Evaluation of the Effects of Vitrectomy with Primary Epiretinal Membrane Peel on Optical Quality Using Double-Pass Aberrometry

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Keywords
Primary epiretinal membrane · Vitrectomy · Double-pass aberrometry · Optical quality · Objective scatter index

Abstract
Introduction: We performed a prospective, single-center, cohort study in order to evaluate the effects of vitrectomy with epiretinal membrane (ERM) peel on optical quality in patients with primary ERM. Methods: Thirty patients treated for primary ERM by vitrectomy with ERM peel were included from our tertiary university hospital ophthalmology department. The main study outcome was a variation in optical quality parameters measured using the HD Analyzer™ between preoperative and 2-month postoperative evaluations in operated eyes. Optical quality parameters comprised point spread function (PSF) width at 10% and 50%, objective scatter index (OSI), and modulation transfer function (MTF) cutoff. Contralateral non-operated eyes were used as an internal control for measurement reproducibility. Results: Mean PSF width at 10% (42.22 vs. 27.37 arc/min; \( p = 0.0002 \)) and mean OSI (3.32 vs. 2.32; \( p = 0.0003 \)) were significantly improved between pre- versus postoperative evaluations. Mean PSF width at 50% and mean MTF cutoff showed no changes. Subgroup analysis according to crystalline lens status gave similar results, demonstrating that improvements in mean PSF width at 10% and OSI were not lens-related. Non-operated eyes showed no changes in any of the parameters analyzed. Conclusion: Reduced light scattering measured by OSI indicates improved optical quality following vitrectomy with ERM peel among patients with primary ERM. OSI measurement could thus be a new parameter of interest in the preoperative assessment of primary ERM and other pre-vitrectomy assessments.

Introduction
High-contrast visual acuity is no longer sufficient for the qualitative assessment of visual function \cite{1, 2}. Instead, nowadays, the objective assessment of optical quality has taken over with the development of user-friendly devices. Optical quality is affected by three distinct phenomena: (1) light scattering or dispersion, which is increased by loss or partial loss in transparency of the optical system; (2) light diffraction, the extent varying according to pupil diameter; and (3) second-order optical
aberrations (spherocylindrical refractive errors) and high-order optical aberrations (HOAs). The latter is related to the ocular surface (approximately 90% of cases) and the crystalline lens [3]. Thus, at a given high-contrast visual acuity, optical quality may indeed be very different.

Several standard wavefront aberrometers have been developed to study optical aberrations by measuring the light distortions generated from several point source objects upon passing through an optical system [4]. However, the estimation of the optical quality provided by these aberrometers is only valid in the case of preserved ocular media transparency [5] or in the absence of multifocal intraocular lenses [6]. The HD Analyzer® (Visiometrics, Terrassa, Spain), the third version of the Optical Quality Analysis System, is the only commercially available double-pass optical quality aberrometer providing a quantitative and objective assessment of optical quality. It directly measures the combined effect of HOAs and light scattering [2, 7]. Briefly, an isolated light source produced by an infrared light beam (780 nm diode laser) forms an image on the foveal retina. The HD Analyzer® analyzes the size and shape of the light source after reflection on the retina and double-pass through the ocular media. This gives a direct measure of the point spread function (PSF), from which can be deduced the objective scatter index (OSI) and the modulation transfer function (MTF) [1, 5]. Several teams have used the HD Analyzer® to quantify and correlate the extent of intraocular light scattering in eye diseases, including dry eye diseases [8, 9], anterior uveitis [10], keratoconus [11], and lens opacities [7, 12], contributing in turn to our understanding of the potential effects of these diseases on visual quality. In contrast, few studies have addressed the influence of vitreoretinal diseases on optical quality [13]. Likewise, the value of pre- and postoperative measurements of optical quality has not been evaluated in indications for vitreoretinal surgery, such as primary epiretinal membrane (ERM).

ERMs consist of nonvascularized fibrocellular tissue that has proliferated on the retinal surface in the macular area [14]. When ERMs become contractile, they cause varying degrees of macular folding, which can lead to functional discomfort in the form of decreased visual acuity or metamorphopsia. ERMs are idiopathic in more than 70% of cases [15] and related to age [16], developing secondary to retinal breaks or vascular/inflammatory retinal diseases [17]. First described in 1978 by Machemer [18], treatment for ERM is surgical and consists of vitrectomy associated with ERM peeling in cases with significant functional discomfort.

The aim of this study was to prospectively evaluate for the first time the effects of vitrectomy with ERM peel on optical quality in a cohort of 30 patients with primary ERM. For this, we used the HD Analyzer® to calculate variations between pre- and postoperative PSF width at 10% and 50%, OSI, and MTF cutoff.

Methods

Study Design

We performed a prospective, nonrandomized, single-center, cohort study on 30 patients with primary ERM who underwent unilateral vitrectomy with ERM peel. Patients were enrolled between December 2014 and July 2017 from our tertiary ophthalmology department at Toulouse University Hospital Center. The study protocol and data collection were prospectively approved and carried out according to the Ethics Committee of the French Society of Ophthalmology (IRB#1 0008855). All patients included in the study received clear oral and written information and gave free and written informed consent to participate. All data have been anonymized for publication purposes. Only one eye of each patient was operated on. The contralateral non-operated eye was used to perform an internal control of optical quality measure-ment reproducibility.

