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Research Article

# Epiretinal Membrane Surgery With and Without a Systematic Use of Blue Dye: Functional Outcome and Surgery Duration

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## Abstract

**Purpose:** To compare the outcome of macular pucker (MP) surgery and the duration of surgery with and without the systematic use of blue dye.

**Material and Methods:** All patients undergoing a 23-G vitrectomy with MP peeling at the Strasbourg University Hospital between January 2010 and May 2012 were included. Before June 2011 patients had dye-assisted surgery only on the surgeon's request (group 1). After June 2011, patients had systematic dye-assisted surgery (group 2). Best corrected visual acuity (VA), central macular thickness (CMT) were measured before and after surgery. The duration of surgery was recorded.

**Results:** 155 patients (162 eyes) were included: 110 eyes in group 1 and 52 in group 2. The mean initial, 3-month and final VA did not differ between the groups, neither the CMT changes ($p>0.05$). The duration of surgery was significantly reduced in group 2 (46 min, group 1; 35 min, group 2) ($p=0.0025$). In case of secondary MP, the visual postoperative gain was better in group 2 (57.5%) than in group 1 (24.6%) ($p=0.03$).

**Conclusion:** The systematic use of dye for MP surgery reduces surgical time. It may help to achieve better visual results in cases of MP secondary to retinal diseases.

**Keywords:** Macular Pucker; Vitrectomy; Blue; Chromovitrectomy

## Previous Submission

This article has been previously reviewed by Ophthalmologica. The reviewers asked why we did not make two groups : with or without dye. It was not our purpose, because blue dye is now widely used. We just wanted to evaluate the eventual advantages of a systematic use of blue dye during epiretinal membrane surgery, compared with a non-systematic use. We rewrote this article in order to clarify our purpose.

## Introduction

Epiretinal membrane (ERM) is a common finding during ocular assessment in elderly people, particularly since OCT examination is routinely performed. About 5–10% of the population aged 50 or more is concerned [1-3]. The main risk factors for developing an ERM are age, diabetes, ethnic origin (more frequent in Asians), and ocular diseases. Classically idiopathic ERMs are differentiated from secondary

ERMs associated with other ocular or retinal diseases such as diabetic retinopathy, retinal detachment, myopic retinoschisis, uveitis, macular telangiectasia, retinal vein occlusion, and others.

Surgical treatment is proposed if visual acuity is impaired. Since the early 2000's, macular surgery is facilitated by the use of vital dyes. The usefulness of ERM staining has been widely evaluated during the last decade. The staining capacity of the dyes has been compared. Schumann et al. [4] showed the selectivity of internal limiting membrane (ILM) staining of Brilliant Blue G (BBG), Teba [5] confirmed the utility of trypan blue dye in ERM and ILM delineation and removal. Henrich et al. [6] showed the superiority of indocyanine green (ICG) in membrane staining in comparison with trypan blue (TB) and BBG. However, few studies have compared the functional outcome of dye-assisted vitrectomy. Haritoglou et al. [7] and Li et al. [8] found no difference in visual outcome or histological morphology between MP surgery with or without dye. Mackenzie [9] noted a better central macular thickness in the group with staining, but no difference in terms of visual acuity.

As no visual benefit has been proved with the use of dye, some surgeons do not systematically use it, but only when they think they need it, for example in difficult cases. The systematic use of dye in ERM surgery has not been evaluated yet.

The present study compared the anatomical and functional results and the cost-effectiveness of dye assisted ERM surgery whether the dye is used only on surgeon's demand or systematically.

## Material and Methods

All patients operated for MP at Strasbourg University Hospital between January 2010 and May 2012 was included. This retrospective study was conducted in accordance to the tenets of the Declaration of Helsinki. The surgeon had more than 6 years of experience in membrane surgery. Patients all underwent a 23-G vitrectomy with ERM peeling. Patients operated before June 2011 had dye-assisted surgery only on the surgeon's request (group 1). After June 2011, patients underwent systematic dye-assisted surgery (group 2).

Briefly, all patients had a central vitrectomy, the posterior hyaloid membrane was detached from the optic disc if the posterior vitreous detachment was not already present (Constellation, Alcon, Fort Worth, TX, USA). In group 1, the ERM was peeled, blue dye was injected in the eye if the surgeon considered the dye mandatory to accomplish the peeling. In group 2, blue dye was first injected and the ERM was then peeled. The type of blue dye used was MembraneBlue ® (trypan blue 0.15%, DORC, Zuidland, The Netherlands)

Best corrected visual acuity (VA) (LogMAR) and central macular thickness (CMT) were measured before surgery, 3 months after surgery and at the end of follow-up. The follow-up period was at least 3 months long and 80% of the eyes had a follow-up longer than 6 months. All CMT measures were performed with a spectral domain OCT (Spectralis, Heidelberg Engineering, Heidelberg, Germany). The type of epiretinal membrane (idiopathic or secondary) and the lens status were noted for all patients.

The duration of surgeries between antiseptic skin preparation and bandage time was systematically recorded by the operating room nurse, using a computer software.

