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● *Original Contribution*

USING AN ULTRASOUND ELASTICITY MICROSCOPE TO MAP THREE-DIMENSIONAL STRAIN IN A PORCINE CORNEA

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Abstract—An ultrasound elasticity microscope was used to map 3-D strain volume in an *ex vivo* porcine cornea to illustrate its ability to measure the mechanical properties of this tissue. Mechanical properties of the cornea play an important role in its function and, therefore, also in ophthalmic diseases such as keratoconus and corneal ectasia. The ultrasound elasticity microscope combines a tightly focused high-frequency transducer with confocal scanning to produce high-quality speckle over the entire volume of tissue. This system and the analysis were able to generate volume maps of compressional strain in all three directions for porcine corneal tissue, more information than any previous study has reported. Strain volume maps indicated features of the cornea and mechanical behavior as expected. These results constitute a step toward better understanding of corneal mechanics and better treatment of corneal diseases. (E-mail: kyle.hollman@soundsightresearch.com) © 2013 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Elasticity, Strain, Cornea, Keratoconus, High-frequency imaging, 3-D imaging.**

INTRODUCTION

Because of its function, mechanical behavior and elastic properties are important to the cornea. To focus, the cornea must maintain its shape, and yet, to protect itself and other parts of the eye, it needs some flexibility. Elastic properties play a significant role in some diseases affecting the cornea, most prominently post-LASIK (laser-assisted in situ keratomileusis) ectasia and keratoconus. It is also important to fully understand corneal elasticity because trauma and healing may affect mechanical behavior. Clinical applications that could potentially benefit from better measurements of corneal tissue mechanics using high-frequency ultrasonic strain imaging include keratoconus and post-LASIK ectasia.

Keratoconus is a disease in which mechanical properties of the cornea weaken, leading to progressive thinning and distortion of the cornea, as well as visual distortion. It affects about 1 in 2000 people in the general population (Kennedy et al. 1986). In early stages and mild cases, glasses or contact lenses can be used to maintain visual acuity. If these conservative approaches are not helpful, surgical treatment is often recommended. In approximately 20% of cases, keratoconus progresses to the point where corneal transplant is required (Rabinowitz 1998). Recently, a new experimental method of corneal collagen cross-linking with ultraviolet A (UVA) and the photosynthesizer riboflavin has been shown to slow or stop the progression of keratoconus (Mazzotta et al. 2007; Mencucci et al. 2007; Wollensak 2006).

High-resolution corneal mechanical measurements with ultrasonic imaging could lead to better understanding and improved treatment of keratoconus. Most current techniques track gross deformations so they measure only average mechanical properties. Higher-resolution measurements could determine if the keratoconus affects the entire corneal thickness or if it is more

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localized. Better *in vivo* mechanical measurements can also lead to earlier detection of this condition. In assessing UVA/riboflavin treatment, high-resolution measurements could determine how localized the treatment is and provide information regarding penetration depth. Post-treatment monitoring would also benefit from reliable elasticity measurements. *In vivo* elasticity measurements would be valuable in assessing the long-term effects of this new treatment. Accurate *in vivo* elasticity measurements could also be helpful in planning corneal transplant surgery for patients with keratoconus.

Post-LASIK ectasia is another condition in which there is corneal thinning and distortion. It is a rare but dreaded complication of corneal refractive surgery that occurs when too much structural corneal tissue is removed during surgery (Guirao 2005; Jaycock et al. 2005a, 2005b). Although pre-screening procedures are intended to prevent this complication, the criteria are based primarily on pre-operative corneal curvature and predicted post-operative corneal thickness. In other words, will there be enough tissue left after surgery to sustain structural integrity? However, total structural integrity is a combination of both thickness and stiffness. Further, if stiffness is non-homogenous throughout the thickness of the tissue, the total strength of any tissue is more complicated.

Elasticity maps from a high-frequency ultrasound elasticity microscope would provide critically useful information for improved screening to prevent post-LASIK ectasia. It could screen out softer-than-normal corneas whose thickness would otherwise allow surgery. It may also allow surgery in stiffer corneas that would otherwise be screened out as too thin. Finally, high-resolution mechanical measurements could lead to better predictions of post-operative shape in corneas that pass screening.

There are a number of techniques for measuring corneal elasticity, many of which have been reported in the literature. Unfortunately, they measure gross average properties throughout the corneal thickness or are destructive and cannot be used *in vivo*. The cornea is not homogeneous. Components such as the epithelium, Bowman's layer, stroma and endothelium have different elastic moduli. It is not even known if the largest component of the cornea, the stroma, is elastically homogeneous. The stroma consists of alternating layers of collagen fibers. Because of mechanical behavior, fibers near the epithelium and Bowman's layer experience different forces than those close to the endothelium, and therefore, it is conceivable that they have different mechanical properties. However, the technological capability to measure elastic differences as a function of corneal depth has not been available until now.

As this study reveals, a 3-D elasticity microscope can create a 3-D map of normal strains in an *ex vivo* porcine cornea. These strain maps are a key development toward recreating volume maps of elastic moduli that can be used to understand the local and global mechanical properties of the cornea.

METHODS

As shown in Figure 1, the 3-D elasticity microscope consists of a high-frequency single-element transducer precisely scanned with a stepper motor-driven three-axis positioning system. A fourth axis (not shown in

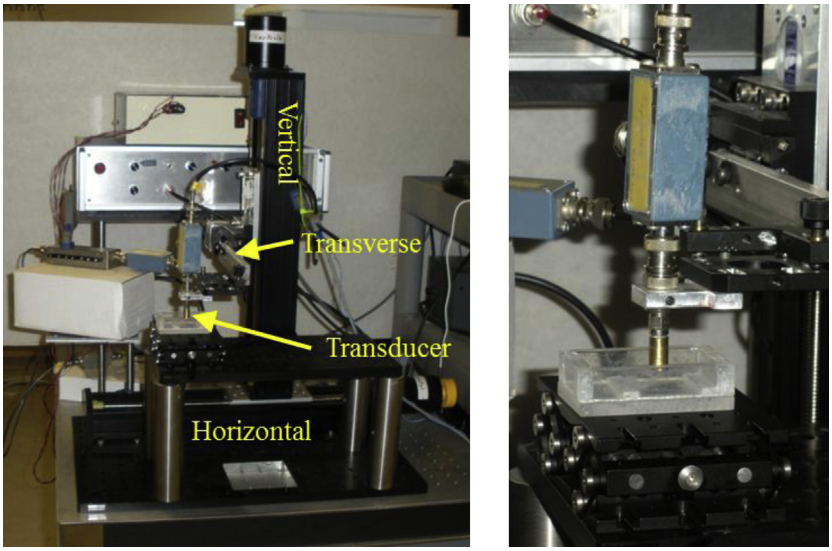

Fig. 1. Photograph of elasticity microscope equipment. There are three imaging axes: horizontal, vertical and transverse. The deformation axis and slit pushing plate are not shown. On the right is a close-up of the high-frequency ultrasonic transducer (brass-colored cylinder).