High Field Magnetic Resonance Angiogram of the Mouse Eye

Gangchea Lee[1], Minjung Kim[2], and Thomas Neuberger[1,3]

[1]Biomedical Engineering, Pennsylvania State University, University Park, PA, United States, [2]Biology, Pennsylvania State University, University Park, PA, United States, [3]Huck Institutes of the Life Sciences, Pennsylvania State University, University Park, PA, United States

Introduction:

Magnetic Resonance Imaging (MRI) is used widely in both the medical and the research field due to its high achievable spatial resolution and its non-invasive character. Furthermore, MRI can be used to acquire three dimensional images for structure analysis of tissues. The proper function of the eye is maintained by the delivery of nutrition and oxygen of the ocular circulation. Malfunction of these vessels can lead to severe results such as vision loss. Currently, eye angiography is limited to two dimensional images, using fluorescein or indocyanine green angiography [1]. Due to the small dimensions of the blood vessels, it is challenging to track the ocular circulation of the eye using MRI. To accomplish this task, a high signal to noise ratio (SNR) and a high spatial resolution are required. In this work, a 14 tesla MRI system and a dedicated home-built radio frequency surface coil were used to acquire *in vivo* a three dimensional angiogram of the mouse eye. The results of this non-invasive study could be used to investigate ocular diseases.

Method:

C57BL/6 mice were anesthetized with 4% isoflurane using 1L/min air flow. After the anesthetization, 30uL of magnevist (Bayer, Germany) was injected through the tail intravenously to increase SNR of the blood vessels. The mouse was placed into a home-built mouse bed, and fixed with a biting bar (Figure 1). The 8mm ID home-built RF surface resonator was placed on top of the left eye. To inhibit the motion of the eye due to eye dryness, artificial tears ointment was applied to both eyes. Imaging was performed on a 14.1 tesla, 8.9cm vertical bore system, operated with an Agilent Direct Drive Console (Agilent Technologies, Santa Clara, CA, USA). The respiration was monitored during the experiments, and isoflurane was adjusted in between 1.1% and 1.7% to keep 45-60 breath/min. A three dimensional gradient echo sequence with flip angle of 70 degree was used to record an angiogram of the mouse eye. With a field of view of 6mm x 7.2mm x 7.2mm and a matrix size of 200 x 180 (partial Fourier: 240) x 240, an isotropic 30 um spatial resolution was achieved. A repetition time (TR) of 40ms and an echo time (TE) of 4.5ms were chosen to maximize the contrast between blood vessels and the surrounding tissues of the eye. With two averages the total experimental time was 57.6 minutes. Data reconstruction was performed using MatLab (The MathWorks, Natick, MA, USA). To segment blood vessels, the reconstructed data was loaded into Avizo 8.0 (FEI, Burlington, MA, USA). By selecting high SNR vessels using the magic wand tool (connected threshold tool), an angiogram could be created.

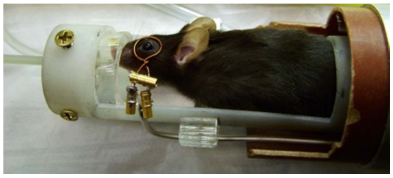

Figure 1: The mouse ready to be imaged.

Results:

A three dimensional model of the blood vessels structure of the mouse eye was acquired. Figure 2 shows a slice of a mouse angiogram for both with and without magnevist. The SNR of the orbital sinus was calculated using ImageJ (National Institutes of Health, Bethesda, MD, USA). With and without the magnevist, the average SNR of the orbital sinus were 52 and 18 respectively. A high signal of the blood vessels compared to the surrounding tissue was observed. For the eye image without the magnevist injection, both choroidal and retinal blood vessels did not show high contrast compared to the surrounding tissue. However, the eye image with the magnevist injection did show high contrast between the retinal vessels and the surrounding tissues.

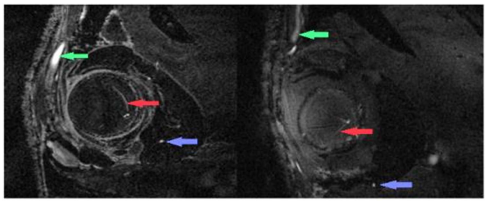

Figure 2: A slice of a mouse angiogram with (left) and without (right) the magnevist. Orbital sinus (green arrow), retinal vessels (red arrow), and vessels around the eye (blue arrow) are shown.

Discussion:

The high static magnetic field allowed us to reach 30um isotropic resolution, enabling us to capture the major ocular blood vessels of the left mouse eye, which in later was segmented using Avizo (Figure 3). The vessels significantly smaller than one pixel size could not be resolved. However, the use of magnevist increased both SNR and contrast to segment the major retinal vessels of the mouse eye. The high contrast was enhanced by the presence of the blood retinal barrier which blocked the flow of the magnevist into the retina. On the other hand, choroidal vessels could not be segmented even with the use of magnevist, because the magnevist leaked out to the surrounding tissue due to lack of tight junctions such as the blood retinal barrier [2]. In addition, motion of the animal was a limiting factor for the experiment. If the isoflurane level was too high, the mouse started to show singultus. A low level of isoflurane caused the mouse to wake up. In both cases, the moving artifacts smeared the signal of the blood vessels. Therefore, it was crucial to control the breathing rate during the experiment. To the best of our knowledge, this work is the first attempt to visualize the blood vessels of an *in vivo* mouse eye by using MRI. The presented work could be used to study other eye vascular disease such as diabetic retinopathy.

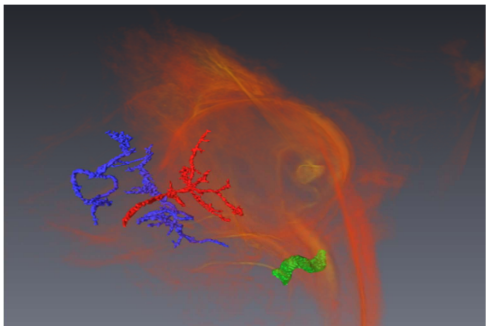

Figure 3: The segmentation of blood vessels using magnevist. The overall shape of the mouse eye is indicated in orange. Orbital sinus (green), retinal vessels (red), and vessels around the eye (blue) are segmented.

References:

[1] H. Shimada, A. Kawamura, R. Mori, and M. Yuzawa, "Clinicopathological findings of retinal angiomatous proliferation.," *Graefes Arch. Clin. Exp. Ophthalmol.*, vol. 245, no. 2, pp. 295–300, Feb. 2007.

[2] M. Saint-Geniez and P. a D'Amore, "Development and pathology of the hyaloid, choroidal and retinal vasculature.," *Int. J. Dev. Biol.*, vol. 48, no. 8–9, pp. 1045–58, Jan. 2004.