MRI Laminar Resolution of the Human Retina

Q. Peng[1,2], Y. Zhang[2], and T. Q. Duong[1,2]
[1]Radiology, UT Health Science Center at San Antonio, San Antonio, TX, United States, [2]Research Imaging Institute, UT Health Science Center at San Antonio, San Antonio, TX, United States

INTRODUCTION The retina consists of highly structured cellular and synaptic layers. In rodents, anatomical MRI of the retina was capable of revealing multiple layers of the thin retina (1,2). Manganese-enhanced MRI following intraocular injection of manganese (Mn) showed 7 layers, consistent with histological assignments (3). More recently, a novel application of high-resolution balanced steady state free precession (bSSFP) MRI revealed 7 layers without using contrast agent in mouse retinas (4).

MRI of the human retina is challenging because the thin retina is located in a region of high magnetic susceptibility (air-tissue interface), is susceptible to eye motion in awake human, and high spatial resolution may be limited by weaker field gradients on human scanners. Moreover, retinal thickness does not scale significantly from rodent to human (in contrast to the brain), although the eye ball size does scale somewhat which allows a thicker imaging slice. Previous studies failed to detect laminar resolution of the human retina (5,6). In this study, we reported on our initial experience on pushing spatial resolution and contrast to visualize anatomical layers in the in vivo human retina at 3T.

METHODS Experiments were performed on 2 normal human volunteers with 2-3 repeated measurements made on each subject. MRI studies were performed on a 3T Philips Achieva equipped with 80mT/m gradient system. A custom-made circular eye coil of 6 cm in diameter was SNR-optimized for the adult human retina. A dynamic scan of a single 2D b-SSFP (bFFE) was performed, each dynamic took 10 s, and 2 s pause was given before the next dynamic acquisition. Subjects were asked to blink during pause but otherwise fixate on a point during MRI. The b-SSFP sequence parameters were TR/TE/FA = 20/2.1/40°, readout bandwidth = 5.3 kHz, and spatial resolution of 100x200x2000 μm. The higher resolution dimension (100 μm) was set in the readout direction (up-and-down). Oversampling was employed in the phase-encoding direction (left-right) to avoid aliasing artifacts. A total of 10 dynamics was acquired leading to 2 minutes per scan. Co-registration was performed as needed. Signal intensity profiles across the retinal thickness were analyzed, and peak FWHM was used to determined laminar thicknesses.

RESULTS SNR of the custom-made surface coil at 3cm depth was 218% of a standard 8-channel head coil. **Figure 1** shows representative high resolution MRI of the retina obtained in 2 mins. Three bright-dark-bright layers were observed. The sclera behind the retina appeared relatively dark as expected. The retinal thicknesses for the three layers are summarized in **Table 1** for the temporal and nasal quandrants on either side of the optic nerve.

The imaging slice thickness yielded up to 14% partial volume effect (PVE) due to the retinal curvature, meaning that the retinal thickness was overestimated by up to 14%. With PVE correction, the total retinal thicknesses including the choroid were 592 μm and 705 μm in the nasal and temporal quandrant, respectively. Thicknesses of the nasal and temporal quandrants were different in all scans.

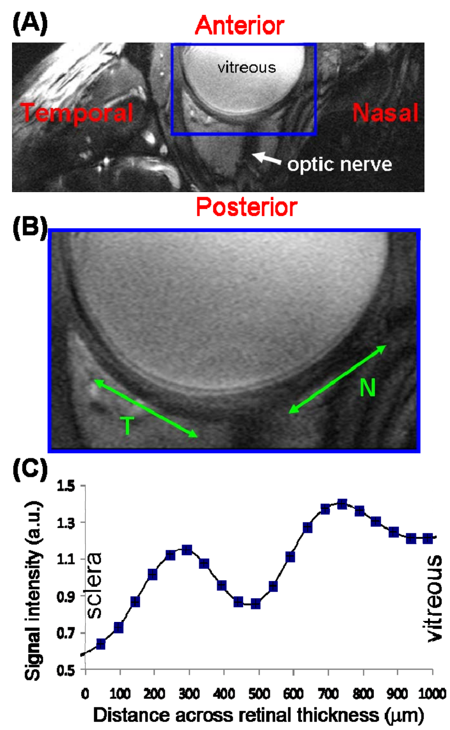

Figure 1. (A) Scout image. **(B)** In vivo human retina at 100x100μm obtained using a surface coil at 3T in 2 mins. **(C)** Spatial profile across the retinal thickness, indicating the bright-dark-bright layers. The signal at the vitreous boundary is high.

Table 1. Laminar thicknesses over the region N and region T as shown in Figure 1B.

	Region N	Region T
"Inner" layer	232 ± 8	294 ± 20
"Middle" layer	227 ± 11	254 ± 54
"Outer" layer	217 ± 29	256 ± 67
Total	675 ± 35	804 ± 80
$Total_{(PVE)}$	592 ± 31	705 ± 71

$Total_{(PVE)}$: Corrected for partial volume effect (14%) due to slice thickness

DISCUSSION This study demonstrates a novel MRI application to detect laminar resolution in the in vivo human retinas at high spatiotemporal resolution. This was made possible by using a custom-made Rx-only surface radiofrequency coil, choosing the appropriate imaging protocol, optimizing imaging parameters, minimizing eye movement as well as image co-registration.

The 3 layers herein are similar to those reported in cats (2) and rats (1). In those studies, intravenous administration of Gd-DTPA – to which retinal and choroid/retinal pigment endothelium were impermeable – was used to set the boundaries of the retinal thickness and helped layer assignments. We tentatively assigned: 1) the "inner" bright layer to include the vascularized ganglion cell layer, inner plexiform layer, inner nuclear layer and outer plexiform layer, 2) the "middle" dark layer to include the avascularized outer nuclear layer and the photoreceptor inner and outer segments, and 3) the "outer" bright layer to include the vascularized choroid. These assignments of course remain to be validated.

The thickness of the in vivo human neural retina (excluding the choroid) varied significantly, even within the OCT literatures – 236 μm (7) and 200-310 μm (8). Reports of in vivo human choroidal thickness are sparse but have been quoted to be 293-307 μm by partial coherence interferometry (9) and 318-335 μm by OCT (10). Together, the total retinal thickness including the choroid ranged from 500-650 μm. By comparison, MRI-derived total retinal thickness, although within the ranges reported by OCT, was on the high side. Possible explanations include limited spatial resolution, movement artifact, and long readout window which degraded resolution. Further studies are needed to resolve this discrepancy.

In conclusion, we demonstrate, for the first time, the feasibility of achieving anatomical laminar resolution on the human retina using MRI at 3T. Future studies will aim to improve spatial resolution and contrast, as well as to explore implementations of physiological MRI techniques, such as BOLD and blood flow MRI, in the human retinas.

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