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An improved spinning lens test to determine the stiffness of the human lens

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ABSTRACT

It is widely accepted that age-related changes in lens stiffness are significant for the development of presbyopia. However, precise details on the relative importance of age-related changes in the stiffness of the lens, in comparison with other potential mechanisms for the development of presbyopia, have not yet been established. One contributing factor to this uncertainty is the paucity and variability of experimental data on lens stiffness. The available published data generally indicate that stiffness varies spatially within the lens and that stiffness parameters tend to increase with age. However, considerable differences exist between these published data sets, both qualitatively and quantitatively. The current paper describes new and improved methods, based on the spinning lens approach pioneered by Fisher, R.F. (1971) 'The elastic constants of the human lens', Journal of Physiology, 212, 147–180, to make measurements on the stiffness of the human lens. These new procedures have been developed in an attempt to eliminate, or at least substantially reduce, various systematic errors in Fisher's original experiment. An improved test rig has been constructed and a new modelling procedure for determining lens stiffness parameters from observations made during the test has been devised. The experiment involves mounting a human lens on a vertical rotor so that the lens spins on its optical axis (typically at 1000 rpm). An automatic imaging system is used to capture the outline of the lens, while it is rotating, at pre-determined angular orientations. These images are used to quantify the deformations developed in the lens as a consequence of the centripetal forces induced by the rotation. Lens stiffness is inferred using axisymmetric finite element inverse analysis in which a nearly-incompressible neo-Hookean constitutive model is used to represent the mechanics of the lens. A numerical optimisation procedure is used to determine the stiffness parameters that provide a best fit between the finite element model and the experimental data. Sample results are presented for a human lens of age 33 years.

1. Introduction

1.1. Accommodation, presbyopia and lens stiffness

The human lens is suspended within the globe of the human eye by a set of zonular fibres, that connect the lens to the ciliary muscle. When the normal young eye views a distant object, the ciliary muscle is relaxed and tension in the zonules is maximal. In this state the eye is said to be unaccommodated. To bring a nearby object into focus, the ciliary muscle contracts with the consequence that the tension in the zonules reduces and the lens adopts a thicker and more rounded shape. The deformations that develop in the lens during this process cause the optical power of the eye to increase. In this state the eye is said to be accommodated. It is well known that the effectiveness of this accommodation mechanism decreases with increasing age and that, from middle-age onwards, the accommodation range is minimal. This limiting condition is known as presbyopia.

In recent years there has been considerable interest in the development of new forms of surgical intervention to restore some measure of accommodation to presbyopes. A detailed understanding of the mechanical performance of the individual components of the accommodation apparatus would be of assistance in assessing and optimising these proposed interventions. Also, at a more fundamental level, there is continued interest in developing a more secure understanding of the natural ageing processes in the human eye and the way in which these processes lead to the development of presbyopia.

Although presbyopia has been attributed in various ways to different ageing mechanisms, e.g. Charman (2008), it is generally assumed that age-related changes in the stiffness of the lens are a significant contributing factor. To test this assumption, robust

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numerical data are needed on lens stiffness, and on the way in which the stiffness develops with age. Current published experimental data on lens stiffness (e.g. Fisher, 1971; Heys et al., 2004; Hollman et al., 2007; Weeber et al., 2007) indicate that the lens becomes stiffer with age. However, significant differences exist between the numerical values of lens stiffness data reported in the literature. This lack of uniformity in the published data reflects, to varying degrees, the difficulties in obtaining high quality post-mortem lenses, sample swelling and damage during transport and storage (e.g. see Augusteyn et al., 2006), technical challenges associated with working at a small scale and with soft materials, systematic errors associated with the various test procedures that have been adopted and genuine biological variations between samples obtained from different donors.

1.2. Mechanics of the lens

The lens is a complex structure. It consists of an intricate arrangement of specialised cells, known as lens fibres, enclosed within a thin and relatively stiff collagen-rich nearly acellular membrane known as the capsule. The internal, cellular, regions of the lens (referred to in this paper as the lens substance) and the external capsule are distinct biological structures. It is therefore convenient to treat them separately for the purpose of developing an understanding of the mechanical characteristics of the lens. Certain features of the lens substance are known to vary spatially within it. It is currently understood, for example, that the stiffness of the lens substance (e.g. Heys et al., 2004; Weeber et al., 2007) and the refractive index (e.g. Navarro et al., 2007; Kasthurirangan et al., 2008) both vary with position. The lens substance is also known to be non-homogeneous in a structural sense. The nucleus, for example, is a central portion of the lens that is generally regarded as being distinct from the surrounding cortex (e.g. Augusteyn, 2007, 2010).