Patients

Adult patients with phakic or pseudophakic eyes presenting with primary ERM with surgical indication for treatment, defined by an initial visual acuity measured in logMAR ≥0.2 and/or metamorphopsia affecting daily living, were included for study. Patients were excluded if either eye presented trauma, pupillary abnormalities, pseudophakic multifocal intraocular lens, previous ocular surgery (with the exception of uncomplicated cataract surgery >90 days before inclusion), active intraocular inflammation or infection, significant dry eye disease, corneal conditions, or preexisting vitreous disease. We also excluded patients undergoing combined phaco-vitrectomy or with intraoperative posterior capsulotomy, as well as patients developing postoperative keratitis, posterior capsule opacification, or progressive cataract during the 2-month postoperative follow-up period to reduce the effects of lens opacification. The degree of lens opacification for phakic eyes was defined according to the International Lens Opacities Classification System III (LOCS III) by the same certified operator (vitreoretinal surgeon) both pre- and postoperatively. Patients with unsatisfactory optical quality measurements (uncorrected subjective refraction or outside automatically corrected values, absence/excess blinking, incorrect artificial pupil diameter setting) were also excluded.

Surgery of Primary ERM

All patients were managed in outpatient surgery after consulta-
tion with an anesthesiologist. The procedure was performed under general or locoregional anesthesia and consisted of a three-port transconjunctival 25- or 27-gauge pars plana vitrectomy. The vitrectomy was performed with a noncontact wide-angle optical system (RESDIGHT®, Zeiss, Oberkochen, Germany) using a CONSTELLATION® vision system (Alcon, Fort Worth, TX, USA). A disposable concave lens made of PMMA (FCI, Paris, France) allowed for better visualization of the posterior pole. The ERM and
internal limiting membrane were dissected using a 25-gauge forceps (GRIESHABER Revolution® DSP; Alcon) after injection of Membrane Blue-Dual® (DORC, Zuidland, The Netherlands). Sclerotomies were not sutured given their self-sealing nature. All surgeries were performed by the same vitreoretinal surgeon.

Evaluation of Outcomes

The primary study outcome was the evaluation of optical quality based on variations between pre- and 2-month postoperative optical quality parameters measured using the HD Analyzer™ in operated eyes. The secondary outcomes were based on differences between preoperative and 2-month postoperative best corrected distance visual acuity (BCDVA) and central retinal thickness in the operated eyes. Primary and secondary endpoint measures were evaluated in patients in both eyes, thus including the contralateral non-operated eyes. Measurements made in these eyes served as intra-individual controls of optical quality measurement reproducibility.

All patients were interviewed about the onset of visual defects in both eyes. The following evaluations were performed for both eyes at the initial preoperative and final postoperative evaluations 2 months after surgery: the presence or absence of metamorphopsia according to the Amsler grid, BCDVA after objective refraction measurement by an autorefractor keratometer (Tonoref® III; Nikom, Gamagori, Japan), dilated fundus examination with slit-lamp, macular optical coherence tomography (SPECTRALIS® HRA + OCT; Heidelberg Engineering, Heidelberg, Germany), and HD Analyzer™ optical quality parameter measurements (PSF width at 10% and 50%, OSI, and MTF cutoff). Visual acuity was measured in logMAR under the same distance and lighting conditions. Central retinal thickness was measured by spectral domain optical coherence tomography.

Optical Quality Parameter Measurements

We used the HD Analyzer™ based on the double-pass aberrometry technique for optical quality parameter measurements. This allows the capture of asymmetries in retinal images which can derive from diffraction, aberrations, and scattering. We used the following three optical quality parameters as primary study endpoint measures: PSF width at 10% and 50%, OSI, and MTF cutoff.

The PSF is directly measured by the HD Analyzer™ and represents the spatial distribution of the light intensity of the image on the retinal focal plane. It takes into account the effects of diffraction and aberrations in the case of loss of ocular media transparency upon double-pass through the ocular media. The lower the PSF, the better the resolution of the eye. The width of the PSF at 10% and 50% of its maximal height was measured (in arc/min), and a mean value for each was selected for analysis (the mean of the four most reproducible individual acquisitions among six obtained per patient).

The MTF curve, directly computed from the Fourier transformation of the double-pass retinal image, represents the loss of contrast produced by the optics of the eye as a function of spatial frequency. The lower the contrast attenuation, the better the optical quality of a system for a given spatial frequency [19]. The parameter studied was MTF cutoff; this value is the cutoff point of the MTF on the x-axis in cycles per degree (cpd), representing the point at which the spatial frequency is maximal. It predicts the theoretical maximum visual acuity, and the higher the MTF cutoff, the better the resolution of the eye.

The OSI, also computed from the PSF, is an objective index of intraocular light scattering. It is the ratio between the integrated light in the periphery and the central peak of the double-pass image. The higher the OSI, the higher the level of intraocular light scattering related to the loss of transparency of one or more ocular structures.

All patients underwent a complete refractive examination and the measurements were performed with spherical-lindrical correction to achieve the best possible optical quality. Spherical ametropias between −8 diopters (D) and +5 D were automatically corrected by the HD Analyzer™, while higher spherical ametropias and astigmatisms above 0.50 D were corrected with an external test lens. All measurements were performed by the same operator throughout the study and after blinking, given tear film quality is likely to affect light scattering [20]. The diameter of the natural pupil was measured by the instrument, but the measurements recorded for study were with a fixed pupil diameter chosen by the operator (3–6 mm).

