery. Although these authors used different ILM staining methods, the results are very similar and, not only BCVA, but also retinal sensitivity and fixation stability improve after surgery.

Limitations of our study are relatively short follow-up and small sample size and lack of control group. In summary, the study shows a significant benefit in BCVA for patients with macular hole after surgery and an even greater improvement in microperimetry analysis of retinal sensitivity, fixation stability and location. The MP-1 microperimetry sensitivity map overlaid onto other devices' images using dedicated MP-1 software allows successful evaluation of fixation location in patients with a macular hole before surgery. With microperimetry findings, we can also measure functional macular changes more precisely than using BCVA alone after macular hole surgery.

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