Mapping of the optic nerve in multiple sclerosis patients with and without optic neuritis

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Target Audience: Physicists and clinicians focused on understanding multiple sclerosis disease etiology and the effects of both multiple sclerosis and optic neuritis on the size of the optic nerve.

Purpose: The optic nerve (ON) and surrounding cerebrospinal fluid (CSF) have been manually measured(1,2). Optic neuritis is a sudden inflammation of the ON and is marked by pain on eye movement, and visual symptoms such as a decrease in visual acuity, color vision, contrast and visual field defects (3). The ON is closely linked with multiple sclerosis (MS) and patients have a 50% chance of developing MS within 15 years (4). Further, we know that the post-mortem optic nerve is atrophic in patients with remote optic neuritis. Despite this, there is no in vivo radiological biomarker of the ON that predicts eventual development of MS. We hope to better understand optic neuritis disease etiology as it relates to MS using MRI to examine the ON anatomy along the length of the nerve. The goal of this work is to compare the ON of MS patients with and without optic neuritis to healthy controls using an automated tool to measure the size of the ON and cerebrospinal fluid (CSF) independently derived from high-resolution orbital MRI.

Method: Anatomical T2-weighted VISTA scans were obtained on a 3T Philips Achieva (Philips Medical Systems, Best, The Netherlands) using a 2 channel body coil for transmission and an 8 channel head coil for reception. After tri-planar localization, we acquired the T2-weighted volume in the axial plane. The VISTA sequence parameters were: 3D FSE (TR/TE/α = 4000ms/404ms/90°), FOV= 180 x 180 x 42mm^3, nominal resolution = 0.6 x 0.6 x 0.6mm^3, SENSE factor = 2, fat saturation = SPIR, and total scan time = 5:20. It should be noted that the TE is long due to the nature of the asymmetrically sampled k-space pattern of the VISTA (SPACE on Siemens, and CUBE on GE) acquisition but does provide excellent tissue:CSF contrast. We reformat the data into the coronal plane and utilize a model to fit the ON and surrounding CSF. The model is initialized using the result of a previously described multi-atlas segmentation protocol (5). We then fit the model to the ON using a conjugate gradient descent non-convex optimization method. A graphic outline of this pipeline can be seen in Figure 1. The model measures the underlying radius of the ON and the surrounding CSF at each slice. A total of 58 subjects are evaluated. 32 are healthy controls (55%) and 26 are relapsing-remitting MS patients. Of the 26 MS patients (45%), 14 (24%) have a history of optic neuritis, 8 unilateral and 6 bilateral. This yields a total of 64 healthy ONs, 24 MS patient ONs, and 20 optic neuritis ONs which are measured along the length and compared. The slice-wise measurements were interpolated over the length of the ON to be the same length as the longest observed ON which is 36.25 mm (58 slices). The shape of the ONs often results in appearance over a different number of slices from volume to volume. Interpolation more closely aligns corresponding parts of the ON across subjects. A three-element moving window median filter is applied across slices to reduce noise in the measurements.

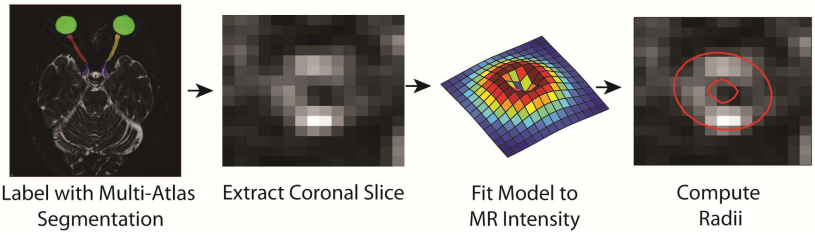

Fig 1. Processing pipeline utilized to automatically measure the optic nerve and surrounding CSF radii

Results: The median ON and surrounding CSF radii are significantly different between healthy controls and MS patients with a history of optic neuritis ($p<0.05$; assessed slice-wise by Wilcoxon rank-sum test) in 19 slices for the inner radii and 22 slices for the outer radii (**Fig 2b**). These slices were mostly grouped in the anterior region of the ON. The differences survive Bonferroni correction. Differences between healthy controls and MS patients without a history of optic neuritis (Fig 2a) were smaller; only 2 slices for the inner radii and 11 slices for the outer radii were significant ($p<0.05$; assessed slice-wise by Wilcoxon rank-sum test). Differences did not survive Bonferroni correction.

Conclusions: ON atrophy is seen to manifest near the eye globe in relapsing-remitting patients with a history of optic neuritis and we can detect this atrophy on high-resolution in-vivo MRI. Furthermore, the CSF surrounding the ON reduces in size with the presence of MS with a history of optic neuritis. There is a possible reduction in the size of CSF surrounding the ON in MS patients without a history of optic neuritis but there is currently not enough data to support this. These results are the first radii measurements of this fully-automated pipeline in a patient population and confirm prior manual studies which suggest ON size differences between patients and controls. This may provide an opportunity to compare optic nerve atrophy in large-scale patient populations in the future and may provide a novel biomarker for disease progression.

References: 1. Repka MX, et al. Ophthalmology 1989;96(1):26-32. 2. Newman W et al. British journal of ophthalmology 2002;86(10):1109-1113. 3. Richa C. Optometry-Journal of the American Optometric Association 2010;81(9):423-424. 4. Group ONS. Archives of neurology 2008;65(6):727. 5. Panda et. al. JMI. 2014;1(2):024002-024002.

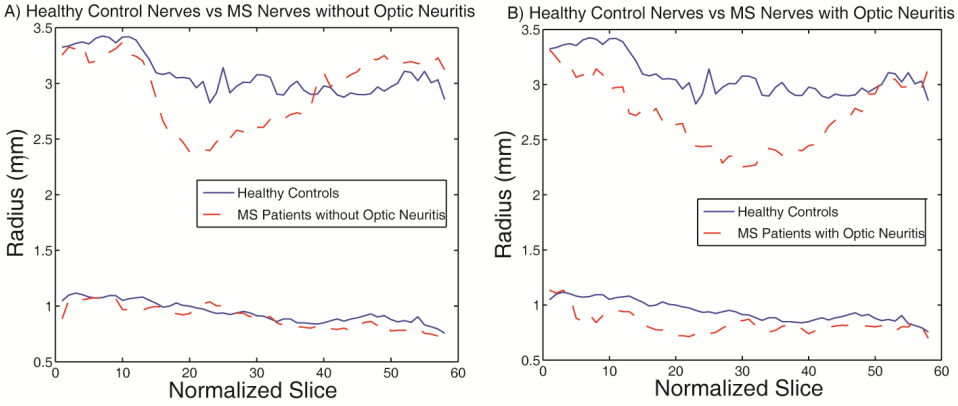

Fig 2. Median filtered radii measurements comparison across populations. Healthy controls vs relapsing-remitting MS patients with a history of optic neuritis (left) and healthy controls vs relapsing-remitting MS patients without a history of optic neuritis (right)