Statistical Analysis

The Wilcoxon signed-rank test for paired samples was used to compare primary and secondary endpoints between pre- and postoperative eyes of the same patients. For comparisons between pseudophakic and phakic patient subgroups, sex (qualitative variable) was compared using the Fisher’s exact test. Comparisons between quantitative variables for pseudophakic versus phakic patient subgroups or 25- versus 27-gauge pars plana vitrectomy were made using the Mann-Whitney U test. Correlations between reduction in central retinal thickness and changes in optical quality parameters/BCDVA of operated eyes were calculated using the two-tailed Pearson correlation test. All results are presented as mean ± standard deviation. A value of $p < 0.05$ was considered statistically significant. Statistical analyses were performed using the R software (version R-3.4.3).

Results

Description of the Patient Cohort

Thirty-seven patients were enrolled for the study, of which seven were excluded for unsatisfactory HD Analyzer™ measurement acquisition (n = 4), intraoperative capsulotomy (n = 1), and early postoperative cataract development (n = 2). As a result, 30 patients (30 eyes) having undergone vitrectomy for primary ERM peel were included. Table 1 summarizes the demographic and clinical characteristics of the patients included for study. A total of 27 contralateral non-operated eyes were included as three eyes were excluded from analysis: two due to cataract surgery during the postoperative follow-up period and one due to unsatisfactory HD Analyzer™ measurement acquisition at final evaluation. The mean patient age was 68.67 ± 7.74 years (51–85 years) and 16 (53%) patients were male. The main functional signs were the sensation of decreased visual acuity (n = 19; 63% patients)
and the appearance of metamorphopsia \((n = 9; 30\% \text{ patients})\). Among the operated eyes, 17 (57\%) were phakic and 13 (43\%) pseudophakic. It is noteworthy that 12 (40\%) patients presented with bilateral primary ERM at study inclusion; however, only one eye among these patients presented with ERM of surgical indication, i.e., the operated eyes. The contralateral non-operated eyes of these patients presented with initial visual acuity <0.2 logMAR and remained unchanged throughout the study with no signs of metamorphopsia. Twenty-five (83\%) patients underwent 25-gauge vitrectomy and 5 (17\%) patients underwent 27-gauge vitrectomy for primary ERM peel. We found no difference in both baseline or postoperative optical quality parameters, BCDVA, or central retinal thickness based on the performance of 25- versus 27-gauge vitrectomy on operated eyes (online suppl. Table 1; see www.karger.com/doi/10.1159/000524237 for all online suppl. material).

### Optical Quality Outcomes

The pre- and 2-month postoperative optical quality parameters measured using the HD Analyzer™ are summarized in Table 2. The preoperative mean PSF width at 10% was 42.22 ± 27.18 arc/min in operated eyes and 21.05 ± 13.83 arc/min in contralateral non-operated eyes at initial evaluation. Mean PSF width at 10% showed significant improvement 2 months after surgery in operated eyes (27.37 ± 8.72 arc/min; \(p = 0.0002\)) but no change in non-operated eyes (22.39 ± 16.76 arc/min; \(p = 0.28\)). The preoperative mean OSI was 3.32 ± 1.63 in operated eyes.

### Table 1. The demographic and clinical characteristics of the patients included for study

| Demographic characteristics |  |
|----------------------------|---|
| Patients enrolled for study, \(N\) | 37 |
| Patients excluded, \(n\) | 7 |
| Unsatisfactory HD Analyzer™ measurement acquisition, \(n\) | 4 |
| Intraoperative posterior capsulotomy, \(n\) | 1 |
| Early postoperative cataract development, \(n\) | 2 |
| Patients included for study, \(n\) (%), | 30 (100) |
| M:F sex ratio, \(n\) (%) | 16:14 (53) |
| Age, years, mean ± SD | 68.67±7.74 |

| Clinical characteristics of operated eyes, \(n\) | 30 |
| Functional signs, \(n\) (%) |  |
| Decreased visual acuity | 19 (63) |
| Metamorphopsia | 9 (30) |
| Relative central scotoma | 3 (10) |
| Binocular diplopia | 1 (3) |
| Visual discomfort experienced by the patient | 4 (17) |
| Lens status, \(n\) (%) |  |
| Phakic | 17 (57) |
| Pseudophakic | 13 (43) |
| Refractive status, \(n\) (%) |  |
| Myopic | 7 (23) |
| Hyperopic | 20 (67) |
| Emmetropic | 3 (10) |
| Pars plana vitrectomy for primary ERM, \(n\) (%) |  |
| 25-gauge | 25 (83) |
| 27-gauge | 5 (17) |

| Clinical characteristics of contralateral non-operated eyes | 27 |
| Primary ERM, \(n\) (%) | 10 (37) |
| Lens status, \(n\) (%) |  |
| Phakic | 16 (59) |
| Pseudophakic | 11 (41) |
| Refractive status, \(n\) (%) |  |
| Myopic | 7 (26) |
| Hyperopic | 20 (74) |
| Emmetropic | 0 (0) |

SD, standard deviation.
and 1.71 ± 1.16 in contralateral non-operated eyes. Similar to PSF width at 10%, mean OSI was significantly improved following surgery in operated eyes (2.32 ± 0.86; \( p = 0.0003 \)), showing no difference in non-operated eyes (1.84 ± 1.30; \( p = 0.07 \)). The mean PSF width at 50% remained unchanged after surgery in both operated (7.16 ± 4.33 vs. 6.11 ± 2.09 arc/min; \( p = 0.29 \)) and non-operated (4.62 ± 1.99 vs. 4.48 ± 2.09 arc/min; \( p = 0.46 \)) eyes. Finally, the mean MTF cutoff also showed no significant variation between preoperative and 2-month postoperative evaluations in both operated (19.27 ± 7.74 vs. 20.01 ± 8.12 cpd; \( p = 0.81 \)) and non-operated (30 ± 12.31 vs. 29.82 ± 10.81 cpd; \( p = 0.86 \)) eyes.

