Numerical Modeling of Ophthalmic Response to Space

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INTRODUCTION

To investigate ophthalmic changes in spaceflight, we would like to predict the impact of blood dysregulation and elevated intracranial pressure (*ICP*) on Intraocular Pressure (*IOP*). Unlike other physiological systems, there are very few lumped parameter models of the eye [1, 2]. The eye model described here is novel in its inclusion of the human choroid and retrobulbar subarachnoid space (rSAS), which are key elements in investigating the impact of increased *ICP* and ocular blood volume. Some ingenuity was required in modeling the blood and rSAS compartments due to the lack of quantitative data on essential hydrodynamic quantities, such as net choroidal volume and blood flowrate, inlet and exit pressures, and material properties, such as compliances between compartments.

MATERIALS AND METHODS

The model is comprised of four compartments (Fig 1a). Due to the scarcity of data, a single blood compartment is a proxy for the vasculature of the eye. We derived an equation for the net arterial inflow Q_a (Fig 1b) by drawing inspiration from prior works [3-5]. We have assumed that the retina is well-regulated so that its effect on *IOP* changes can be ignored.
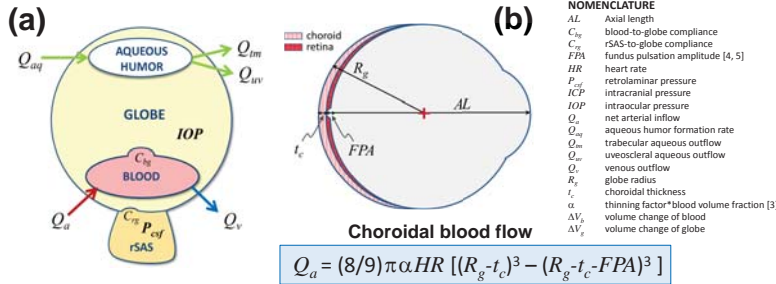

NOMENCLATURE

AL	Axial length
C_{bg}	blood-to-globe compliance
C_{rg}	rSAS-to-globe compliance
FPA	fundus pulsation amplitude [4, 5]
HR	heart rate
P_{csf}	retrolaminar pressure
ICP	intracranial pressure
IOP	intraocular pressure
Q_a	net arterial inflow
Q_{aq}	aqueous humor formation rate
Q_{tm}	trabecular aqueous outflow
Q_{uv}	uveoscleral aqueous outflow
Q_v	venous outflow
R_g	globe radius
t_c	choroidal thickness
α	thinning factor*blood volume fraction [3]
ΔV_b	volume change of blood
ΔV_g	volume change of globe

Choroidal blood flow

$$Q_a = (8/9)\pi\alpha HR\ [(R_g-t_c)^3 - (R_g-t_c-FPA)^3]$$

Figure 1. Schematic of: (a) 4-compartment lumped parameter eye model; and (b) calculation of net choroidal flow.

Researchers have injected saline into the anterior chamber of the eye to study its effect on *IOP*. Fig 2a shows a compilation of such data for the net volume change of the globe, ΔV_g, and *IOP* for enucleated eyes (blue) and living eyes (red) [6]. From this, we can determine C_{bg}. Park *et al.* [7] documented the change in position (x_{LC}, y_{LC}) of the anterior surface of the lamina cribrosa (LC) resulting from surgical intervention for relief of high *IOP* (Fig 2b). Unlike chronic glaucoma patients, these individuals experienced elevated *IOP* for a short time (here, 2.57±1.32 days). It is unlikely that substantial tissue remodeling could have occurred over this relatively brief period, so we will assume that the change in LC position represents an elastic response of the tissues of the posterior eye.
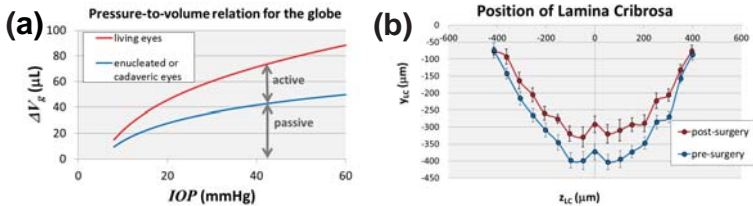

