Morphometry of the Retrobulbar Human Optic Nerve: Comparison between Conventional Sonography and Ultrafast Magnetic Resonance Sequences

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PURPOSE. To compare different methods for quantification of optic nerve and nerve sheath diameter. To apply a novel magnetic resonance protocol using half-Fourier acquired single-shot turbo spin-echo (HASTE) sequences to analyze optic nerve dimensions.

METHODS. Measurements were taken in right eyes of 33 subjects whose median age was 25 years. A-scan ultrasonography was repeated three times in straight gaze. B-scan ultrasonography was repeated three times in straight gaze and abduction. HASTE sequences were applied in straight gaze, analyzed twice by two different radiologists, and completely repeated in a subset of 10 subjects; 95% confidence intervals and coefficients of variation were calculated.

RESULTS. HASTE sequences yielded high contrast between cerebrospinal fluid and optic nerve parenchyma. Acquisition time for each sequence was 1.5 seconds per slice. Optic nerve diameters decreased from 3.23 mm at 5 mm to 2.67 mm at 15 mm behind the eye. Sheath diameters decreased from 5.72 mm to 3.98 mm. A- and B-scan ultrasonography yielded significantly smaller diameters. For HASTE sequences, the coefficients of variation ranged from 2% to 7% and were significantly smaller than those obtained with ultrasonographic measurements (5%–13%).

CONCLUSIONS. The precision of magnetic resonance imaging exceeds that of ultrasonographic methods for determining optic nerve and nerve sheath diameters. HASTE sequences appear particularly appropriate for investigating the retrobulbar optic nerve complex and may be useful in future studies quantifying axonal loss within the optic nerve. (Invest Ophtalmol Vis Sci. 2007;48:1913–1917) DOI:10.1167/iovs.06-1075

Since the introduction of A-scan ultrasonography for measuring optic nerve thickness in 1977,1–3 the diameter of the retrobulbar optic nerve and its sheath has been widely used as a diagnostic parameter in various diseases such as anterior ischemic optic neuropathy, optic neuritis,4 and elevated intracranial pressure.5–9 The diameter and cross-sectional area of the optic nerve have also been shown to correlate with axonal degeneration such as in glaucoma,10–13 demyelination after optic neuritis or multiple sclerosis,14–17 and hereditary optic neuropathies.18,19 Hence, precise documentation of acute swelling or chronic axonal loss in the retrobulbar optic nerve may serve as a useful quantitative diagnostic parameter. It may also serve as a means for future evaluation of neuroprotective strategies.16

To correctly interpret optic nerve measurements, precise normative data are necessary. Accordingly, the retrobulbar optic nerve and its sheath have often been investigated in healthy subjects using methods such as A-scan ultrasonography,20–23 B-scan ultrasonography,24–27 three-dimensional ultrasonography,25,26 computerized tomography,27–29 and magnetic resonance imaging (MRI).30–32 However, these data vary tremendously. Factors contributing to this variation are personal experience, interobserver variability, test-retest variability, and eye movement artifacts occurring during long acquisition times of up to several minutes in certain MRI protocols.5,12,14,15,18,19,30–34

The purpose of this study was to measure optic nerve diameters in healthy subjects and to compare our data with those in the literature, motivated by the aforementioned variability of anatomic data presented thus far. We chose A- and B-scan ultrasonography and MRI. In the latter, we applied modified ultrafast half-Fourier acquired single-shot turbo spin-echo sequences (HASTE) published recently by our group.35 This type of T2-weighted spin-echo sequence provides high contrast between optic nerve parenchyma and cerebrospinal fluid and is sensitive enough to show a statistically significant thinning of the optic nerve in 30° abduction compared with straight gaze. Because of the very short acquisition times, this new MRI protocol may be less sensitive to eye motion artifacts, possibly blurring the image.35

METHODS

This study was performed according to the tenets of the Declaration of Helsinki. Informed consent was obtained from all subjects after explanation of the nature and possible consequences of the study, which had been approved by our institutional Ethics Committee. Thirty-three healthy subjects whose median age was 25 years (range, 22–67 years) were included. Only right eyes were studied. Exclusion criteria were refraction anomalies exceeding 5 D, any optic nerve disease, elevated intraocular pressure, any orbital disease, intracranial abnormalities, and metallic implants or foreign bodies.

