

Update on Chromovitrectomy and Macular Hole Repair

BY CHI-CHUN LAI, MD

Recently, enzymatic vitrectomy has been applied to macular hole (MH) repair. A clinical trial indicated that 40% of MH cases could be treated with a single injection of ocriplasmin (Jetrea, ThromboGenics).¹ These results are exciting, but the remaining 60% of patients still require surgery, specifically pars plana vitrectomy (PPV) and internal limiting membrane (ILM) peeling for hole repair. It is widely accepted that ILM peeling can contribute to better anatomic and functional results during MH surgery.² However, removing the barely visible ILM can be technically challenging even for experienced surgeons. Hence, chromovitrectomy, or the use of dyes to enhance the visibility of the ILM to facilitate membrane removal, and thus increase the safety of intentional peeling of the ILM, has become a popular procedure over the past few decades.³

CONCEPTS OF CHROMOVITRECTOMY

Currently, 2 major methods have been employed to increase the visibility of the ILM: staining dyes and coating materials. Each of these methods has pros and cons for MH repair (Figure 1). Commonly used staining dyes, including indocyanine green (ICG), trypan blue (TB), and brilliant blue G (BBG), are able to increase visibility by selective staining and penetration of the ILM, resulting in a well-visualized margin during membrane peeling.⁴ However, the difficulty of removal after dye application may result in the long-term retention of dye, which may raise safety concerns.⁵

Other coating materials, including triamcinolone acetonide (TA), whole blood, and blood clumps, only coat the membrane surface rather than stain the ILM.⁶⁻⁸ They can be removed almost completely at the end of surgery. Despite the fact that there is no long-term retention, the use of these materials may be complicated by their dispersion during application.

	Staining Dyes	Coating materials
Representatives	ICG, TB, BBG	TA, Blood, BC
Enhanced visibility of ILM	++	++
Selective staining and penetration	+	-
Dispersion	-	+
Retention	+	-
Toxicity reported in cell study	ICG, TB	TA (preservative)
Toxicity reported in human case	ICG, TB	-

Figure 1. Pros and cons for staining dyes and coating materials for MH repair.

COMMON DYES FOR CHROMOVITRECTOMY

Indocyanine Green

ICG continues to be used by vitreoretinal surgeons worldwide for staining the ILM. It was the first dye used to stain the ILM and shows a good ability to stain this tissue, most likely due to its high affinity for the matrix components of the ILM, such as collagen type 4 and laminin.^{3,9} Staining the ILM with ICG not only enhances its visibility but also increases the biomechanical stiffness of the ILM, thereby facilitating the peeling procedure.¹⁰ Although there are safety concerns regarding ICG, several methods have been introduced to decrease its toxicity. They include reducing the concentration, iso-osmolality, shortening the exposed time, selective staining, and protecting the central macular area during application.¹¹

Tricks that might be used to reduce dispersion during the application of ICG and other chemical dyes include mixing the dye with 5% glucose water to produce a heavier solution and applying these mixtures using a

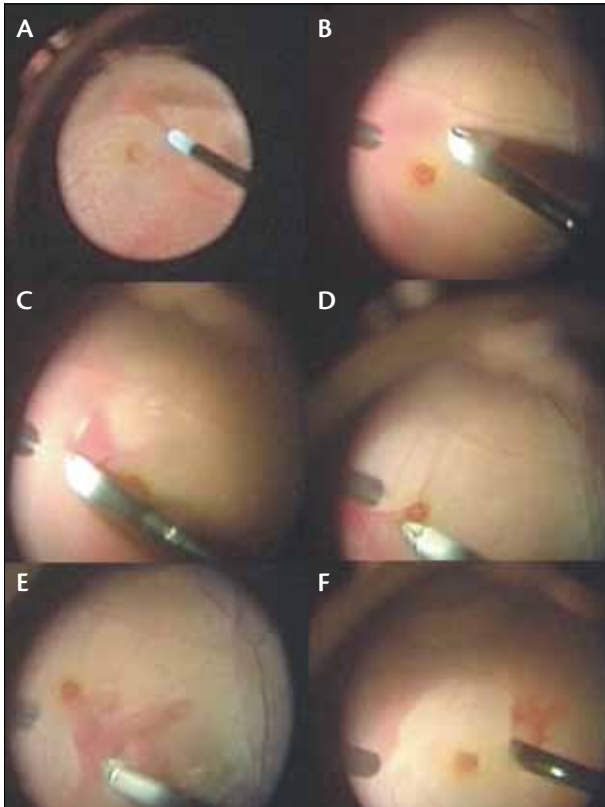


Figure 2. An autologous blood clump was produced by 5-10% blood in 5% glucose water (A). The blood clump was applied using a back-flush needle (B-E). The blood clump-coated ILM was removed in a circumferential manner around the MH. Note the obvious visibility of the ILM (F). The margin of the peeled area was well defined.

