Binocular iPad Treatment of Amblyopia for Lasting Improvement of Visual Acuity

Repeated experience with dichoptic perceptual learning tasks and dichoptic game play have been shown to be effective in improving the visual acuity of amblyopic children and adults. However, whether the visual acuity gains achieved with binocular treatment are long lasting has not yet been addressed. We examined the durability of visual acuity improvements obtained as a result of binocular iPad game play in childhood amblyopia.

Methods | This study protocol was approved by the University of Texas Southwestern Medical Center Institutional Review Board. Written informed consent was obtained from a parent or guardian prior to enrollment in the study. Amblyopic children aged 4 to 12 years who participated in our previous study of binocular iPad games, had best-corrected visual acuity (BCVA) improvement of at least 0.1 logMAR (1.0 line; Snellen equivalent 20/25) in the amblyopic eye after 4 to 8 weeks of compliant binocular iPad game play, and did not patch after cessation of iPad game play were eligible for enrollment in the follow-up study. For comparison, we also enrolled children whose amblyopic eye BCVA had improved at least 0.1 logMAR after 4 to 12 weeks of compliant binocular iPad game play but who did patch after cessation of binocular iPad game play. The referring pediatric ophthalmologist decided whether the child had concurrent patching treatment (at a different time of day) during the binocular iPad game play or afterward. The inclusion criteria and protocol of our previous study are available online. The BCVA was obtained for each eye with the Amblyopia Treatment Study HOTV method (for those aged <7 years) or electronic Early Treatment Diabetic Retinopathy Study method (for those aged ≥7 years) at the baseline and outcome visits and 3, 6, and 12 months after the outcome visit.

Results | Eight amblyopic children aged 4.8 to 12.7 years were enrolled in the primary group with binocular iPad game play and no patching after outcome, and 10 children aged 4.0 to 10.2 years were enrolled in the group with binocular iPad game play and patching after outcome. Amblyopic eye BCVA at each time is illustrated in the Figure. For the primary group with binocular iPad game play and no patching after outcome, the mean (SE) baseline BCVA improved from 0.30 (0.04) logMAR to 0.15 (0.05) logMAR (Snellen equivalent, improvement from 20/40 to 20/25) after 4 to 8 weeks of binocular iPad game play. For the group with binocular iPad game play and patching after outcome, the mean (SE) baseline BCVA improved from 0.43 (0.08) logMAR at baseline to 0.29 (0.07) logMAR (Snellen equivalent, improvement from 20/54 to 20/39) after 4 to 12 weeks of binocular iPad game play. A 2-way repeated-measures analysis of variance (visit by postoutcome treatment) found a main effect of visit on visual acuity (F<sub>1,16</sub> = 10.77; P < .001) but was not able to identify an effect of patching after outcome on visual acuity (F<sub>4,64</sub> = 2.41; P = .14). Pairwise post hoc comparisons found that baseline BCVA was significantly different from the BCVAs at the outcome visit and the 3-, 6-, and 12-month postoutcome visits (P < .001), but the BCVAs did not differ between the outcome and postoutcome visits (P ≥ .58).

Discussion | To our knowledge, this study provides the first evidence that BCVA improvements obtained with binocular iPad game play are retained for at least 12 months after the treatment ends. Along with our previous study, this demonstrates that home-based binocular iPad games may be an effective treatment for amblyopia. Compared with the traditional patching treatment, which usually takes months to years, the binocular iPad game play appears to improve visual acuity rapidly (in only weeks).

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Figure. Best-Corrected Visual Acuity of Amblyopic Eyes at Each Visit

Best-corrected visual acuity of amblyopic eyes at each visit for participants in the primary group with binocular iPad game play and no patching after outcome vs those in the group with binocular iPad game play and patching after outcome. Each data point represents the mean; error bars, standard error.
In Vivo Biomechanical Mapping of Normal and Keratoconus Corneas

Corneal mechanical strength is critical to withstanding intraocular pressure and maintaining normal shape.\textsuperscript{1-3} In keratoconus, the mechanical stability is compromised,\textsuperscript{4} which may lead to progressive morphological changes. Therefore, a noninvasive technique capable of accurately measuring the mechanical properties of the cornea may help us understand the mechanism of keratoconus development and improve detection and intervention in keratoconus. We previously developed Brillouin microscopy based on light scattering from inherent acoustic waves in tissues\textsuperscript{4} and showed that this technique can provide quantitative estimates of local longitudinal modulus,\textsuperscript{5} which correlate to the Young and/or shear moduli of the cornea.\textsuperscript{6,7} Using a clinically viable instrument, for the first time, to our knowledge, we mapped the elastic modulus of normal and keratoconic corneas in vivo. We found distinctive biomechanical features that differentiate normal and keratoconic corneas and therefore have the potential to serve as diagnostic metrics for keratoconus.

Methods | The study recruited 6 volunteers with normal corneas (mean [SD] age, 37 [15] years) and 5 patients with advanced keratoconus (mean [SD] age, 43 [7] years). All participants signed an informed consent form and the study was approved by the Partners Human Research Committee (Partners Healthcare Institutional Review Board), in accordance with the principles of the Declaration of Helsinki. We constructed a laser-scanning confocal Brillouin microscope (wavelength, 780 nm; power, 1.5 mW; lateral/axial resolution, 5 μm/30 μm; sensitivity, approximately 10 MHz). The instrument was equipped with wide field-of-view imaging to allow real-time pupil detection and beam positioning (lateral accuracy of <0.5 mm). For participants with normal corneas, areas measuring about 5 × 5 mm in the central region of the cornea were scanned. For patients with keratoconus, similar regions, but including the center of the cone, were scanned as confirmed by their topographic images (Pentacam; OCULUS). To construct Brillouin maps, axial scans were taken at various transverse locations; the anterior mean Brillouin shift was computed from each axial scan by averaging the measured Brillouin shift values of the anterior portion of the corneal stroma. A color-coded elasticity map was obtained by 2-dimensional interpolation of the mean Brillouin shift in the anterior portion.

Results | Normal corneas were found to have relatively uniform anterior Brillouin shifts in the central region (Figure 1A). By contrast, keratoconic corneas presented strong spatial variations in Brillouin shifts (Figure 1B). Figure 2 shows the average anterior Brillouin shifts of normal (n = 7) and keratoconus (n = 6) corneas in the cone region (<1 mm from thinnest point) and outside the cone region (>3 mm away from thinnest point). A highly statistically significant decrease (unpaired t test, P < .001) was found in the keratoconic cone region with respect to normal corneas. Also, a highly statistically significant difference (paired t test, P < .001) was observed between the cone region and outside the cone region. The regions outside the cone showed no statistically significant difference compared with the normal corneas.

Discussion | We have described the distribution of elastic modulus in keratoconus and normal corneas in vivo. The elasticity maps show remarkable spatial variations around the cone. The reduction of 100 MHz in the keratoconic cone region (Figure 2) corresponds to an approximately 3% decrease in longitudinal modulus and approximately 70% reduction in shear modulus.\textsuperscript{5} The regions away from the cone in the keratoconic corneas have similar Brillouin shifts as normal corneas, which is consistent with our ex vivo data.\textsuperscript{2} This finding supports the long-standing hypothesis that keratoconus involves a spatially localized mechanical alteration in the cornea.\textsuperscript{1} It also emphasizes the need for spatially resolved measurements for accurate analysis of the biomechanical anomalies in keratoconus. Future research is warranted to understand the relationship between the focal or heterogeneous mechanical weakening and morphological changes (ie, thinning and steepening) and to develop biomechanics-based metrics for improved diagnosis and...