### Visual Outcomes and Central Retinal Thickness Changes

The preoperative mean BCDVA was 0.38 ± 0.24 logMAR in operated eyes and 0.08 ± 0.14 logMAR in contralateral non-operated eyes, showing a significant improvement 2 months after surgery in operated eyes (0.22 ± 0.23 logMAR; \( p = 0.0001 \)) but no change in non-operated eyes (0.07 ± 0.1 logMAR; \( p = 0.328 \)). Preoperative mean spherical power was 0.32 ± 2.54 D in operated eyes and 0.06 ± 2.75 D in contralateral non-operated eyes at initial evaluation. Spherical power significantly decreased in operated eyes following surgery (−0.2 ± 2.49 D; \( p = 0.0001 \)), but remained unchanged in non-operated eyes (0.03 ± 2.77 D; \( p = 0.960 \)). Preoperative mean central retinal thickness was 484.1 ± 80.25 µm in operated eyes and 305.85 ± 49.12 µm in contralateral non-operated eyes at initial evaluation. This was significantly reduced only in operated eyes (398.73 ± 50.34 µm; \( p < 0.0001 \)) after surgery. These data are summarized in Table 2.

#### Phakic versus Pseudophakic Outcomes

Subgroup analysis was performed on pre-versus postoperative variations in optical quality parameters and visual characteristics of operated eyes according to their phakic or pseudophakic crystalline lens status (data summarized in Table 3). Changes in optical quality parameters were comparable between both subgroups, showing a significant improvement in mean OSI for both phakic (3.04 ± 1.1 vs. 2.48 ± 0.86; \( p = 0.008 \)) and pseudophakic (3.68 ± 2.13 vs. 2.26 ± 0.9; \( p = 0.013 \)) operated eyes between pre- versus postoperative evaluations. Likewise, mean PSF width at 10% showed a significant improvement in both phakic (37.51 ± 16.83 vs. 29.3 ± 9.4; \( p = 0.008 \)) and pseudophakic (48.385 ± 36.53 vs. 26.42 ± 8.22; \( p = 0.013 \)) operated eyes between pre-versus postoperative evaluations. These results thus remain in line with the significant improvements observed in all operated eyes in Table 2 (not according to lens status). Again, in agreement with the variations observed in all operated eyes, the changes in mean PSF width at 50% and mean MTF cutoff were not statisti-

### Table 2. Comparison of pre- to postoperative optical quality parameters, visual acuity, and central retinal thickness in operated and contralateral non-operated eyes

|                     | Operated eyes | Non-operated eyes |
|---------------------|---------------|-------------------|
|                     | preoperative  | post-operative    | \( p \) value\(^a\) (difference between pre- vs. postoperative) | preoperative  | post-operative    | \( p \) value\(^a\) (difference between pre- vs. postoperative) |
| OSI (mean±SD)       | 3.32±1.63     | 2.32±0.86         | 0.0003\(***\) | 1.71±1.16     | 1.84±1.30         | 0.069 |
| PSF width at 10%, arc/min (mean ± SD) | 42.22±27.18 | 27.37±8.72 | 0.0002\(***\) | 21.05±13.83 | 22.39±16.76 | 0.279 |
| PSF width at 50%, arc/min (mean ± SD) | 7.16±4.33 | 6.11±2.09 | 0.289 | 4.62±1.99 | 4.48±2.09 | 0.464 |
| MTF cutoff, cpd (mean ± SD) | 19.27±7.74 | 20.01±8.12 | 0.080 | 30±12.31 | 29.82±10.81 | 0.659 |
| Best corrected distance visual acuity, logMAR (mean ± SD) | 0.38±0.24 | 0.22±0.23 | 0.0001\(****\) | 0.08±0.14 | 0.07±0.1 | 0.328 |
| Central retinal thickness, µm (mean ± SD) | 484.1±80.25 | 398.73±50.34 | <0.0001\(****\) | 305.85±49.12 | 303.63±46.84 | 0.202 |
| Sphere, D (mean ± SD) | 0.32±2.54 | −0.2±2.49 | 0.0001\(****\) | 0.06±2.75 | 0.03±2.77 | 0.960 |
| Sphere, D (mean absolute ± SD) | 1.77±1.62 | 1.55±1.93 | 0.093 | 1.80±2.05 | 1.86±2.02 | 0.532 |
| Total astigmatism, D (mean ± SD) | 0.98±0.51 | 0.95±0.59 | 0.331 | 1.19±0.79 | 1.21±0.76 | 0.785 |
| cpd, cycles per degree; D, diopters; MTF, modulation transfer function; OSI, objective scatter index; PSF, point spread function; SD, standard deviation. \(^a\)Wilcoxon signed-rank test. \(*** p \) value ≤0.001; \(**** p \) value ≤0.0001.
cally significant for both phakic and pseudophakic eyes following surgery (Table 3). Mean spherical power was only significantly decreased among eyes in the phakic subgroup (0.34 ± 3.36 vs. −0.40 ± 3.27 D; p < 0.0001) and remained unchanged for eyes in the pseudophakic subgroup (0.29 ± 0.72 vs. 0.06 ± 0.76 D; p = 0.120) at final evaluation.

