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Biomechanical Characterization of Mouse Sclera in Myopia

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Abstract: Myopia, or near-sightedness, is a common ocular condition in which the eye elongates excessively. Development of myopia is associated with, and thought to be facilitated by, changes in the biomechanical properties of the sclera (the white part of the eye). We characterized scleral biomechanics in a mouse model of myopia using unconfirmed compression testing and biphasic theory to extract scleral permeability, in- plane scleral tensile modulus, and through-plane scleral compressive modulus. We find that myopia reduces in-plane tensile modulus and permeability, consistent with scleral tissue remodeling. Such biomechanical outcome measures may offer advantages over more traditional assessments of myopia-associated changes in the small mouse eye.

Keywords: Biphasic model; myopia; unconfined compression; mouse

1 Introduction

Myopia (near-sightedness) is a very common condition, with more than 90% of young adults being myopic in some populations [1]. High myopia is a risk factor for more serious ocular conditions, including retinal detachment, glaucoma, and cataract. In most cases, myopia is due to excessive elongation of the eye during development, i.e. the eye is "too long" for its refractive power. This increased ocular axial length is accompanied, and thought to be facilitated by, by remodeling of the sclera (the white part of the eye) and altered scleral biomechanics.

The mouse is a powerful mammalian model to study myopia, yet its scleral biomechanics have not been characterized in part because of the mouse's very small eye size and thin sclera (~ 80 μm). Here, we present results from unconfined compression testing of mouse sclera in control and myopic eyes, and extract in-plane scleral tensile stiffness, compressive modulus, and permeability using the Biphasic Isotropic Conewise Linear Elastic model [2].

2 Methods

Unilateral myopia was induced at P28 in naïve, male C57BL/6J mice (n=6) by form deprivation, a well-accepted model of myopia [3]. The contralateral eyes were untreated and served as control. Refractive power and dimensions of each eye were measured using an automated photorefractor and optical coherence tomography imaging at baseline and after ~3 weeks of form deprivation, at which point animals were sacrificed. Eyes were enucleated immediately after sacrifice and stored in PBS until mechanical testing. Scleral samples (1 mm diameter) were taken ~1 mm from the optic nerve, and unconfined compression stress-relaxation experiments were performed using the Microsquisher (CellScale, Waterloo, Canada) at 37 °C in an isotonic saline bath at 3 increasing strain levels (5%, 10% and 15%; Fig. 1). The compression test was run in strain-controlled mode. An transfer function in the frequency domain was created from experimental data for each strain step, and the biphasic model was fit to this function to determine material properties. Two-way repeated measures ANOVAs were used to test for significance.

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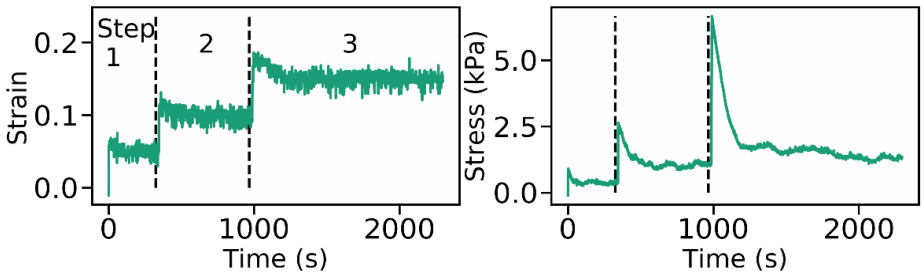

Figure 1: Typical strain *vs.* time (left) and stress *vs.* time (right) data for testing of mouse scleral sample. The 3-step strain- controlled protocol can be seen in the left panel.

3 Results

Mice were significantly myopic (-3.7 ± 0.4 Diopters) after 3 weeks of form deprivation treatment ($p < 0.001$). Associated with this change, myopic sclera was significantly less stiff than contralateral control (31.8 ± 12.6% decrease, $p < 0.001$; Fig. 2). Tissue tensile properties were strain-dependent for mouse sclera ($p < 0.001$), increasing with increasing strain. Further, myopic sclera had significantly increased permeability to saline over contralateral controls (224.4 ± 205.5% increase, $p = 0.006$). There was no significant change in compressive modulus or scleral thickness. Surprisingly, and in distinction to other animal models of myopia, while there was a significant change in measured refractive power, myopia and altered scleral biomechanics were not accompanied by discernible changes in mouse ocular dimensions.

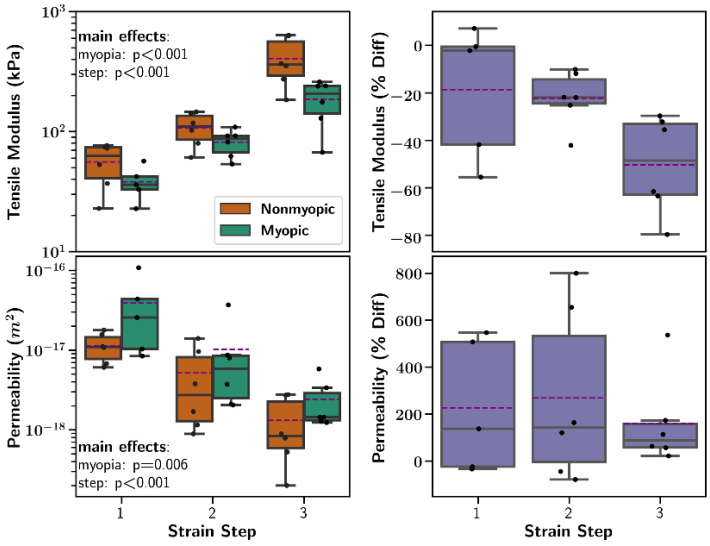

Figure 2: Changes in scleral tensile modulus (top) and permeability (bottom) due to myopia in mice. The left panels show box and whisker plots of measured values at each strain step, averaged over all mice. The right plots show percentage differences in measured quantities, i.e. (myopic- control)/control values. These changes are consistent with scleral tissue remodeling in myopia.

4 Discussion

Mouse scleral biomechanics are altered in a manner consistent with that seen in other mammals in response to induced myopia, but paradoxically, the typical elongation of the eye seen in other models and in humans was not observed. This may be due to the very small size of the mouse eye, precluding reliable measurements of elongation (predicted ~5 um elongation/Diopter refractive error [4]). This result highlights the utility of biomechanical measurements as a complementary outcome measure, together with refractive

power, for monitoring myopia progression in transgenic or pharmacologically-treated mice.

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