back-flush needle to achieve better control during the staining procedure.

Brilliant Blue G

BBG has been certified as a safe food additive in Europe and may be used as a marker for cardiovascular and neurologic disease proteins. In a clinical study, Enaida et al did not find any adverse effects while using BBG to stain the ILM and ERM.¹² Although a recent study reported retinal pigment epithelium and ganglion cell necrosis after more than 5 minutes of exposure, the current literature indicates low toxicity for this dye.¹³

BBG has gained popularity and has recently become a widely used agent due to its reputation of being non-toxic to retinal tissue. Several studies demonstrate that this chemical dye is an effective stain that is able to achieve favorable anatomic and functional results. BBG is considered as an alternative to ICG for staining the ILM because of its high affinity and lack of significant adverse effects.

Triamcinolone Acetonide

TA can be used to stain the transparent vitreous. It shows a good affinity for the vitreous gel and facilitates visualization during the induction of posterior vitreous detachment and removal of the complete anterior vitreous base.¹⁴ During MH repair, TA was sometimes applied using a double-staining technique involving 2 different dyes in macular surgery. The first dye (for example, TA) is typically used to stain the vitreous. After removing the vitreous and posterior hyaloid, a second dye with a high affinity to the ILM is applied. The white steroid crystal can also deposit on the surface of the ILM and enhance its margin during peeling.⁶

Autologous-blood

Autologous-blood has long been used during vitreo-retinal surgery, and its components, such as platelets, have been used during MH repair.^{15,16} Autologous heparinized whole blood has been used for MH repair since 2005. It was first used to cover the ILM and RPE for protection against ICG during MH surgery, reducing potential toxicity.¹⁷ Later, autologous heparinized whole blood was also used alone to coat the surface of the ILM and enhance visualization of the ILM margin during peeling.⁷

Recently, this technique was further improved by generating a blood clump solution by mixing autologous heparinized whole blood with 5% glucose water.⁸ This solution can be introduced to stain the posterior vitreous. It is also able to form a thin, evenly distributed layer of blood clump coating on the surface of the ILM over the macular area, allowing the ILM margin to be identified during peeling (Figure 2). The benefits of auto-blood include its cost and availability.

THE FUTURE OF CHROMOVITRECTOMY

The primary goal of chromovitrectomy is to make this surgical process safer and easier. Vital dyes facilitate the visualization of nearly transparent structures such as the vitreous cortex, ERM, and ILM. Because the ILM has a thickness of just a few microns, its peeling presents a challenge to all vitreoretinal surgeons.

When the ILM became the first target of chromovitrectomy, many efforts focused on developing an ideal dye that would be able to thoroughly stain the structure while causing the least toxicity to the retinal tissue. The initial enthusiasm for ICG has gradually decreased because of its narrow safety margin. BBG seems to have a better safety profile, although its long-term effects require further investigation.¹⁸ Therefore, there is a need for new dyes that show better safety profiles, as well as great staining contrast for optimal visualization and possibly neuroprotective effects.

The candidates for future vital dyes may come from substances present in nature. One candidate may be the anthocyanins; they were reported to stimulate the regeneration of rhodopsin in frog rod outer-segment membranes and could accumulate in the retina and offer the additional benefit of improving visual function.¹⁹ A study in cadaver eyes demonstrated the efficacy of these compounds for staining the ILM.²⁰ However, additional preclinical studies are needed to demonstrate their feasibility for chromovitrectomy.

In conclusion, chromovitrectomy could improve the ease and safety of surgery, especially for beginners who are performing ILM peeling. With cautious application, the adverse effects of current dyes could be prevented, improving the surgical outcomes for MH repair. ■

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