Journal of Biomechanics 46 (2013) 1752–1758

Contents lists available at SciVerse ScienceDirect

Journal of Biomechanics

journal homepage: www.elsevier.com/locate/jbiomech
www.JBiomech.com

An experimental and theoretical analysis of unconfined compression of corneal stroma

Hamed Hatami-Marbini*, Ebitimi Etebu

School of Mechanical and Aerospace Engineering, Oklahoma State University, Stillwater, OK 74078, USA

ARTICLE INFO

Article history:
Accepted 18 March 2013

Keywords:
Corneal mechanics
Unconfined compression behavior
Stress relaxation experiments
Biphasic theory

ABSTRACT

The cornea is a transparent connective tissue with dual functions of protecting the eye (mechanical properties) and refracting the light (optical properties). Both of these properties are derived from the corneal intricate and pseudo regular extracellular matrix, the stroma. From the mechanics point of view, the corneal extracellular matrix is a hydrated structure composed of collagen fibrils, proteoglycans, and the interstitial fluid. The objective of this study was to investigate compressive biomechanical properties of the cornea using an experimental and numerical framework. The unconfined compression stress-relaxation tests were performed to measure the corneal behavior experimentally and the transversely isotropic biphasic theory was used to analyze the experimental data. It was observed that the behavior of the corneal stroma under stepwise stress-relaxation compression is similar to that of the other soft hydrated tissues and is composed of an immediate stiff response, a transient relaxation phase, and a final steady-state stage. Within the range of deformation considered in this study, maximum and equilibrium reaction stresses were linearly dependent on the compressive strain. The linear transversely isotropic biphasic model curve fitted experimental measurements with the coefficient of determination $r_{fit}{}^2=0.98\pm0.01$. The mechanical parameters of the porcine corneal stroma were calculated as a function of the engineering strain. The corneal out-of-plane modulus was almost independent of the compressive strain, the transverse Young's modulus linearly increased with increasing strain, and the permeability coefficient decayed exponentially with increasing strain. The average mechanical parameters under unconfined compression were found to be: the out-of-plane modulus $\overline{E}_z=5.61\ KPa$, the transverse Young's modulus $\overline{E}_r=1.33\ MPa$, and the permeability coefficient $\overline{\kappa}_r=2.14\times10^{-14}\ m^4/N.s$.

1. Introduction

The cornea is a transparent connective tissue which connects the front of the eye to outside world. It serves as the principal refractive element of the eye and as an effective protective shield for the eye against external injuries and trauma. From the anterior to posterior, the human cornea is composed of epithelium, Bowman's membrane, stroma, Descemet's membrane, and endothelium. While all these layers are essential for the normal function of the eye, the mechanical properties of the cornea are mainly derived from the stromal layer. The stroma constitutes 90% of the corneal thickness and its microstructure has certain similarities to load-bearing soft tissues such as articular cartilage and intervertebral disc. The stromal thin collagen fibrils are embedded in a soft hydrated matrix formed by proteoglycans and interstitial fluid. The collagen fibrils have a uniform diameter and are arranged in flat bundles known as lamellae. Keratocytes, the principal cellular component of the cornea, lie between the collagen lamellae. They occupy about 2–5% of total volume of the stroma and maintain the corneal extracellular matrix by actively synthesizing and secreting collagen and proteoglycans (Brightbill et al., 2009; Hassell and Birk, 2010). In addition to the relevance of the mechanical properties of the stroma in defining the shape and stability of the cornea, they are important to understanding cell behavior, tissue homeostasis, and wound healing.

The cornea under physiological conditions is mainly subjected to (i) membrane stresses caused by intraocular pressure and (ii) concentrated anterior stresses applied by external objects (e.g. eye rubbing and eyelid pressure). The in-plane biomechanical properties of the cornea have mainly been characterized using strip extensometry and inflation tests (Boschetti et al., 2012; Boyce et al., 2007; Elsheikh and Alhasso, 2009; Jue and Maurice, 1986; Kampmeier et al., 2000). A number of studies have also been undertaken to determine the mechanical behavior of the cornea in compression. Nevertheless, these studies have been primarily

* Correspondence to: 218 Engineering North, School of Mechanical and Aerospace Engineering, Oklahoma State University, Stillwater, OK 74078-5016, USA. Tel.: +1 405 744 5900; fax: +1 405 744 7873.
E-mail addresses: hhatami@okstate.edu, hamed.hatami@gmail.com (H. Hatami-Marbini).

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http://dx.doi.org/10.1016/j.jbiomech.2013.03.013

