Flow in the Canal of Schlemm and its Influence on Primary Open Angle Glaucoma

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1 POAG in Human Eyes

POAG (Primary Open Angle Glaucoma) is a major cause of blindness, affecting 65-70 million sufferers worldwide ([ERC04]). The eye produces aqueous humour (AH: a water-like substance secreted by the ciliary body) which flows behind the iris, through the pupil aperture, out into the anterior chamber (AC) and drains from the eye via the drainage angle. From the drainage angle the AH passes through a biological filter (the trabecular meshwork, or TM) into the canal of Schlemm (SC), the main drainage route from the eye, and finally exhausts into "collector channels". POAG occurs when this drainage mechanism is somehow compromised [FW92]. Essentially the AH cannot be removed quickly enough and as a result the intraocular pressure (IOP) increases in the eye. Contrary to popular belief, glaucoma and elevated IOP are not synonymous. Though very often associated with elevated IOP, glaucoma is, in reality, an optic nerve neuropathy. Notwithstanding this, elevated IOP is always regarded as potentially harmful to the eye. In the current study we therefore seek to model the flow of AH from the AC through the TM and into the SC and to couple this flow to predictions of changes in IOP.

2 Governing Equations

2.1 Fluid Modelling

The flow of AH through the TM, into the SC and out into the collector channels was studied in [JK83], [TA89] and [AS06]. None of these studies appeared to realise that the flows involved may be thought of as lubrication theory flows. Though in each case the final equations were very similar to the equations derived in Section 2.3 below, none of these studies attempted to couple the SC flow to a model for the evolution of overall IOP changes, which is the main aim of the current study.

The SC typically has half-length (i.e. length between a symmetry axis and a collector channel) $L = 600\mu$m, ([JK83]) undeformed depth $h_0 = 25\mu$m ([JK83]) and breadth $B = 300\mu$m ([JK83]). The aspect ratio $\epsilon = h_0/L$ is thus about 0.04. Using the values $\mu = 0.75 \times 10^{-3}$Pa s ([JK83]) and $\rho = 1003$kg/m^3 ([FW92]) for the density and dynamic viscosity respectively, the Reynolds number is $Re = LU/\nu \sim 4$ and the reduced Reynolds number $\epsilon^2 Re \sim 0.004$. The lubrication theory equations may therefore indeed be used (see, for example [Ock95]). The BVP to be studied (see Fig. 1 for nomenclature) is therefore

$$p_x = \mu u_{zz}, \quad p_z = 0, \quad u_x + w_z = 0 \quad (x \in [0, L], 0 \leq z \leq h(x)) \tag{1}$$

with boundary conditions

$$u(x,0) = w(x,0) = 0, \quad u(x,h(x)) = 0, \quad w(x,h(x)) = w_h(x),$$
$$p_x(0,z) = 0, \quad p(L,z) = p_{out}, \tag{2}$$

Here p denotes pressure, $\mathbf{q} = (u(x,z), w(x,z))$ fluid velocity, subscripts denote derivatives, w_h is the flow speed through the TM and $p_{out} \sim 9$mmHg ([JK83]) is the IOP at a collector channel.

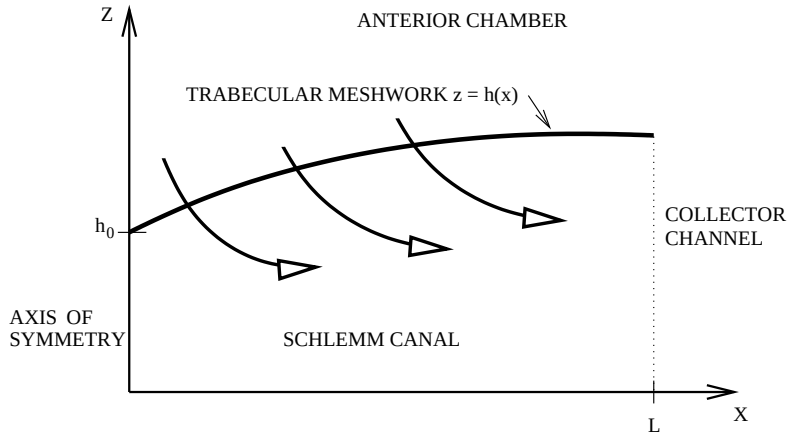

Fig. 1. Schematic diagram of flow through the TM into the SC

2.2 Friedenwald's Law

To close the model we must relate the eye's AH production and removal to the IOP. It has long been accepted that the volume and IOP of a human eye are related by Friedenwald's law [F37]. This states that two IOPs p_1 and p_2 are related to respective ocular volumes V_1 and V_2 (measured in $\mu\ell$) via