## Results

A total of 155 patients (162 eyes) were included: 110 eyes in group 1 and 52 in group 2. There was no difference between the two groups in terms of age and gender, mean preoperative VA, lens status (phakic or pseudophakic) or vitreous status (posterior vitreous detachment) ($p>0.05$). 2 patients had chronic open angle glaucoma, 8 patients had a history of retinal detachment, 1 patient had a Wegener disease. No patient had cataract before surgery. MPs were either idiopathic (96 eyes, 59.3%) or secondary (66 eyes, 40.7%). The proportion of secondary MPs did not differ significantly between the two groups (45.87% in group 1 vs 32.07% in group 2, $p>0.05$). The main cause of secondary membranes was diabetes (65%), followed by myopia (14%), retinal detachment (9%), uveitis (6%), retinal vein occlusion (1,5%), an some other causes such as macular telangiectasia (4,5%). The mean follow-up was 17.5 months (± 12.4 months). In group 1, 73% of the vitrectomies were performed without membrane staining, whereas all of group 2 received blue dye ($p=0.0001$) (Table 1).

The mean 3-month VA (0.34, group 1; 0.34, group 2) and final VA (0.32, group 1; 0.31 group 2) did not differ in the two groups ($p>0.05$). The difference from preoperative to postoperative CMT was not statistically different at 3 months (101.1 µm, group 1; 99.5 µm, group 2) and at the end of follow-up (102.6 µm, group 1; 99.5 µm group 2) ($p>0.05$). Surgery duration was significantly reduced in group 2 (46 min, group 1; 35 min, group 2) ($p=0.0025$) (Table 2) (Figure 1).

The subpopulation study revealed that postoperative VA for secondary MP seemed to be better in group 2 (0.36) than in group 1 (0.43) ($p=0.07$), as did the visual postoperative gain (57.5%, group 2; 24.6%, group 1) ($p=0.03$) (Figure 2). In this subpopulation, the CMT reduction did not differ between the two groups (25.5%, group 1; 27.4% group 2) ($p>0.05$) (Table 3).

| | Blue dye used at the surgeon's request | Blue dye used systematically | *p* (95%) |
|---|---|---|---|
| Age (years) | 70.67 | 69.57 | >0.05 |
| Gender (percentage of men) | 45.87 | 52.8 | >0.05 |
| Phakic (%) | 68.22 | 62.26 | >0.05 |
| Operated eye (percentage of right eye) | 54 % | 49 % | >0.05 |
| General health (percentage of diabetics) | 32 % | 36 % | >0.05 |
| General health (percentage of patients suffering from hypertension) | 58 % | 47 % | >0.05 |
| Preoperative visual acuity (LogMAR) | 0.54 | 0.57 | >0.05 |
| Central macular thickness (µm) | 474.74 | 483.69 | >0.05 |
| Complete posterior vitreous detachment (%) | 59.79 | 45.83 | >0.05 |
| Proportion of secondary epiretinal membrane | 45.87 | 32.07 | >0.05 |

