HEAT TRANSFER, FLUID FLOW AND DRUG TRANSPORT IN THE ANTERIOR EYE

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Summary This study numerically investigates the temperature distribution and aqueous humor flow field in the human eye, and their effects on the transport process of drugs topically applied on the corneal surface. The results can help to understand heat and mass transfer processes in the human eye, and improve the drug delivery efficacy in the treatment of eye diseases such as glaucoma.

INTRODUCTION

Aqueous humor (AH) in the anterior human eye forms part of the pathway for topically applied drugs in the treatment of intraocular diseases. Compared with mechanisms such as constant replenishment of aqueous humor from the ciliary body (CB) to trabecular meshwork (TM), phakodenesis and rapid eye movement during sleep, natural convection has been shown to be the dominant cause of aqueous humor flow, which results from the temperature gradient across the eye [1,2]. Since a non-invasive measurement in the human eye is still practically impossible, it is of fundamental importance to develop mathematical models of heat transfer, AH flow and drug transport in the eye. Compared with the vast literature available on drug transport in the posterior eye [3,4], drug transport in the anterior human eye has rarely be studied. Recently, Lin et al [5] proposed a mathematical model of the transport of ethacrynic acid (ECA), a topically applied drug for the treatment of primary open-angle glaucoma (POAG), and predicted the spatial and temporal evolution of ECA concentration in the anterior eye. However, they only considered AH production and outflow, and neglected temperature inhomogeneity and the resulting natural convection of AH. The goal of this work is to investigate the effects of natural convection and eye orientation on the AH flow and ECA transport in the anterior eye, and help to improve the efficacy of drug delivery in the treatment of intraocular diseases.

METHODOLOGY

A two-dimensional model of the human eye is developed, including the cornea, anterior chamber, posterior chamber, iris, TM, CB, lens and vitreous body, as shown in Fig. 1. Temperature distribution is governed by the transient bioheat equation, with heat loss due to convection, radiation and tear evaporation specified on the corneal surface and a heat flux boundary condition specified on the sclera surface. Steady 2D incompressible Navier-Stokes equations are used to simulate the AH flow in the anterior and posterior chamber, in which the buoyancy force due to temperature gradients is modeled using the Boussinesq approximation. We assume that there is only one inlet, i.e., CB, and one outlet, i.e., TM, and no-slip conditions are specified on other boundaries. Finally, evolution of ECA concentration is governed by a transient convection diffusion equation, with a constant concentration C_0 as the boundary condition on the pre-corneal surface. The coupled heat transfer, fluid flow and mass transfer problem is solved in Comsol Multiphysics 3.5a.

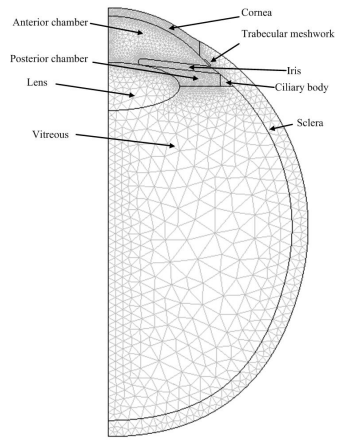

Fig. 1.

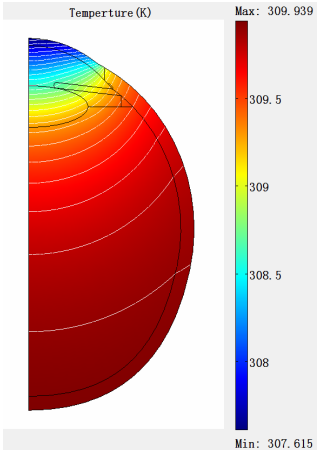

Fig. 2.

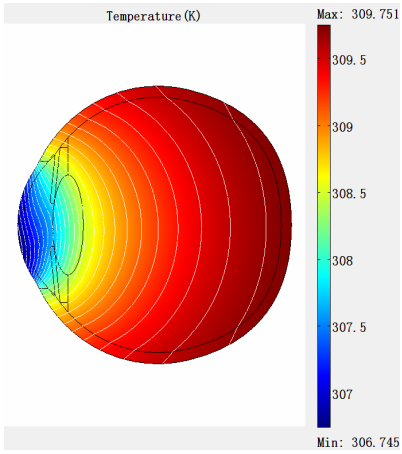

Fig. 3.

