NEW ACQUISITION AND ANALYSIS FOR SEGMENTATION OF THE INTRAORBITAL OPTIC NERVE IN VIVO AT 3T

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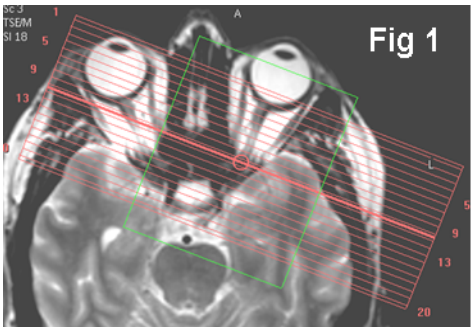
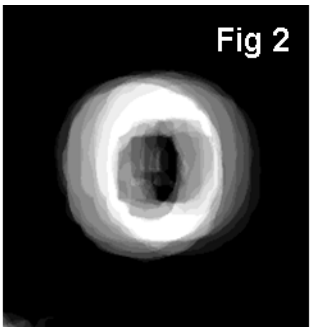
TARGET AUDIENCE: Neurologists studying multiple sclerosis (MS) and Neuro-ophthalmologists. In addition, physicists working on developing new methods for structural and quantitative MR measurements of the optic nerve.

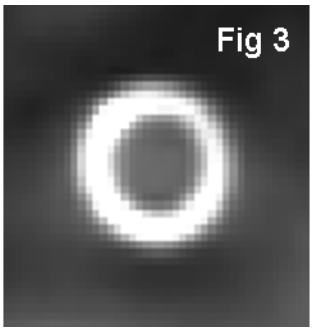
PURPOSE: To develop a fast and reliable method for measuring the mean cross-sectional area of the optic nerve *in vivo* at 3T.

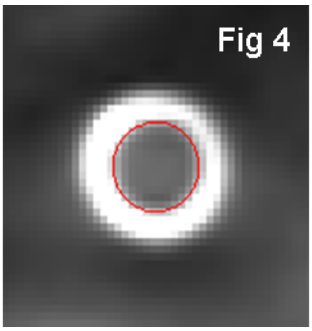
INTRODUCTION: The ability to reliably measure the mean cross-sectional area (CSA) of the intraorbital optic nerve (ION) *in vivo* can be very important when studying neurological conditions such as glaucoma [1] and multiple sclerosis (MS) [2, 3]. This is because these pathological conditions are likely to be associated with axonal loss and progressive atrophy and, therefore, reliable methods for measuring the CSA of the ION not only can aid in the diagnosis but can also be invaluable when assessing neuroprotective strategies. However, imaging the ION is technically challenging due to the small size of the structure, the influence of the surrounding cerebrospinal fluid (CSF) and fat, but more importantly the inherent motion of the ION during imaging examinations. Typically, the ION mean CSA can be measured by means of semi-automated image analysis of high-resolution MR images acquired with a variety of pulse sequences and types of image contrast (e.g. T1-weighted, T2-weighted) and with reported coefficient of variation > 4% [2-4]. While the image analysis methods currently employed for segmenting the ION may only suffer from operator dependent errors, image acquisition strategies can be more problematic. For example, the higher the resolution required the longer it takes to acquire the images with consequent motion artefacts, especially in the anterior portion of the ION, while faster acquisitions may depict the anterior portion of the ION more clearly but can suffer from lack of conspicuity in the mid and distal portions [2, 4]. In this work, we propose a new and robust segmentation method of the ION, which is based on a) an improved image acquisition scheme that combines separately acquired volumes by registering them to account for motion related artefacts associated with long acquisitions and b) a semi-automated image analysis method that is less operator dependent and which is based on an active surface model (ASM) that has been shown to be invaluable in measuring the spinal cord mean CSA [5], a small and discrete structure similar to the ION.

METHOD: A) Study participants: Five healthy control subjects were recruited (mean age 29 years, range 27-31, 3 male). Informed consent was obtained from all participants and the study was approved by the local institutional review board. B) MR Imaging: Using a 3T Philips Achieva MRI system (Philips Medical Systems, Best, Netherlands) and the manufacturer's product 32-channel head coil, the left ION was imaged in the coronal-oblique plane (i.e. slices orthogonal to the ION longitudinal axis; see Fig. 1) with the following sequence parameters: a fat-suppressed heavily T2-weighted multi-slice 'single-shot' 2D-TSE with TR = 16sec; TE = 74ms; flip angle $\alpha = 90°$; FOV= 160 x 160 mm^2; voxel size = 0.5 x 0.5 x 3 mm^3; NEX = 1; 20 contiguous slices (no gap); scanning time = 32 secs ; number of repeated dynamics = 15 (total scan time 7min 58secs). In order to minimise the effect of motion during imaging, the volunteers were asked to focus their vision on a coloured marker positioned in front of them for each one of the 32sec dynamic scans, with a short break in-between each dynamic scan. All subjects were imaged 3 times with the same imaging protocol on 3 separate occasions. B) Image analysis: The 15 acquired volumes were registered slice-by-slice using the 2D registration options provided by the 'imregister' command in MATLAB 2012a (Mathworks, Natick, MA, USA). Using Jim Software (Xinapse systems, www.xinapse.com), the ASM segmentation option was used to segment 8-10 slices starting from 3mm behind the globe to the orbital apex (the number of slices depended on the length of the ION between the globe and the orbital apex in each volunteer). Scan-rescan reproducibility of all measurements was recorded from the coefficient of variation as a percentage value (COV%)









RESULTS: Despite the acquisition of fast individual volumes, motion of the optic nerve during imaging was unavoidable. Figure 2 shows an example of the same slice taken from each volume and added together (i.e. after thresholding and binarisation, for demonstration only). Figure 3 shows the result of the image registration for a single slice following addition of the registered volumes and Fig 4 shows an example of the segmentation using the ASM. The mean ± SD CSA of the ION in the 5 volunteers was 5mm ± 0.8 and the mean scan-rescan COV was 3.9%. Table 1 shows the results obtained from all volunteers in more detail.

Table 1	Scan 1 (mm^2)	Scan 2 (mm^2)	Scan 3 (mm^2)	Scan-rescan (%COV)
Case 1	4.6	4.1	4.6	5.9
Case 2	5	5.1	5.6	6.3
Case 3	4.4	4.6	4.5	2.2
Case 4	6.3	6.3	6.3	0.5
Case 5	4.5	4.9	4.5	4.7

CONCLUSION: A new MR acquisition and analysis protocol has been presented for fast and reliable segmentation of the ION which utilises an improved acquisition scheme and a robust image analysis method. Future investigations will be directed at evaluating the image acquisition and analysis protocol presented here in disease states and, if the high reproducibility is confirmed, ION atrophy measured with this methodology could become a feasible and clinically relevant biomarker.

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