$$K(V_1 - V_2) = \log_{10} p_1 - \log_{10} p_2$$

where $K \sim 0.025/\mu\ell$ [FW92] is a known constant. Denoting normal conditions using a subscript n ($p_n \sim 14$mmHg ~ 1867Pa ([BRM05])) and altered conditions using a subscript i, we therefore find that $p_i = p_n \exp(\tilde{K}(V_i - V_n))$ where $\tilde{K} \sim 5.75646 \times 10^7/\mathrm{m}^3$. Differentiation now shows that

$$\frac{dp_i}{dt} = \tilde{K} p_i (\dot{V}_{in} - \dot{V}_{out}) \tag{3}$$

where $\dot{V}_{in}$ ($\sim 2\mu\ell/$min ([BRM05])) and $\dot{V}_{out}$ ($\mathrm{m}^3/$sec) denote the respective total amounts of fluid flowing in and out of the eye.

2.3 Fluid Flow/IOP Evolution Equations

We assume that the temporal changes in the IOP take place on a much longer time scale than that associated with the passage of an individual fluid particle from the AC to a collector channel, so that the flow may be treated as quasi-steady. The flow problem (1)-(2) may now be solved to yield

$$u = \frac{p_x}{2\mu}(z^2 - hz), \quad w = \frac{p_{xx}}{2\mu}\left(\frac{hz^2}{2} - \frac{z^3}{3}\right) + \frac{p_x h_x z^2}{4\mu}$$

where the flow pressure $p(x)$ satisfies

$$\left(\frac{p_x h^3}{12\mu}\right)_x = w_h(x) \quad (p(L) = p_{out}, \quad p_x(0) = 0).$$

In general both $w_h(x)$ and $h(x)$ are unknown and must be determined. The outflow $\dot{V}_C$ ($\mathrm{m}^3/$s) from a single collector channel is therefore

$$\dot{V}_C = \int_0^{h(L)} Bu\,|_{x=L}\; dz = -\frac{B}{12\mu}(h^3 p_x)\,|_{x=L}$$

so that $\dot{V}_{out} = N\dot{V}_C$ where N is the total number of collector channels ($N \sim 30$ for a human eye ([ERC04])) and the IOP $p_i(t)$ is determined by (3) with $p_i(0) = p_{io}$.

3 Results

We now examine a number of different cases, relating aqueous outflow to changes in IOP for various structure submodels.

3.1 Simple modelling cases

First we consider the (unrealistic) case where $h(x) \equiv h_0$ and $w_h(x) \equiv \alpha < 0$ are both constant. We find that

$$p = p_{out} - \frac{6\alpha\mu}{h_0^3}(L^2 - x^2), \quad \dot{V}_{out} = -NB\alpha L$$

and thus

$$\frac{dp_i}{dt} = \tilde{K}p_i(\dot{V}_{in} + NB\alpha L) \quad (p_i(0) = p_{io}).$$

Thus $p_i = p_{io}\exp(\beta t)$ where $\beta = \tilde{K}(\dot{V}_{in} + NB\alpha L)$. The IOP thus increases/decreases exponentially depending on whether the quantity $-\alpha$ is less than/greater than $\dot{V}_{in}/NBL$. A "worst-case" scenario arises if all aqueous outflow ceases so that $\dot{V}_{out}$ suddenly becomes zero. The IOP rises exponentially, on a timescale $(\tilde{K}\dot{V}_{in})^{-1} \sim 520$s. Starting from a normal IOP of 14mmHg, the IOP rises to a dangerous value of 30mmHg in just under seven minutes.