RESULTS AND DISCUSSIONS

Fig. 2 and 3 plot the temperature distribution inside the human eye at supine and standing positions, respectively, when the ambient temperature is 298K and the body temperature is 310K. In Fig. 3, the temperature contours in the anterior chamber are distorted due to the non-axisymmetric gravity force. Fig. 4 and 5 depict the AH flow fields at supine and standing positions, respectively, in which subfigures (a) and (b) are results with and without considering natural convection, respectively. Since temperature on the surfaces of lens and iris is higher than that on the corneal

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surface, the warmer fluid which has a lower density will rise, and the cooler fluid with a higher density will descend near the corneal surface. Hence, a constant circulation of AH is generated in the anterior chamber. ECA concentration distribution with and without considering natural convection is shown in Fig. 6(a) and Fig. 6(b), respectively, after 6 hours of ECA administration. From Fig. 4 and Fig. 6, it can be clearly seen that natural convection leads to stronger AH circulation, as well as increased overall ECA concentration in the anterior chamber, especially in the central region. Fig. 7 plots the time-dependent change in ECA concentration at TM for the supine eye position when the ambient temperature is 298K. As can be seen, natural convection of AH lowers the steady state ECA concentration at TM by approximately 15%. This is because when the ambient temperature is lower than the body temperature, AH circulation in the anterior chamber is counter clockwise and points from TM to the corneal center along the corneal inner surface. In this case, diffusion transport dominates convective transport of ECA. As the ambient temperature is further decreased, convection overpasses diffusion and more ECA is convected along the lower half of AH circulation (left half of the curve in Fig. 8). On the other hand, when the ambient temperature is higher than the body temperature, AH circulation becomes clockwise and the aforementioned trend is reserved (right half of the curve in Fig. 8). It is also indicated in Fig. 8 that higher ambient temperature can help to increase the steady ECA concentration at TM. Fig. 9 compares ECA concentration at TM between the supine eye position and standing eye position when the ambient temperature is 298K. Since the AH circulation in Fig. 5(b) is counter clockwise, the lower part of TM has a higher concentration than the upper part, which has about the same ECA concentration for the supine eye position.

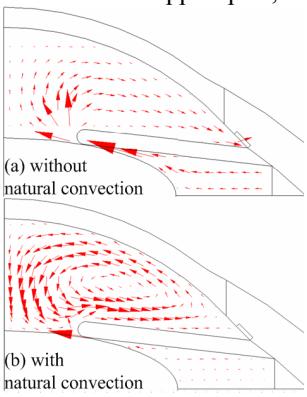
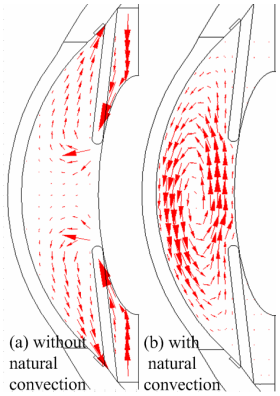


Fig. 4.



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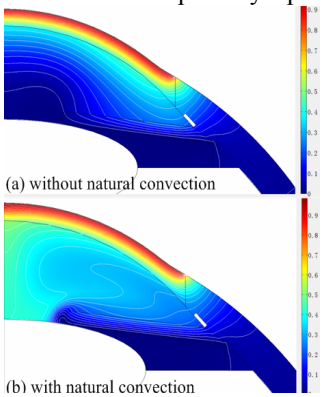

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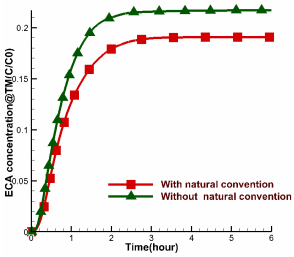

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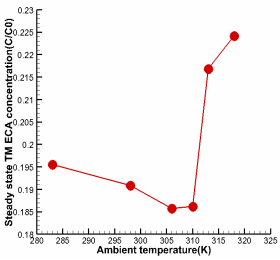

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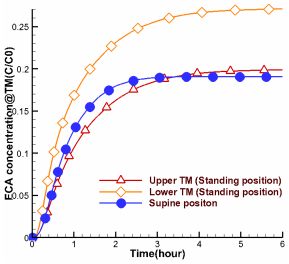

Fig. 9.

CONCLUSIONS

In this study，we numerically invesigate temperature distribution, AH flow and drug transport in the anterior human eye. The concentration of ECA at its target location, TM, depends on several factors，including ambient temperature and eye orientation. Our results show that natural convection causes AH circulation in the anterior chamber whose direction is reversed when the temperature gradient across the eye changes sign. The results on the transport of topically applied ECA is that ECA concentration at TM first decreases, then increases, with increasing ambient temperature. At the standing eye position, lower TM has higher ECA concentration than upper TM, the latter being about the same as the uniform ECA concentration at the supine eye position. Our results may provide guidelines to improve the delivery of ECA, as well as other therapeutic agents for intraocular diseases. E.g., one may apply a warm towel to enhance the efficacy of ECA administration by increasing the corneal temperature.

References

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