New approaches to managing open globe eye injuries with a thermoresponsive sealant

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Traumatic eye injury is the leading cause of unilateral blindness worldwide, especially in developing countries. Open globe injuries, which have the tendency to lead to severe visual impairment, account for about 10% of these injuries (1). The risk for open globe injury was highest in young adults (2) who were actively engaged in economic activities; therefore, open globe injuries not only affect the quality of life and economic condition of patients, but also cause a great deal of cost for society as a whole (3).

Many clinicians would agree that there has been an unmet need in the treatment of open globe injuries. Publications have reported that visual prognosis deteriorates with increasing time to intervention (4,5). With prolonged time to the primary closure of an open wound, intraocular tissue may be infected by microbes from conjunctiva flora or foreign bodies, and that the vitreous body may prolapse out of the globe, which promotes subsequent retinal detachment and proliferative vitreoretinopathy. Nevertheless, the time to interventions for open globe injuries have often been delayed due to various reasons; this contrasts with the fact that the concept of the golden period has been established for the management of acute myocardial infarction, acute stroke, and major trauma (6-9). Much effort has been made for decades to provide proper early intervention to improve the prognosis of patients with such diseases and traumatic conditions. On the contrary, patients with traumatic eye injuries from mass-casualty incidents are usually triaged behind others with more critical injuries. Furthermore, for patients with multiple trauma, it is often necessary to treat more urgent wounds before treating open globe injuries. Patients may be separated from medical services, including surgical interventions by skilled physicians, that require the use of microsurgical instruments and surgical microscopes. Due to these circumstances, adequate management may have not been provided to patients who could avoid developing profound visual impairments if timely intervention had been applied.

Recently, an innovative research group suggested a new approach to manage open globe injuries using a thermoresponsive sealant (TRS), which they developed (10). This approach involves temporarily occluding the open wound early, with the TRS, without specialized equipment such as surgical instruments, which provides the patient a larger window time to subsequently undergo complete surgical intervention. The developed TRS consists of cross-linked N-propylacrylamide copolymerized with butylacrylate and has the property of reversible transition, from liquid to solid. Below body temperature, the TRS remains in the liquid state and can be injected and moldable, and when raised to body temperature, the TRS solidifies by body heat-induced gelation. At first, the efficacy of the TRS was evaluated in an *ex vivo* cadaveric porcine eye model of ocular trauma, where TRS was applied to lacerated eye models after an incision procedure. Intraocular pressure (IOP) was then raised by infusion with warm saline. Depending on the TRS formulation, it withstood IOPs of up to 77 mmHg without leakage. This research group also developed TRS deployment equipment, for ease of use. To prevent premature transition, a controlled-environment

injector tool was proposed. With the deployment technique, an *in vivo* validation study was performed in a rabbit model of ocular trauma. After creating a 3-mm full-thickness laceration in the sclera, the tool was inserted into the laceration and the hydrogel was deployed. In this *in vivo* study, wound sealing improved significantly, and the TRS did not induce any neurotoxicity, retinal tissue degradation, or significant chronic inflammation after 30 days of exposure.

Although the new tissue repair technology demonstrated sustained efficacy and sufficient biocompatibility, an important hurdle needs to be overcome to achieve an actual contribution to the improvement of visual prognosis of open globe injuries in clinical situations. In the researcher's *in vivo* assessment, the scleral laceration wound was near the limbus, and conjunctival laceration and chemosis were well-controlled, which would not be expected in real clinical situations. When clinicians encounter cases of open globe injury, severe chemosis usually accompanies the injury. Careful exploration of the entire wound under chemosis is necessary, which sometimes makes the surgery complex and unpredictable. Therefore, if a surgical microscope and sufficient expertise are not available, adequate exploration and proper exposure of the open laceration wound might not be possible, which limits management of the wound with utilization of TRS in urgent situations. This problem could seriously undermine clinical efficacy, which the approach using the TRS originally intended to achieve.

This research demonstrates that tissue repair technology using a TRS can provide sustained efficacy and sufficient biocompatibility in ex-vivo and in-vivo assessments. The clinical application of the TRS approach would be more feasible if convenient methods to control chemosis or expose the location of open wound under the conjunctiva can be developed. In addition to this result, further experimental research and clinical studies need to be performed to make this approach a comprehensive solution for open globe injuries, which may help clinicians save a substantial number of eyes with open globe injuries worldwide.

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