It is noteworthy that there was no difference in sex when comparing pseudophakic versus phakic patient subgroups, but patients were older in the pseudophakic operated group (72.9 ± 8.1 vs. 65.5 ± 5.9 years; p = 0.022). We found no differences in baseline optical quality parameters, BCVA, central retinal thickness, mean spherical power, or total astigmatism between pseudophakic versus phakic patient subgroups. These findings consolidate that the significant changes observed in optical quality in both pseudophakic and phakic eyes result from the surgery and are not influenced by variations in baseline optical quality parameters. We found, as expected, a significant difference between mean absolute sphere; this was lower in pseudophakic eyes given that patients previously operated for cataract generally have a postoperative target refraction close to 0 D (emmetropia), whereas phakic patients have a “natural” refraction. These data are summarized in online supplementary Table 2.

### Discussion

Advances in aberrometer technology over recent years have resulted in progress in the objective assessment of optical quality in clinical practice [3]. Using the HD Analyzer™ based on the double-pass aberrometry technique, we show for the first time that vitrectomy with ERM peel can significantly improve optical quality in patients with primary ERM.

In order to avoid bias due to variations in the measurements of optical quality parameters, we compared results from operated eyes with a “control group” having not undergone intervention: contralateral non-operated eyes of the same patients. Accordingly, no significant variations were recorded for any of the optical quality parameters measured in the non-operated eyes during follow-up. This allowed us to affirm that the significant improvements observed in the operated eyes were indeed due to the surgical procedure itself and not inconsistent measurement acquisitions. Indeed, the repeatability and reproducibility of measurements made by the HD Analyzer™ have already been well documented [21].

This is the first study examining the effects of vitreoretinal surgery, and hence surgery for primary ERM, on optical quality. Indeed, the benefits of surgery for primary ERM have already been previously assessed in terms of visual acuity and functional discomfort experienced by the patient. According to the authors, visual acuity was

### Table 3. Comparison of pre- to postoperative visual characteristics and optical quality parameters analyzed in operated eyes according to their phakic or pseudophakic crystalline lens status

|                        | Phakic (mean ± SD) | Pseudophakic (mean ± SD) | p valuea | (difference between pre- vs. postoperative) |
|------------------------|--------------------|--------------------------|----------|--------------------------------------------|
| Optical quality parameters |                    |                          |          |                                            |
| OSI (mean ± SD)        | 3.04±1.1           | 2.48±0.86                | 0.008**  |                                            |
| PSF width at 10%, arc/min (mean ± SD) | 37.51±16.83         | 29.3±9.4                 | 0.008**  |                                            |
| PSF width at 50%, arc/min (mean ± SD) | 6.47±2.52           | 6.7±2.47                 | 0.854    |                                            |
| MTF cutoff, cpd (mean ± SD) | 20.49±7.26         | 17.44±5.72               | 0.243    |                                            |
| Best corrected distance visual acuity, logMAR (mean ± SD) | 0.4±0.26           | 0.19±0.23                | 0.018*   |                                            |
| Central retinal thickness, µm (mean ± SD) | 482.47±83.21        | 402.8±34.53              | 0.001*** |                                            |
| Sphere, D (mean ± SD)  | 0.34±3.36          | −0.40±3.27               | <0.0001**** |                                            |
| Sphere, D (mean absolute ± SD) | 2.69±1.92         | 2.28±2.31                | 0.03*    |                                            |
| Total astigmatism, D (mean ± SD) | 1±0.5           | 0.99±0.54                | 0.813    |                                            |
| Best corrected distance visual acuity, logMAR (mean ± SD) | 0.4±0.26           | 0.19±0.23                | 0.018*   |                                            |
| Central retinal thickness, µm (mean ± SD) | 482.47±83.21        | 402.8±34.53              | 0.001*** |                                            |
| Sphere, D (mean ± SD)  | 0.34±3.36          | −0.40±3.27               | <0.0001**** |                                            |
| Sphere, D (mean absolute ± SD) | 2.69±1.92         | 2.28±2.31                | 0.03*    |                                            |
| Total astigmatism, D (mean ± SD) | 1±0.5           | 0.99±0.54                | 0.813    |                                            |

cpd, cycles per degree; D, diopters; MTF, modulation transfer function; OSI, objective scatter index; PSF, point spread function; SD, standard deviation.

* Wilcoxon signed-rank test. * p value ≤0.05; ** p value ≤0.01; *** p value ≤0.001; **** p value ≤0.0001.
improved by a ≥ two-line improvement in 60–90% of cases [22–24] and metamorphopsia was significantly reduced [25] or even disappeared in 75–85% of cases [22]. Accordingly, we demonstrate a significant improvement in visual acuity in the operated eyes of our cohort at 2 months after vitrectomy with primary ERM peel. However, our study expands on these criteria by showing that optical quality is also significantly improved 2 months after surgery. This was demonstrated by significantly improved PSF width at 10% and resulting OSI values in operated eyes, indicating thus a clinically-relevant reduction in light scattering following vitrectomy with ERM peel in patients with primary ERM.

Visual quality parameters may be affected by many factors, including the refractive system, the fundus, and ocular surface conditions. Adding to these factors, our surgical procedure consisted of a central and limited peripheral vitrectomy associated with an ERM peel with internal limiting membrane peeling, resulting in a significant decrease in central retinal thickness. It is therefore not possible to decipher the respective attributions of these independent events on the significant decrease in light scattering we observed.

