In vivo biometry in the mouse myopic eye using 11.7T MRI

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Purpose

Major difficulties in the investigation of the mouse myopic eye are that the ocular dimensions cannot be measured in vivo and that post-mortem histological techniques suffer from limited resolution. Indeed, Optical Coherence Tomography (OCT), a classical tool used for routine in vivo eye parameters, is not adapted to myopia research. We tested the potential of a newly developed MRI protocol at ultra-high field. Using this technique, ocular biometry was performed in mice with normal vision and severe myopic shift.

Materials & Methods

Eleven transgenic mice and eleven control mice were used in the study (2 at P20 (20 days old)), 3 at 3 months, 3 at 6 months, and 3 at 12 months). MRI was performed using a 11.7T spectrometer (117/16 USR Biospec, Bruker) interface with a cryoprobe after an intraperitoneal injection of a Gadolinium-based contrast agent (Dotarem®, Guerbet), to highlight the anterior chamber of the eye and to provide signal enhancement. Spin-echo MR images were recorded in each mouse (2D, 40 slices, TR/TE=1500/10.5ms, voxel size: 50x50x120µm^3, scan time: 13 min). Measurement of axial length (AL), Equatorial Diameter (EQ), Anterior Chamber Depth (ACD), Anterior Chamber Width (ACW), Vitreous Chamber Depth (VCD), Lens Thickness (LT) and Area were performed offline using ImageJ (http://rsb.info.nih.gov/nih-image) for each animal.

Results

The use of a gadolinium-based contrast agent increased both signal to noise ratio in MR images (6.6 dB gain in vitreous chamber) and contrast between anterior and vitreous chamber (2.7 dB gain). This allowed the clear delimitation of the two chambers (Fig. 1) and distinction between the different eye structures.

Comparison between transgenic and control mice at each time point (P20, 3 months, 6 months and 12 months respectively) showed statistically significant difference between the two groups for Area (p=0.057, 0.011 ,0.015 and 0.008), AL (p=0.049, 0.009, 0.001 and 0.009), VCD (p=0.007, 0.005, 0.001 and 0.010) and ED (p=0.032, 0.018, 0.012 and 0.003). No significant statistical difference was found for ACD, ACW and LT.

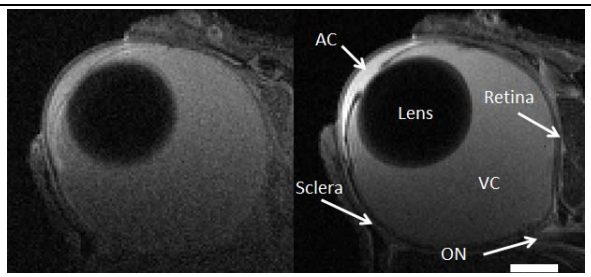

Fig. 1: Increased signal to noise ratio in the MR images of transgenic mice before (left) and 5 min after injection of a gadolinium-based contrast agent. (right). Images are presented with the same dynamic scale, In plane resolution 50µm². Various structures of the eye can be distinguished (AC: Anterior Chamber, VC: Vitreous Chamber, ON: Optic Nerve) Scale bar represents 1mm.

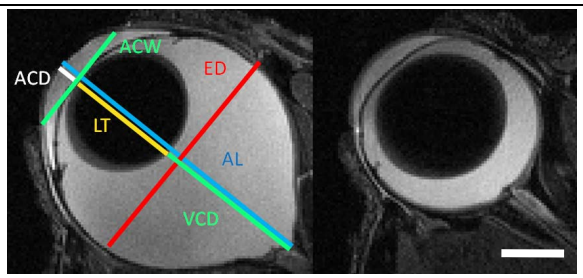

Fig. 2: Comparison of images obtained on transgenic (left) and control (right) mouse at 12 months. Images acquired 50 min after injection of the contrast agent. In plane resolution 50µm². Color lines represent ACD, ACW, LT, ED, VCD and AL. Scale bar represents 1mm.

Conclusion

In vivo mouse eye morphology evaluation is crucial to analyze the consistency of mouse models of myopia. MRI seems to be a very promising tool as it is unaffected by histology bias which can lead to the misevaluation of different parameters. This new MRI protocol provides, for the first time, high resolution biometrical data of mouse myopic eyes in vivo. Axial eye length, corneal thickness, anterior chamber depth, anterior chamber width, lens thickness and vitreous chamber depth can be measured with very good repeatability and very small standard deviations. This protocol achieved a significant improvement in performance over current techniques to measure myopic eyes (OCT; biometry in frozen sections [2-3]), or measurements in standard histological sections of fixated tissue [4].

References

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