Previous experimental studies on the mechanics of the lens substance have mostly proceeded on the basis that it can be represented by an isotropic linear elastic constitutive model. (A constitutive model is a mathematical framework to represent the mechanical behaviour of a material). The non-homogeneous nature of the lens substance is treated by allowing the stiffness parameters to vary with position. The use of isotropic linear elasticity is arguably the simplest constitutive model that can sensibly be employed in this context. It requires the specification of only two independent material parameters; for the purpose of modelling the lens it is convenient to choose the shear modulus G and the bulk modulus K as these parameters. It is typically assumed in the interpretation of data from experimental studies that the lens substance is incompressible; this has the consequence that $K = \infty$. (In practice, to avoid numerical difficulties in a finite element analysis, the bulk modulus is normally set to a large but finite value.) As a consequence, only one parameter, the shear modulus G, is needed to characterise the stiffness of the lens. This view of the lens substance as an incompressible material is supported by MRI studies that indicate that total lens volume is conserved during accommodation (e.g. Hermans et al., 2009). (It should be noted, of course, that although MRI studies may indicate that the total volume of the lens is conserved during accommodation, they do not demonstrate the more restrictive condition that each individual material point in the lens behaves in an incompressible way. It is plausible, for example, that fluid flow may occur within the lens as a result of the stress gradients set up by the accommodation process. This flow would cause the volume of some parts of the lens to reduce and other parts to increase but, on the basis that water is assumed to be effectively incompressible, the total lens volume is conserved.)

Although linear isotropic elasticity provides a convenient approach, it is important to note the possibility that the behaviour of the lens substance may depart significantly from this rather simple model. For example, the highly organised and directional structure of the lens fibres (e.g. Taylor et al., 1996) suggest that the lens substance may behave in an anisotropic manner. Also, dynamic mechanical analysis (DMA) data from Weeber et al. (2005) indicate that the lens exhibits time-dependent behaviour (a feature that is not captured in linear elasticity). Any time-dependency in the lens might derive from visco-elastic behaviour inherent in the molecular structures of the various proteins within the lens. Alternatively (or perhaps in addition) it may arise as a consequence of localised fluid flow within the lens in response to gradients of stress. In spite of these open questions, it is considered that the relative simplicity of the isotropic elasticity approach means that it provides a useful and robust framework within which to describe the mechanics of the lens substance.

Conventional linear elastic theory is formulated in the framework of linear continuum mechanics. It is generally understood, however, that geometric non-linear effects associated with finite displacements may need to be included within any computational model of the mechanics of the lens to achieve realistic results (e.g. Burd et al., 1999). Although linear elasticity is capable of being embedded within a geometric non-linear computational framework, this leads to procedures that lack the rigorous theoretical basis of mathematical formulations that are based on non-linear continuum mechanics and developed within the framework of hyperelasticity (e.g. Bonet and Wood, 1997; Holzapfel, 2000). In view of this, a non-linear continuum mechanics hyperelastic approach is adopted in the finite element analyses described later in this paper. Geometric non-linear effects are captured, in a rigorous way, in this approach. The finite element analysis is based on the neo-Hookean constitutive model to represent the mechanics of the lens. This is a relatively simple hyperelastic model that may be specified in terms of a shear modulus and a bulk modulus that, for small strains, provide equivalence with parameters of the same name that are conventionally adopted in linear elasticity theory.

1.3. Spinning lens concept

The purpose of this paper is to describe an experimental method, based on the spinning lens concept devised by Fisher (1971), to determine numerical values of parameters to describe the stiffness of the human lens substance. One of the principal applications of the data is in the development of numerical models (e.g. based on the finite element method) of the natural accommodation process (e.g. Burd et al., 2002; Weeber and van der Heijde, 2007). The data may also be useful to assist in the assessment of the likely effectiveness of proposed surgical treatments for presbyopia, particularly those that involve modifications to the mechanical characteristics of the lens substance (e.g. Schumacher et al., 2009).

In Fisher's original experiment, the lens was spun on its optical axis and the cross-section of the spinning lens was imaged using flash photography. The observed changes in axial thickness and equatorial diameter were used, in conjunction with an approximate analytical model of the deformations induced in the spinning lens, to infer values of lens substance Young's modulus (which is closely related to the shear modulus). Fisher (1971) presented data on a total of 40 lenses, in the age range 0–67 years. A study by Burd et al. (2006) raised various questions about possible systematic errors in the procedures adopted by Fisher. For example, the analysis of the data given by Fisher (1971) ignored the constraining effect of the capsule whereas it seems implausible that the mechanical effect of the capsule can be neglected in this way without introducing systematic errors in the computed stiffness data.