DRUG DELIVERY TO ANTERIOR AND POSTERIOR SEGEMENT OF THE HUMAN EYE

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ABSTRACT

The eye is a complex physiological system controlled by mechanical, biochemical, and neurological factors, which, under normal conditions, maintain stability and regulation of the intra-ocular pressure. This stability and regulation are essential for the maintenance of the eye’s visual functions and for the nourishment of its tissues. Understanding the details of the ocular fluid flow in the human eye is of interest to ophthalmologists so that they can adapt treatment procedures in case of eye disease. However, many aspects of fluid flow within the eye have not yet been fully examined or quantitatively explained. Many difficulties occur for in vivo experiments on human eye because of their small size, low velocities, etc., and developing numerical models constitutes an attractive approach to study the human eye.

Numerical computations of the ocular fluids dynamics in a human eye are presented in this study to delineate the basic flow mechanisms. The calculations are based on a geometrical model of the eye including: the trabecular meshwork, as a ring-like porous gutter of specific pore diameter and void fraction; the anterior segment, filled with aqueous humor, and the vitreous cavity, filled with vitreous humor.

Characteristics of the porous zone are tailored in the numerical simulation so that the pressure drop of 6 mm Hg occurs through the trabecular meshwork. Flow patterns in both anterior and posterior segments are described and shear stresses on the lens, iris and retina are examined to locate their maximum values. The outer surface of the cornea is assumed to be at fixed temperature (i.e., at ambient temperature), while the iris surface iris is assumed to be at the core body temperature. Aqueous flow in the anterior chamber is driven by buoyancy due to the temperature difference between the cornea and the iris. Large recirculation with very low velocities occurs in the posterior segment as show in the Fig. 2.

Ophthalmic drug delivery is one of the most interesting and challenging endeavors facing the mechanical community. The anatomy, physiology, and biochemistry of the eye render this organ exquisitely impervious to foreign substance. Current methods for ocular delivery include topical administration (eye drops), subconjunctival injections, pericocular injections, intravitreal injections, surgical implants, and systemic routes. However, all of these methods have limitations. Therapeutic levels of many drugs may be difficult to achieve in ocular tissues and systemic toxicities are of concern when the oral and
intravenous routes of administration are used. Intravitreal injections, periocular injections, and sustained-release implants can be used to achieve therapeutic levels of drugs in ocular tissues, but invasive methods are inherently risky due to the potential for bleeding, infection, retinal detachment, and other local injuries. A typical ophthalmic dropper delivers 30 µl, most of which is rapidly lost through nasolacrimal drainage immediately after dosing. It has been estimated that typically less than 5% of a topically applied drug penetrates the cornea and reaches intraocular tissues. Eye drops are useful in treating conditions affecting either the exterior surface of the eye or tissues in the front of the eye, but cannot penetrate to the back of the eye for treatment of retinal diseases. The majority of the topically applied drugs enter the eye by passage across the cornea. This is an extremely inefficient process owing largely to the resistance exerted by the corneal epithelium to drug penetration. The corneal epithelium contributes over 90% of the corneal resistance to penetration to the topically applied drug. A measure of the corneal penetration efficiency of drugs is the permeability coefficient. This is generally on the order of 0.1-4.0E5 cm/s. Computational simulation of flow of the drug in the anterior chamber through the cornea is therefore very useful in producing the necessary understanding of the flow mechanisms. This is one goal of the present work and results from these simulations will be presented.

An intravitreal injection provides the most direct approach to delivering the drugs to the tissues of the posterior segment, and therapeutic tissue drug levels can be achieved. Mass transport in the vitreous can occur by both convective and diffusive transport. The transport usually depends on the state of the system, which includes temperature, pressure, and solute properties. In the present study we have simulated the injection and transport of drug in the vitreous chamber. In order, to simplify the calculation, we assumed that the drug formed a sphere after injection and was homogeneous within it. The injection size was 0.075 cm of diameter and the injection position was 1.28cm away from the retinal surface. Preliminary results from these simulations will be presented.

Posterior uveitis and retinitis secondary to glaucoma also contribute considerably to loss of vision. Trans pars plana vitrectomy (TPPV) is used to treat many different retinal disorders such as Proliferative diabetic retinopathy (including vitreous hemorrhage), Macular hole, Intraocular infections (endophthalmitis), etc. These conditions affect tissues at the back of the eye, where drug treatment is difficult to administer. Vitrectomy is a microsurgical procedure in which specialized instruments and techniques are used to repair retinal disorders, many of which were previously considered inoperable. The initial step in this procedure is usually the removal of the vitreous gel through very small (~1.4mm) incisions in the eye wall, hence the name "vitrectomy". The vitreous is removed with a miniature handheld cutting device and replaced with a special saline solution or silicon oil similar to the liquid being removed from the eye. A complicating factor can be liquefaction of the vitreous in the patients who have undergone vitrectomy. It can be expected to lead the fluid circulation and the abolishment of gradients in the drug concentration within the liquefied portion which leads to the reduced half life of the drug in the vitreous chamber. Therefore, it is important to study the effect of drug kinetics when vitreous is replaced by saline solution or silicon oil. The present study will analyze the role of the vitreous fluid properties in the delivery of the drug.

REFERENCES