Few studies have investigated the optical quality parameters measured by the HD Analyzer™ in the context of macular diseases and variation in central retinal thickness. Lee et al. [13] demonstrated an improvement in optical quality parameters in 29 patients with resolved central serous chorioretinopathy. In line with our results (online suppl. Table 3), the authors found no significant correlations between the improvement of these optical quality parameters and reduction in central retinal thickness. On the other hand, a statistically significant positive correlation (low coefficients) was found between OSI and central retinal thickness in 88 patients with macular edema (defined as central retinal thickness >300 μm) [26]. However, this was in a context of age-related macular degeneration, diabetes, or central retinal vein occlusion. It can be predicted that when retinal surfaces are edematous and irregular, presenting with macular edema, for instance, intraocular light would be reflected. Therefore, it can also be expected for reduction in central retinal thickness/irregularity following ERM peeling to contribute to improvements in light scattering. However, given that the ERM is very close to the inner layers of the retina, thus likely having a minor influence on the distribution of light on the retinal focal plane, it could be expected for this contribution to be minimal. Indeed, a similar idea has already been evoked in a study having investigated the quantity of light scattering found in patients with uveitis [10]; the mean OSI was significantly higher in eyes with anterior uveitis compared with posterior uveitis, with a plausible explanation being that the scattered light after hitting the anterior chamber cells has to travel a longer distance to reach the retina. A recent study showed a statistically significant reduction in optical quality (increase in OSI >160%) in 44 eyes with idiopathic ERM compared to contralateral control eyes. However, this appeared more related to anatomical changes in the inner retina secondary to the ERM than to the ERM itself [27].

There are arguments favoring the theory that vitrectomy is largely responsible for significant decreases in light scattering. The vitreous is one of the physiological sources of ocular light scattering given its macromolecular composition, including molecules such as hyaluronic acid and collagen, which are necessary for vitreous maintenance and stabilization [28]. The scattering of light generated by its passage is therefore all the more substantial as the vitreous undergoes significant structural changes with age (floaters, gel liquefaction). In light of testing this hypothesis, we also measured pre- and postoperative OSI values in 3 patients who had undergone vitrectomy alone in our ophthalmology department for diagnostic or therapeutic purposes for the following indications: floaters, hyalitis in the context of amyloidosis, and large B-cell lymphoma. A 52–89% decrease in OSI was demonstrated among these 3 patients (data not shown). We thus deduce in our study that it could be the vitrectomy itself that contributes in majority to the improvement in OSI over the reduction in retinal thickness/irregularity following ERM peeling. Despite showing an improvement in OSI, results were not significant due to the small patient numbers. In order to further confirm this hypothesis, a new study could be performed dedicated to the investigation of the effects of vitrectomy alone on optical quality and visual improvements.

To date, there is no study in the literature that has addressed the potential effects of vitrectomy on posterior capsular opacification in pseudophakic eyes. Our current data lead us to believe that the benefit of surgery for primary ERM in terms of optical quality in phakic eyes could be compromised at varying speeds by the evolution of lens opacification, which itself increases light scattering. Boni et al. [29] demonstrated a 47% 3-month postoperative cataract rate following surgery for primary ERM via 25-gauge transconjunctival vitrectomy. Indeed, nuclear cataract is the main complication of ERM surgery in these patients, with the majority requiring phaco-emulsification within 2 years of surgery [30]. In this light, we performed subgroup analysis in order to distinguish between
phakic and pseudophakic operated eyes to assess if the significant improvements in postoperative optical quality parameters in this study were not solely related to the results obtained in pseudophakic eyes. Again, we found a significant improvement in OSI and PSF width at 10% in both subgroups. We thus obtained similar results for variations in optical quality measurements whether grouping all eyes operated on or phakic versus pseudophakic operated eyes separately; crystalline lens status thus did not affect changes in optical quality in this cohort. On the other hand, it would appear that the lenses of the operated eyes underwent early intraclinical postoperative remodeling. Indeed, the postoperative myopic shift observed in phakic operated eyes but not in pseudophakic eyes suggests that this remodeling corresponds predominantly to index myopia. Nonetheless, several different and often controversial hypotheses have been evoked in the literature to explain these refractive changes following vitrectomy for ERM [31, 32]. It can be deduced that even though vitrectomy causes early structural lens changes that remain undetectable in the first few months after surgery, their effects on light scattering remain negligible. We cannot completely rule out the progression of nuclear cataract among the phakic eyes included in our study, in turn underestimating improvements in optical quality. However, our short 2-month follow-up period combined with the exclusion of patients with progressive cataract would limit as much as possible the inclusion of patients with sub-clinical cataract progression.

The lack of significant improvement in MTF cutoff in our current study could be partly explained by an insufficient number of patients. However, it could also be due to the fact that MTF cutoff is a function predominantly influenced by light diffraction and HOAs, and to a lesser extent by light scattering [19]. Firstly, consistent with improved light scattering following surgery (reduced OSI), we did observe a slight trend for improved MTF cutoff values after surgery. However, taking into consideration that all measurements were made with an identical exit pupil diameter to limit the effect of diffraction on contrast loss, we did not expect light diffraction to substantially change in the operated eyes of our study, thus limiting changes in MTF cutoff. Secondly, we also assumed no difference in HOAs following surgery. Indeed, the ocular diopters were not modified in our cohort, i.e., the cornea and the lens, contributing again to limiting changes in MTF cutoff values.

