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A poroelastic model for the perfusion of the lamina cribrosa in the optic nerve head

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ABSTRACT

In this work we present a mathematical model for the coupling between biomechanics and hemodynamics in the lamina cribrosa, a thin porous tissue at the base of the optic nerve head which is thought to be the site of injury in ocular neurodegenerative diseases such as glaucoma. In this exploratory two-dimensional investigation, the lamina cribrosa is modeled as a poroelastic material where blood vessels are viewed as pores in a solid elastic matrix. The model is used to investigate the influence on the distributions of stress, blood volume fraction (or vascular porosity) and blood velocity within the lamina cribrosa due to the application of different levels of the intraocular pressure (IOP) and the enforcement of different mechanical constraints at the lamina's boundary. The model simulations suggest that the degree of fixity of the boundary constraint strongly influences the lamina's response to IOP elevation. Specifically, when the boundary is mechanically clamped, IOP elevation leads to an increase in stress close to the lamina's boundary, making it more susceptible to tissue damage. On the other hand, when rotations are allowed at the boundary, the most vulnerable region appears to be located at the lamina's central axis, in proximity of the eye globe, where increased stress and reduced vascular porosity and blood velocity are predicted for increased levels of IOP.

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1. Introduction

Elevated intraocular pressure (IOP) is one of the major risk factors for the irreversible vision loss in glaucoma, which is the second leading cause of blindness world-wide [1]. Many studies have indicated that chronical IOP elevation induces significant structural changes in a thin porous tissue at the base of the optic nerve head called lamina cribrosa [2–6]. Elevated IOP may lead to vision loss by inducing mechanical damage on the retinal ganglion cells axons passing through the lamina (mechanical hypothesis) [7,8] and/or by altering the blood flow within the lamina's tissue (hemodynamical hypothesis) [9,10]. It is reasonable to expect that the mechanical deformations of a living tissue would affect blood flow within the tissue, and therefore the mechanical and hemodynamical hypotheses should be addressed as one coupled problem [5,11]. In this paper, we develop a mathematical framework that allows, for the first time, to theoretically investigate the coupling between the mechanical and hemodynamical hypotheses concerning the effect of IOP elevation on the lamina's tissue.

Various mathematical models have been developed to theoretically investigate the biomechanical hypothesis, namely the biomechanical response of the lamina cribrosa to IOP elevation. For example, linear and nonlinear elastic models for thin circular plates have been used to show that thickness, radius, and mechanical properties of the lamina cribrosa, along with the degree of fixity offered by the sclera, are among the major factors influencing the IOP-induced deformation of the lamina [12,13]. Elasticity models based on finite elements have been used to simulate the biomechanics of the lamina cribrosa on real geometries (see e.g. [14–16] and in the references therein) and to study the micro-architecture of the collagen fibrils within the lamina (see e.g. [17,6] and the

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references therein). The biomechanical study of the ocular posterior segment is a very active area of research and, without being exhaustive, some recent contributions can be found in [18–21] and the references therein.

The main goal of this paper is to propose a theoretical framework to investigate the relationship between blood flow and mechanical deformation within the tissue of the lamina cribrosa. Mathematical models have been proposed to investigate this biomechanics–hemodynamics relationship in the tissue of the retina (see e.g. [22–24]), of the heart (see e.g. [25,26]), of the brain (see e.g. [27,28]) and of the bones (see e.g. [29,30]), but, to the best of our knowledge, there are no models currently available to describe the biomechanics-hemodynamics relationship within the lamina cribrosa.

In the proposed model, the lamina cribrosa is described as a poroelastic material, where blood vessels are viewed as pores in a deformable elastic matrix. The vascular porosity of the lamina cribrosa, here defined as the blood volume fraction, is assumed to change with the local state of stress and strain, which, in turn, is determined by the intertwined response of the solid and blood phases to the fluid-mechanical environment. Because of the interplay between mechanical and haemodynamical effects in lamina cribrosa microcirculation, the vascular porosity can be considered as an index of the capability of the blood to perfuse the lamina and, for this reason, it is one of the most significant quantities investigated in the present analysis.

The mechanical parameters of the solid component of the tissue are described through a nonlinear function of the local effective stress [13,23,31], while the vascular permeability is represented by a quadratic function of the vascular porosity [25]. For the numerical solution of the whole coupled system, a fixed point iteration algorithm of staggered type between solid displacement and fluid pressure is proposed and implemented. At each step of the staggered loop, an inner fixed-point iteration is used to solve the nonlinear mechanical problem. The algorithm is endowed with a relaxation procedure for convergence acceleration, and employs the backward Euler method for time discretization and the Galerkin finite element method on a triangular grid for space discretization.