Figure 2. Essential data for determining compliances: (a) Pressure/volume curve for the globe in living (red) and enucleated (blue) eyes. (Data derived from [6]) and; (b) the change in position of the lamina cribrosa due to surgical intervention for *IOP* reduction. (Data derived from [7])

RESULTS

In response to imposed volume changes, the living eye incorporates both passive and active behaviors, such as regulation, while nonliving eyes can only show a passive response. We attribute the difference between the curves in Fig 2a to blood flow and blood volume changes. The compliance between the globe and blood compartments, C_{bg}, at a given *IOP* is the ratio of ΔV_b to *IOP* (Fig 3). Note that C_{bg} is of order 1 μL/mmHg at a typical *IOP* of 15 mmHg.
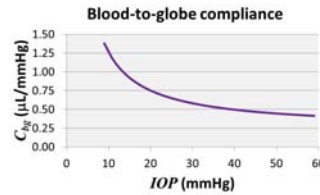

Figure 3. Compliance between the globe and blood compartments as derived from the differential response between living and enucleated eyes. Data obtained from [6].

For adjacent compartments that do not exchange fluid, the compliance governs the extent to which adjoining pressures can influence each other. To calculate compliance between the rSAS and globe, we used clinical data on LC location (Fig 2b) to determine an areal change following *IOP* reduction and swept this area 180° to estimate volume change. We calculated that C_{rg} ~1.1e-3 μL/mmHg. Since this is three orders of magnitude lower than C_{bg}, we predict that P_{csf} plays a minor role in setting *IOP* in comparison to the dynamics of blood flow.

Fig 4 presents experimental and simulated results for *IOP* change (ΔIOP) in parabolic flight as a function of initial IOP_0. Mader *et al.* [8] showed large variation in inter-individual response as measured via TonoPen. The data points may represent the mean value of replicated measurements. We had insufficient information to include error bars on the experimental data due to measurement or device uncertainties.
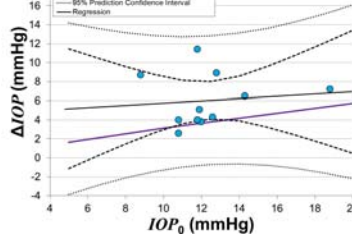

Figure 4. Changes in intraocular pressure during parabolic flight for experimental [8] and simulated results.

The simulation follows the algorithm defined above with parameters that represent a typical healthy middle-aged male. We used an artificially generated Q_a as a sinusoidal forcing function and allowed it to double in magnitude. We were unable to incorporate possible confounding factors, such as the effect of commonly used medications in parabolic flight. The simulation does not include any explicit regulatory response nor does it attempt to cover the entire valid physiological range. Even with this simple framework, the simulated results largely fall within the experimental confidence interval.

Studies of acute ocular blood flow, e.g., due to exercise or postural change, demonstrate that individuals may show a variety of regulatory responses. Our next challenge is to incorporate regulation and demographic variability into our model in a meaningful way.

CONCLUSIONS

We developed a means of computing compliances and flowrates for the rSAS and blood compartment that are currently unavailable in the literature. The estimate of globe-to-rSAS compliance is far smaller than that between the globe and blood compartment, indicating that blood dynamics is more important than retrolaminar pressure in setting *IOP*. However, P_{csf} still plays a major role in setting the biomechanical stress state in the LC. Preliminary validation of the lumped parameter eye model produced encouraging results, which suggest that the dependence of C_{bg} on IOP_0 may play an important role in ocular response to acute hydrostatic pressure change. Following additional development, verification and validation, this code will be used to systematically explore the relative importance of each flow component, compartment pressure, compliance and resistance throughout the relevant physiological ranges.

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