

Vitreoretinal Staining Solutions

Part two of a three-part series in which surgeons share pointers on the optimal use of vital dyes in retina surgery.

Considerations in Vital Dye Staining During Retinal Surgery

By Timothy L. Jackson, PhD, FRCOphth

The use of intraocular vital dyes to enhance tissue visibility during retinal surgery has the potential to improve surgical performance and reduce risk. The ideal retinal vital dye for selective membrane staining during vitreoretinal surgery should be water soluble, reasonably priced, and provide good color contrast, effective staining, and safety. Vital dyes should also offer repeatable, avid staining, yet be easily removable. Internationally, several ophthalmic vital dyes are now available, although only one formulation is currently approved for ophthalmic use by the US Food and Drug Administration (FDA). Characteristics of several vital dyes are discussed below.

COLOR CONTRAST, STAINING QUALITY

In the human visual system, certain color combinations provide better contrast than others (eg, red against green and blue against yellow). Given the

orange-red color of the fundus background, a blue or green dye provides the best color contrast on the retinal surface.

The relationship between dye concentration and tissue staining varies among dyes. Image analysis from one ex vivo study showed that staining increased linearly with dye concentration for some dyes, whereas others displayed an exponential relationship.¹ Given that dyes are variably diluted during application in a saline-filled eye, a linear relationship has advantages, making staining more predictable. However, some dyes provided uneven tissue staining despite a constant concentration. Agents shown to have favorable staining characteristics were Evans blue, rose bengal, naphthol green, natural red, and trypan blue. Some of these dyes (eg, rose bengal) may not have a suitable retinal safety profile.¹

DYES FOR VITREORETINAL PROCEDURES

Adverse effects reported to be associated with the use of indocyanine green (ICG) as a retinal vital stain have included visual field defects, reduced visual acuity, and persistent staining.² There have also been reports of a dose-dependent toxic effect on the retina. These ICG-related effects may be aggravated by low osmolarity, bright endoillumination, and use of concentrations greater than 0.05 mg/mL.³

Trypan blue ophthalmic solution 0.15% (MembraneBlue, DORC) is commonly used to help visualize the epiretinal membrane (ERM) and assist in peeling the internal limiting membrane (ILM). Trypan blue 0.15% also provides effective staining of proliferative vitreoretinopathy (PVR) membranes in eyes with complex retinal detachment. It is the only retinal dye solution approved by the FDA.

There are fewer safety concerns with trypan blue than with ICG. Trypan blue exhibits less avid binding than ICG and has a relative affinity for ERMs. It is easier to rinse out, and, unlike ICG, there is no

At a Glance

- The use of a blue or green dye provides the best color contrast against the orange-red color of the fundus background.
- Many vital dyes have been tested and several commercialized (outside of the United States).
- Trypan blue is a good choice when removing ERM during vitrectomy.
- For staining the ILM during macular hole surgery, BBG is an effective choice.

long-term issue with regard to persistence in the eye after intraocular use. Safety testing comparing ICG and trypan blue using retinal pigment epithelium (RPE) and glial cell cultures showed that the combination of exposure to 0.5% ICG and a xenon endoillumination light source damaged cultured Müller cells, whereas trypan blue did not.³

Brilliant blue G (BBG) 0.025% in combination with 4% polyethylene glycol (PEG; ILM-Blue, DORC) is a posterior dye designed for staining the ILM during vitreoretinal surgery. It is reported to have lower cytotoxicity than trypan blue or ICG, higher affinity for ILM than trypan blue, lower affinity for ERM than trypan blue, and faster staining than trypan blue.⁴ PEG is used as an integrated carrier and to increase the relative molecular weight of the dye, allowing it to fall onto the macula in a fluid-filled eye, staining the targeted tissue only and with little diffusion throughout the vitreous cavity. This increases the tissue concentration and makes it easier to remove.

A dual-combination solution that contains trypan blue 0.15%, BBG 0.025%, and 4% PEG (MembraneBlue-Dual, DORC) was commercially developed to provide a dual dye solution in a single injection that is suitable for ILM, ERM, and PVR membrane staining.^{5,6}

TIPS AND TECHNIQUES

For removal of ERM during vitrectomy, trypan blue is the logical first choice. It is used in the laboratory to stain devitalized tissue, and this characteristic can be exploited during surgery if the edge of the membrane is lost. Restaining will often reveal damaged edges that thereby expose dissection planes. If it is then desired to remove the underlying ILM, a suitable secondary dye such as BBG could be used. However, a simpler option is to use a dual dye solution that contains trypan blue and BBG in a single injection to simultaneously stain the ERM and ILM. Surgeons may need to restain the ILM with the same dye following ERM removal.

BBG is a good option for macular hole surgery, where visualization of the ILM is important; but safety is also important, as the foveal photoreceptors are directly exposed to the dye via the full-thickness retinal defect. An integrated PEG carrier helps concentrate the dye at the macula, eases dye removal, and avoids the need for air-fluid exchange to localize dye on the back of the eye. If a formulation with a PEG carrier is not available, the dye may be refrigerated and used with Hartmann solution as the vitrectomy infusion. This approach should encourage the dye to fall onto the macula.

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CONCLUSION

Vital stains can facilitate macular surgery. Most, though not all, appear to have favorable safety profiles. Future studies may explore the use of fluorophore-labeled antibodies directed against specific macular tissue which, if combined with selective illumination and barrier filters, may lead to highly specific fluorescent staining of ocular tissues.⁷ Whether or not these next-generation dyes will emerge in clinical practice is unknown, but it seems likely that current dyes will remain useful surgical tools for the foreseeable future. ■

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