The modest patient inclusion number was mainly related to increased performance of combined surgery. Indeed, primary ERM is frequently diagnosed among elderly patients, with the majority of cases associated with cataract (prevalence also increasing with age). Cataract can render surgery for ERM difficult given poor fundus visualization. Thus, ERM is now one of the most common indications for combined surgery. Dugas et al. [33] showed that combined surgery gave the same functional and anatomical results as the classic two-stage surgery after 1 year of postoperative follow-up. Additionally, visual recovery was faster with combined surgery and limited the number of patient hospitalizations. For these reasons, combined surgery was indicated for most patients with cataract and primary ERM of surgical indication in our ophthalmology department, therefore reducing the number of patients included in our present study.

It is noteworthy that Ghazi-Nouri et al. [25] described an improved patients’ subjective perception of visual function as indicated by higher VFQ-25 scores 4 months after vitrectomy for ERM with peeling. Patients showed a significant improvement in metamorphopsia, but not in mean visual acuity. In our study, patients demonstrated improved BCDVA 2 months after surgery. In addition, among the 9 (n = 9/30; 30%) patients with functional signs of metamorphopsia affecting daily living before surgery, 4 (n = 4/9; 44%) already indicated improved symptoms 2 months after surgery (data not shown). However, this was assessed qualitatively according to the presence or absence of symptoms using the Amsler grid. New multicentric studies including more patients are needed to further investigate the correlation between improved optical quality and vison-related quality of life.

Conclusion

Vitrectomy with ERM peel for patients with primary ERM significantly improves optical quality by reducing light scattering according to HD Analyzer™ measurement of OSI. OSI measurement could thus be a valuable parameter for integration into the assessment of surgical indication of ERM in the same way as visual acuity, functional discomfort, or metamorphopsia. Moreover, we hypothesize that OSI measurement could also be a valuable parameter in the pre- and post-vitrectomy assessment of more controversial indications, including the highly controversial indication of vitrectomy for vitreous floaters. Indeed, OSI measurement is a simple, objective, and reproducible measurement that can be collected and shared with patients during initial examination, follow-up, or in the event of postoperative functional discomfort.
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Statement of Ethics

All the procedures performed were part of routine care, and both were in accordance with institutional guidelines and with the principles and regulations of the Declaration of Helsinki. This study protocol was prospectively reviewed and approved by the French Society of Ophthalmology (IRB#1 approval number: 00008855). All patients included in the study received clear oral and written information, and then gave free and written informed consent to participate.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

References

1 Güell JL, Pujol J, Arjona M, Díaz-Douton F, Artal P. Optical quality analysis system: instrument for objective clinical evaluation of ocular optical quality. J Cataract Refract Surg. 2004 Jul;30(7):1598–9.
2 Rzemýk V, Cochener B. Quality of vision studied by comparative measurement of light scattering. J Fr Ophtalmol. 2014 Sep;37(7):540–7.
3 McAlinden C, McCartney M, Moore J. Mathematics of Zernike polynomials: a review. Clin Exp Ophthalmol. 2011 Nov;39(8):820–7.
4 Liang J, Grimm B, Goelz S, Bille JF. Objective measurement of wave aberrations of the human eye with the use of a Hartmann-Shack wave-front sensor. J Opt Soc Am A Opt Image Sci. 1994 Jul;11(7):1949–57.
5 Díaz-Douton F, Benito A, Pujol J, Arjona M, Güell JL, Artal P. Comparison of the retinal image quality with a Hartmann-Shack wavefront sensor and a double-pass instrument. Invest Ophthalmol Vis Sci. 2006 Apr;47(4):1710–6.
6 Gatinedo D. Limited accuracy of Hartmann-Shack wavefront sensing in eyes with diffractive multifocal IOLs. J Cataract Refract Surg. 2008 Apr;34(4):528. author reply 528–9.
7 Cabot F, Saad A, McAlinden C, Haddad NM, Grise-Dulac A, Gatinedo D. Objective assessment of crystalline lens opacity level by measuring ocular light scattering with a double-pass system. Am J Ophthalmol. 2013 Apr;155(4):629–35.e1–2.
8 Vandermeer G, Chamy Y, Pisella P-J. Comparison of objective optical quality measured by double-pass aberrometry in patients with moderate dry eye: normal saline vs. artificial tears: a pilot study. J Fr Ophtalmol. 2018 Mar;41(3):238–45.
9 Herbaut A, Liang H, Rabut G, Trinh L, Kessal K, Baudouin C, et al. Impact of dry eye disease on vision quality: an Optical Quality Analysis System Study. Transl Vis Sci Technol. 2018 Jul;7(4):5.
10 Nanavaty MA, Stanford MR, Sharma R, Dhillon A, Slapton DJ, Marshall J. Use of the double-pass technique to quantify ocular scatter in patients with uveitis: a pilot study. Ophthalmologica. 2011;225(1):61–6.
11 Leonard AP, Gardner SD, Rocha KM, Zeldin ER, Tremblay DM, Waring GO. Double-pass retinal point imaging for the evaluation of optical light scatter, retinal image quality, and staging of keratoconus. J Refract Surg. 2016 Nov 1;32(11):760–5.
12 Galliot F, Patel SR, Cochener B. Objective scatter index: working toward a new quantification of cataract? J Refract Surg. 2016 Feb;32(2):96–102.
13 Lee K, Sohn J, Choi JG, Chung SK. Optical quality in central serous choriotenopathy. Invest Ophthalmol Vis Sci. 2014 Dec 2;55(12):8598–603.
14 Dupas B, Tadayoni R, Gaudric A. Epiretinal membranes. J Fr Ophtalmol. 2015 Nov;38(9):861–75.
15 Wang SB, Mitchell P, Plant AJH, Phan K, Liew G, Chilja J, et al. Prevalence and risk factors of epiretinal membrane in a cohort with cardiovascular disease risk, compared with the Blue Mountains Eye Study. Br J Ophthalmol. 2015 Dec;99(12):1601–5.
16 Kawasaki R, Wang JJ, Sato H, Mitchell P, Kato T, Kawata S, et al. Prevalence and associations of epiretinal membranes in an adult Japanese population: the Funagata Study. Eye. 2009 May;23(5):1045–51.
17 Appiah AP, Hirose T. Secondary causes of premacular fibrosis. Ophthalmology. 1989 Mar;96(3):389–92.
18 Machemer R. The surgical removal of epiretinal macular membranes (macular puckers) (author’s transl). Klin Monbl Augenheilkd. 1978 Jul;173(1):36–42.
19 Gatinel D. CASSETTE NB Studio [Internet], MTF – Modulation Transfer Function. [cited 2017 Nov 27]. Available from: https://www.gatinel.com/recherche-formation/acuite-visuelle-definition/qualite-de-vision/.
20 Kobashi H, Kamiya K, Yanome K, Igarashi A, Shimizu K. Longitudinal assessment of optical quality and intraocular scattering using the double-pass instrument in normal eyes and eyes with short tear breakup time. PLoS One. 2013;8(12):e82427.
21 Xu CC, Xue T, Wang QM, Zhou YN, Huang JH, Yu AY. Repeatability and reproducibility of a double-pass optical quality analysis device. PLoS One. 2015;10(2):e0117587.