**Table 1.** Description of preoperative population

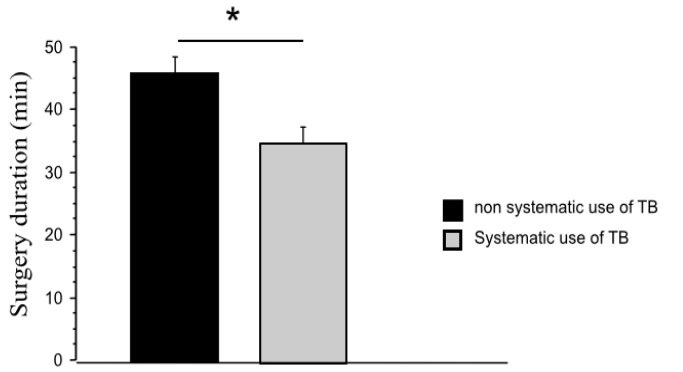


**Figure 1.** The systematic use of blue dye allows to reduce the operation time by 24% (11 min in average )(p=0.038)

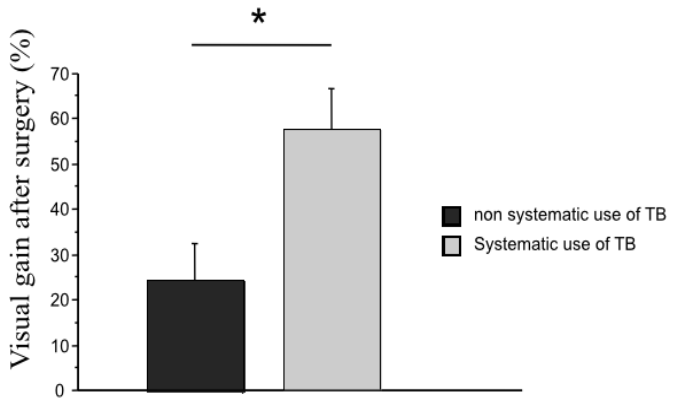


**Figure 2.** In case of secondary macular puckers, visual gain is improved when blue dye is systematically used.

| | Blue dye used at the surgeon's request | Blue dye used systematically | *p* (95%) |
|---|---|---|---|
| Visual acuity at 3 months (LogMAR) | 0.34 | 0.34 | >0.05 |
| Visual acuity at the end of the follow-up (LogMAR) | 0.32 | 0.31 | >0.05 |
| Gain in visual acuity at 3 months | 28.6 % | 36.7 % | >0.05 |
| Gain in visual acuity at the end of follow-up | 33 % | 39.3 % | >0.05 |
| Central macular thickness reduction at 3 months | 21% | 17.7% | >0.05 |
| Central macular thickness reduction at the end of the follow-up | 21.7% | 18.6% | >0.05 |
| Surgical time (between skin desinfection and bandage) | 46 min | 35 min | **0.0025** |
| Blue dye actually used | 27 % | 100 % | <0.001 |
| Complete ILM peeling | 45.1 % | 67.4 % | 0.03 |

**Table 2.** Postoperative results (all patients)

| | Blue dye used at the surgeon's request | Blue dye used systematically | *p* ( 95%) |
|---|---|---|---|
| Phakic (%) | 69.39 | 64.71 | >0.05 |
| Initial visual acuity (LogMAR) | 0.62 | 0.73 | >0.05 |
| Visual acuity at the end of follow-up (LogMAR) | 0.43 | 0.36 | 0.07 |
| Gain in visual acuity at the end of follow-up | 24.6% | 57.5% | **0.03** |
| Initial CMT (µm) | 472.67 | 538.92 | >0.05 |
| Central macular thickness reduction | 25.5 % | 27.4 % | >0.05 |

**Table 3.** Results for secondary epiretinal membranes

## Discussion

Since ERM surgery has long been performed without dye by many surgeons, the systematic use of dye in this surgery is not the gold standard. The cost of dye may be one of the reasons why some surgeons use it only when they think they need it. Another reason is that the use of dye has not yet been proved more efficient in ERM surgery in terms of visual recovery [7,8]. Moreover, the lack of proof of the safety of dyes prevents some surgeons from using them.

In this study, the general visual outcome was not modified by the way of using the dyes. However, when considering only secondary ERM, the systematic way of using blue dye seemed to improve visual results, compared with the « on demand » dye assisted surgery.

A possible explanation for this observation is that secondary ERM are probably more difficult to peel than idiopathic ones. In the present study, secondary ERMs were mainly due to diabetic or myopic retinopathies (Figure 3). These are often associated with vitreoschisis [10-12]. In these cases, it can be difficult to distinguish the posterior hyaloid membrane from the ERM, and the difference is often undetectable on OCT examination. If surgeons do not decide to use dye, they can easily mistake the posterior hyaloid for the ERM [13]. Even if ERM is classically reported to be associated with complete posterior vitreous detachment, a recent small series [14] showed that posterior vitreous detachment may be present in only 50% of the cases.


**Figure 3.** SD-OCT of a diabetic macular pucker, pre-operative and 6 month post operative.

A second explanation is that peeling without any dye is probably more « traumatic » for the retina. In eyes with high myopia or diabetic retinopathy, the retina is abnormal and chronic retinal degeneration is associated. Injecting dye prior to any peeling attempt might allow minimizing retinal touches.

Many patients consulted 3 or 6 months after their vitrectomy and the VA was measured independently of their lens status. Vitrectomy is a well-known cause of cataract development within a few months. This could be a bias for our visual acuity results, but we checked that the lens status did not differ in the two groups.

In the present study, trypan blue was used. The safety of dyes is a recurrent question. Studies using animal models [15,16] suggest that BBG is less toxic than trypan blue. However, trypan blue does not induce changes in the retinal nerve fiber layer (RNFL) thickness [17], just as BBG [18]. Trypan blue has been reported to be safe for surgical use [19]. In the present study, we could not find evidence of any side effects with trypan blue.

Finally, the systematic use of blue dye reduced the surgery by 11 min, corresponding to a 24% reduction in the mean operating time. In our hospital, the cost of the blue dye syringe was three times less than the cost of 11 min of operating room use. The systematic use of dye in our institution probably helped us increase the number of daily surgeries. Moreover, once stained, the visibility of the ERM is sufficient to peel it with simple forceps without the assistance of an expensive scraper or backflush canula. This cost-effectiveness study argues in favour of the systematic use of blue dye in ERM surgery. Likewise, Gupta [20] made an interesting cost-utility study and concluded that ERM surgery is a very cost-effective procedure when compared with other interventions across medical subspecialties.

In summary, the result of this study shows that using systematically blue dye in ERM surgery is beneficial for two reasons. First, patients with ERM secondary to diabetes or high myopia, have better visual outcomes. Second it allows reducing the time of surgery, improving its costs-effectiveness.

## Conflict of Interest Statement

None of the authors has conflict of interest with the submission.

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