In this paper, we explore the feasibility of the proposed modeling approach on a simplified two-dimensional geometry. A comparison between model simulations and experimental measures [32] is performed to assess the capability of our simplified model to provide physiologically reasonable deformations of the lamina cribrosa for different levels of IOP. The model is then used to estimate the effect of IOP elevation on the distribution of the fluid-mechanical variables in the case of different insertion conditions of the sclera, which are possibly connected to individual–specific anatomical characteristics (for example ethnicity) and, in the same individual affected by ocular disease, to the progress of the pathology itself.

2. Methods

In the following, we review some fundamentals of the anatomy and physiology of the lamina cribrosa, the basic assumptions underlying our modeling approach, the mathematical description of the model and the numerical strategy for its solution.

2.1. Anatomy and physiology of the lamina cribrosa

The lamina cribrosa is a thin, sieve-like portion of sclera at the base of the optic nerve head, formed by a multilayered network of collagen fibers that insert into the scleral canal wall (see Fig. 1(left)).

The main functions of the lamina cribrosa are (i) to act as a scaffold for the retinal ganglion cell axons which relay the visual information from the retina to the brain; (ii) to allow the central retinal artery (CRA) and the central retinal vein (CRV) to enter and leave the intraocular space; and (iii) to stabilize the pressure difference between the intraocular pressure (IOP, baseline value 12–15 mmHg) in the intraocular space and the retrolaminar tissue pressure (RLTp, baseline value 7–10 mmHg) in the optic nerve canal (see Fig. 1(right)). Blood supply to the lamina cribrosa is provided by branches of the posterior ciliary arteries (PCAs), and therefore blood enters the lamina from its outer lateral boundary, as shown in Fig. 1(left). Blood drainage occurs through the CRV, approximately located at the centre of the lamina. It is interesting to notice that, although passing through the lamina, the CRA does not contribute to the blood circulation within the lamina, as it ensures blood supply only to the inner retinal tissue [33].

2.2. Basic assumptions

We model the lamina cribrosa as a poroelastic medium composed of an elastic solid (comprising collagen, elastin, extracellular matrix and neural tissue) and an interconnected vascular porous space filled by blood. Blood is treated here as a Newtonian fluid as in [25,26]. Throughout the remainder of the article, we adopt the point of view of the classic poroelastic theory under the assumption of reversibility of the deformations and isothermal conditions (see the fundamental works of Biot [34] and the more recent reviews [35,36]).

We denote by Ω the spatial domain occupied by the poroelastic medium. Since the lamina cribrosa is approximately a cylindrical structure, the reasonable assumption of axially symmetric solutions leads to consider as a simpler exploratory step the rectangular domain $(0,L)\times(-d/2,d/2)$ corresponding to a section of the cylinder (see Fig. 2).

Having fixed a point $\mathbf{x}=(x_1,x_2)^T$ in Ω, we indicate by $V(\mathbf{x},t)$ an (arbitrary) representative elementary volume (REV) centered at $\mathbf{x}$ at time t. Then, denoting by $V_s(\mathbf{x},t)$ and $V_f(\mathbf{x},t)$ the volumes occupied in V by the solid and the fluid, respectively, we can define the quantity

$$N(\mathbf{x},t)=\frac{V_f(\mathbf{x},t)}{V(\mathbf{x},t)} \tag{1}$$

representing the volumetric fraction of the fluid component, or vascular porosity, and the quantity

$$\frac{V_s(\mathbf{x},t)}{V(\mathbf{x},t)}=1-N(\mathbf{x},t) \tag{2}$$

representing the volumetric fraction of the solid component. Notice that Eq. (2) has been obtained under the assumption of fully saturated mixture, namely $V_s(\mathbf{x},t)+V_f(\mathbf{x},t)=1$.

2.3. Balance equations and constitutive assumptions

Denoting by $\mathbf{u}$ the solid displacement and by p the fluid pressure, in the assumptions of small deformations, negligible inertial terms, absence of body forces and volumetric fluid mass sources/sinks, the poroelastic equations describing the lamina cribrosa read:

$$\nabla\cdot\boldsymbol{\sigma}=\mathbf{0}, \tag{3a}$$

$$\boldsymbol{\sigma}=\mathbf{S}-\alpha p\mathbf{I}, \tag{3b}$$

$$\mathbf{S}=\mu(\nabla\mathbf{u}+\nabla\mathbf{u}^T)+\lambda\nabla\cdot\mathbf{u}\,\mathbf{I}, \tag{3c}$$

$$\frac{\partial\zeta}{\partial t}=-\nabla\cdot\mathbf{v}, \tag{3d}$$