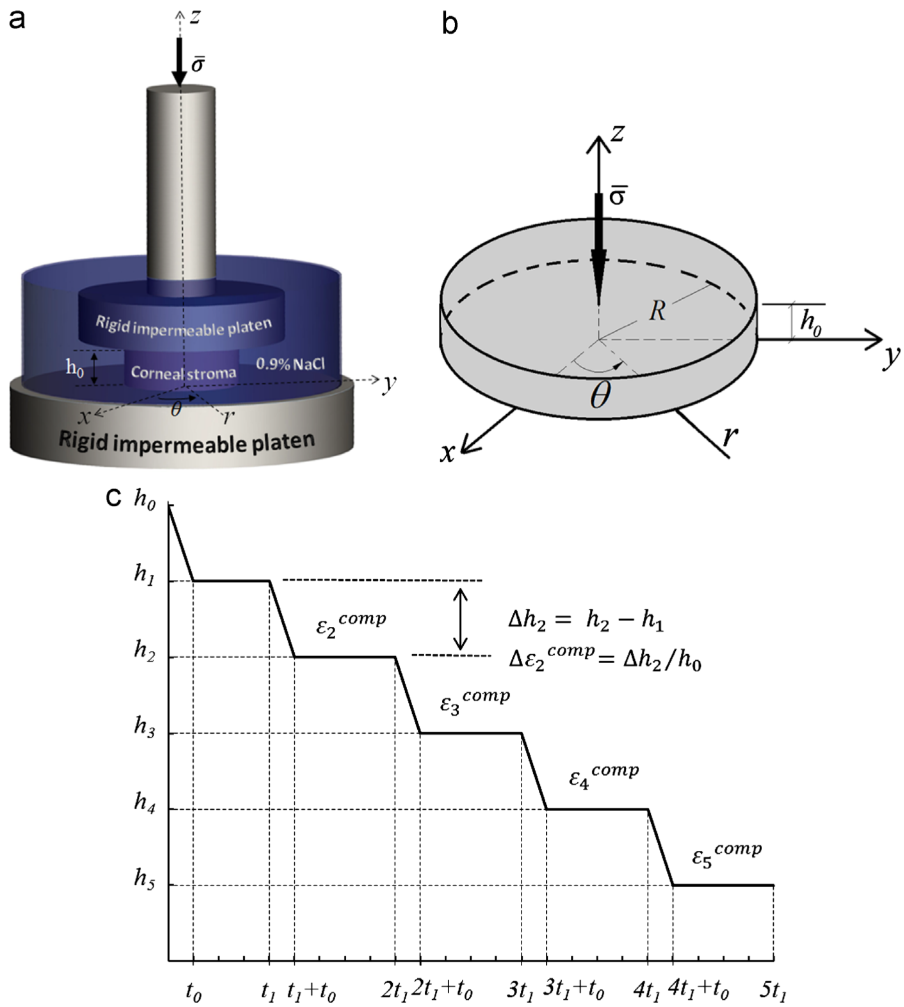

Fig. 1. Schematic plots of (a) the unconfined compression experimental setup and (b) the corneal stromal disc with radius R and initial thickness h_0. The measured reaction force $\overline{\sigma}$, the Cartesian x–y–z coordinate and the cylindrical r–θ–z coordinate systems are shown. (c). A schematic plot of the experimental procedure for conducting stepwise unconfined compression stress-relaxation tests. The initial thickness h_0 of the sample is determined at the tare load equivalent to 1.5 KPa. The corneal sample is compressed with a constant displacement rate Λ=0.15 μm/s from its initial thickness to 20% engineering strain in five equal strain increments $\Delta\varepsilon_j^{comp}=4\%$, $j=1$ to 5. The loading ramp duration is $t_0=(h_{i-1}-h_i)/\Lambda$, $i=1,\ldots,5$, the strain and thickness of the sample at the end of each step are given by $\varepsilon_i^{comp}=\sum_{j=1}^{i}\Delta\varepsilon_j^{comp}$ and $h_i=h_0(1+\varepsilon_i^{comp})$, respectively.

focused on developing the relationship between the tissue swelling pressure and hydration (Hedbys and Dohlman, 1963; Klyce et al., 1971; Olsen and Sperling, 1987). To the best of our knowledge, there is no previous careful analysis of stress-relaxation and transient compressive properties of the corneal stroma under unconfined compression. The unconfined compression experiments have been used to characterize the mechanical behavior of soft hydrated tissue such as articular cartilage, sclera, temporomandibular disk, and even brain tissue (Allen and Athanasiou, 2006; Armstrong et al., 1984; Cheng and Bilston, 2007; Cohen et al., 1998; Mortazavi et al., 2009; Soltz and Ateshian, 2000; Soulhat et al., 1999). In this experiment, a circular piece of tissue is compressed axially between two rigid plates in an ionic solution. Moreover, a mixture theory is used to analyze the experimental data and predict the material parameters (Armstrong et al., 1984; Cohen et al., 1998; Huang et al., 2001; Lai et al., 1991; Mow et al., 1980; Soltz and Ateshian, 2000). A complete review of mixture theories as well as a thorough discussion on thermodynamics-based derivation of governing equations appear in the reference (Hatami-Marbini, in press). The simplest form of mixture theories is the linear biphasic model in which the extracellular matrix is represented as an incompressible homogenous elastic porous solid matrix filled with an incompressible fluid phase (Mow et al., 1980). This theory successfully has explained the creep and stress-relaxation behaviors of the articular cartilage among other soft tissues (Armstrong et al., 1984; Cohen et al., 1998; Korhonen et al., 2002; Mow et al., 1980; Soltz and Ateshian, 2000).

There are clear differences between human and animal corneas both in terms of their morphologic and mechanical properties. Nevertheless, due to the increasing difficulties in obtaining human cornea, various animal models have been considered in corneal research. For example, chicken cornea has been used as a model for investigating wound healing process following the refractive surgery (Martinez-Garcia et al., 2006). Because of its similarity to man and its availability, the porcine cornea is often used as an approximate model system for material property characterization studies (Boschetti et al., 2012; Elsheikh et al., 2008; Kampmeier et al., 2000; Sanchez et al., 2011; Wollensak et al., 2003; Zeng et al., 2001). It has been observed that porcine and human corneas have almost similar tensile strength and stress–strain relation but different tensile stress–relaxation relationship (which might be due to the relatively old age of human donor cornea) (Elsheikh and Alhasso, 2009; Elsheikh et al., 2008, 2010; Kampmeier et al., 2000). In the present study, we selected porcine cornea to investigate the unconfined compressive stress–relaxation behavior of the corneal stroma. Furthermore, we used the linear transversely isotropic biphasic theory to analyze the experimental data and subsequently determine the stromal material parameters, i.e. the