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Author Contributions

F.V. and V.S. contributed to study conception and design. Data collection was performed by F.V., F.M., L.M., P.M., C.G., and P.F. Data analysis and interpretation was performed by F.V. and V.S. The first manuscript draft was prepared by F.V. and all the authors commented on the previous drafts of the manuscript. All the authors have approved the final version of the manuscript. As the corresponding author, V.S. takes responsibility for all aspects of this work and ensures to appropriately investigate and resolve any questions raised.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

Author Contributions

F.V. and V.S. contributed to study conception and design. Data collection was performed by F.V., F.M., L.M., P.M., C.G., and P.F. Data analysis and interpretation was performed by F.V. and V.S. The first manuscript draft was prepared by F.V. and all the authors commented on the previous drafts of the manuscript. All the authors have approved the final version of the manuscript. As the corresponding author, V.S. takes responsibility for all aspects of this work and ensures to appropriately investigate and resolve any questions raised.

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22 Gaudric A, Cohen D. Surgery of idiopathic epimacular membranes. Prognostic factors. J Fr Ophtalmol. 1992;15(12):657–68.
23 Poliner LS, Olk RJ, Grand MG, Escoffery RF, Okun E, Boniuk I. Surgical management of premacular fibroplasia. Arch Ophtalmol. 1988 Jun;106(6):761–4.
24 Rice TA, De Bustros S, Michaels RG, Thompson JT, Debanne SM, Rowland DY. Prognostic factors in vitrectomy for epiretinal membranes of the macula. Ophthalmology. 1986 May;93(5):602–10.
25 Ghazi-Nouri SM, Tranos PG, Rubin GS, Adams ZC, Charteris DG. Visual function and quality of life following vitrectomy and epiretinal membrane peel surgery. Br J Ophtalmol. 2006 May;90(5):559–62.
26 Cho JH, Bae SH, Kim HK, Shin YJ. Optical quality assessment in patients with macular diseases using optical quality analysis system. J Clin Med. 2019 Jun 21;8(6):892.
27 Liu L, Wang Y, Liu J, Liu W. Retinal-image quality and contrast sensitivity function in eyes with epiretinal membrane: a cross-sectional observational clinical study. BMC Ophtalmol. 2018 Nov 7;18(1):290.
28 Bishop PN. Structural macromolecules and supramolecular organisation of the vitreous gel. Prog Retin Eye Res. 2000 May;19(3):323–44.
29 Boni S, Barale PO, Gendron G, Poisson F, Scheer S, Sahel JA. Surgery of the idiopathic epimacular membrane on transconjunctival 25-gauge vitrectomy (TSV): a series of 50 cases. J Fr Ophtalmol. 2010 Oct;33(8):544–50.
30 de Bustros S, Thompson JT, Michaels RG, Enger C, Rice TA, Glaser BM. Nuclear sclerosis after vitrectomy for idiopathic epiretinal membranes. Am J Ophtalmol. 1988 Feb 15;105(2):160–4.
31 Hamoudi H, Kofod M, La Cour M. Refractive change after vitrectomy for epiretinal membrane in pseudophakic eyes. Acta Ophtalmol. 2013 Aug;91(5):434–6.
32 Hamoudi H, La Cour M. Refractive changes after vitrectomy and phacovitrectomy for macular hole and epiretinal membrane. J Cataract Refract Surg. 2013 Jun;39(6):942–7.
33 Dugas B, Ouled-Moussa R, Lafontaine P-O, Guillaubey A, Berrod J-P, Hubert I, et al. Idiopathic epiretinal macular membrane and cataract extraction: combined versus consecutive surgery. Am J Ophtalmol. 2010 Feb;149(2):302–6.