3.2 Flow through TM determined by Darcy's law

The previous case is unrealistic: the TM is acts as a porous filter, so that the speed $w_h(x)$ of the flow into the SC is determined by both the IOP in the AC and the flow pressure. Assuming that $h(x)$ is still given by the constant h_0, we therefore now consider the consequences of using Darcy's law $\mathbf{q} \propto \nabla p$ to model the flow through the TM by setting $w_h = -\frac{k}{d\mu}(p_i - p)$. Here d is the width of the TM and the (constant) permeability k (dimensions m^2) has been measured for the TM in the form of a "TM resistance" $R_T = \mu d/(kBL)$ (dimensions kg $\mathrm{s}^{-1}\mathrm{m}^{-4}$) where d is the width of the TM. Thence

$$p_{xx} - \beta^2 p = -\beta^2 p_i \qquad \left(\beta^2 = \frac{12k}{dh_0^3}\right),$$

the total outflow is given by

$$\dot{V}_{out} = N\frac{B\beta h_0^3}{12\mu}(p_i - p_{out})\tanh\beta L,$$

and the IOP is therefore governed by

$$\frac{dp_i}{dt} = p_i(A + Bp_i) \qquad (p_i(0) = p_{i0}) \tag{4}$$

where

$$A = \tilde{K}\left(\dot{V}_{in} + \frac{N\tanh(\beta L)p_{out}}{R_T\beta L}\right), \quad B = -\frac{\tilde{K}N\tanh(\beta L)}{R_T\beta L}.$$

Equation (4) has two steady states: an unphysical one at $p_i = 0$ and another (which may easily be shown to be stable) at $p_i = -A/B$. Normally the IOP remains constant at $p_i = p_n = 14$mmHg ~ 1867Pa say. Thence

$$p_n = -\frac{A}{B} = p_{out} + \frac{\dot{V}_{in}R_T\beta L}{N}\coth(\beta L).$$

We can now "back out" a value for R_T. Using the parameter values previously considered, we find that $R_T \sim 1.96 \times 10^{13}\text{kg s}^{-1}\text{m}^{-4}$, in very close agreement with measured values ([JK83], [ERC04]). Equation (4) has exact solution

$$p_i(t) = \frac{Ap_{i0}}{(A + Bp_{i0})e^{-At} - Bp_{i0}}.$$

A TM blockage thus causes the IOP to rise on a timescale $1/A$ to its new elevated value. It is now easy to calculate the IOP rise that would occur if collector channels become blocked or the TM resistance should increase for some reason (such as blockage by particles)

4 Conclusions and Further Work

We have neglected both the effects of uveoscleral outflow which is another (much weaker) AH drainage mechanism, and "pseudofacility", whereby the production of AH by the ciliary body is surpressed at elevated IOP. Both could be included if desired. Further study will include cases where (i) the TM is deformable and (ii) The permeability K in Darcy's law is not constant (the pores in the TM close as the pressure difference across it increase).

References

[AS06] Avtar, R., Srivastava, R.: Aqueous outflow in Schlemm's canal. Appl. Math. Comp., **174**, 316–328 (2006)

[BRM05] Broquet, J., Roy, S., Mermoud, A.: Visualization of the aqueous outflow pathway in the glaucoma surgery by finite element model of the eye. Comp. Meth. Biomech. Biomed. Eng., **1**, 43–44 (2005)

[ERC04] Ethier, C.R., Read, T.A., Chan, D.: Biomechanics of Schlemm's canal endothelial cells: influence on F-Actin architecture. Biophys. J., **87**, 2828–2837 (2004)

[FW92] Fatt, I., Weissman, B.A.: Physiology of the eye, 2nd Edition. Butterworth-Heinemann, Boston (1992)

[F37] Friedenwald, J.S.: Contribution to the theory and practice of tonometry. Am. J. Ophthalmol., **20**, 985–1024 (1937)

[JK83] Johnson, M.C., Kamm, R.D.: The role of Schlemm's canal in aqueous outflow from the human eye. Inv. Ophth. Vis. Sci., **24**, 320–325 (1983)

[Ock95] Ockendon, H., Ockendon, J.R.: Viscous Flow. Cambridge University Press, Cambridge (1995)

[TA89] Tandon, P.N., Autar, R.: Flow of aqueous humour in the canal of Schlemm. Math. Biosciences, **93**, 53–78 (1989)