Sonographic measurements were taken by an experienced and specifically trained technician with the subjects in supine position and with the use of state-of-the-art equipment. We intended to cut the nerve approximately 5 mm behind the eye. For A-scan ultrasonography (Ophthascan S mini A; Biophysics Medical, Clermont-Ferront, France),
the probe was placed onto the temporal sclera with the subject looking straight ahead after application of topical anesthesia. The device was set to 80 dB in the orbit mode, and quantification was performed off-line. Diameters of the optic nerve and its sheath were documented three times. For B-scan ultrasonography (Ultrascan Digital B 4000; Alcon, Irvine, CA), subjects were instructed to close their right eyes and to keep their left eyes either looking straight ahead or fixating a target 30° to the right to induce right eye abduction. The probe was placed on the eyelid covered with sonographic coupling gel. Diameters of the optic nerve and its sheath were again documented off-line three times at 80 dB.

On the same day, subjects were investigated with a 3T magnetic resonance scanner (Magnetom Trio; Siemens, Erlangen, Germany) that uses an eight-channel phased-array head coil. Subjects were instructed to fixate on a target inside the scanner, with the right eye in straight gaze. As published previously in more detail,35 an ultrafast T2-weighted HASTE sequence was applied with the following characteristics: half-Fourier acquisition in single-shot turbo spin-echo (HASTE); TR, 1500 ms; TE, 146 ms; number of excitations 1; bandwidth, 195 Hz/pixel; fast sync pulses (duration, 1 ms); FOV, 23 × 18 cm²; matrix, 512 × 367; nominal spatial resolution, 0.45 × 0.49 mm²; slice thickness, 3 mm. The images were then interpolated to a matrix size of 2048 × 1468, leading to a pixel size of 0.11 × 0.12 mm². In these HASTE images, cerebrospinal fluid (CSF) yielded a high, white signal and the optic nerve a low, dark signal. Voxels containing CSF and optic nerve or CSF and adjacent tissue showed a defined gray shade proportional to their fractional contents of CSF and tissue (partial volume effect of MRI36). Hence, quantification of the optic nerve and CSF sheath diameter was facilitated by the high-contrast differences in the nerve compared with its surroundings. As a result, measurement accuracy was then limited by the reproducibility of the region of interest (ROI).37 Three slices perpendicular to the optic nerve were acquired in each subject. They were placed at 5, 10, and 15 mm behind the globe. The exact imaging time was documented for each image.

Outer diameters of the optic nerve and its sheath were determined by a board-certified radiologist on a radiologic work station (J-Vision; Tiani, Vienna, Austria) by placement of circles around their outlines so that the best possible fit was achieved. These measurements were repeated in a blinded fashion by a second radiologist. In addition, a subset of 10 subjects was reevaluated 3 months later in a second round of MRI using the same parameters.

Statistically, the main outcome herein was test–retest variability and precision across methods. Correlation techniques are often used in this situation, which, however, are adversely affected by range normaliza-

![Figure 1](https://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933237/) Transverse (A) and sagittal (B) T2-weighted TSE sequences used as a localizer to plan the orthogonal and coronal HASTE sequences perpendicular to the optic nerve at 5 (C), 10 (D), and 15 mm (E) behind the eye.

**RESULTS**

During MRI, the subjects spent a mean time of 8.4 minutes (± 1.8 SD; range, 5–16 minutes) in the scanner. Times of acquisition for an initial localizer scan were 66 seconds and 82 seconds for fast T2-weighted turbo spin-echo (TSE) sequences in transversal and sagittal orientation, respectively, used for planning. HASTE image acquisition time for optic nerve diameter quantification was 1.5 seconds per slice.

Figure 1 illustrates three typical examples of optic nerve cross-sections at the aforementioned three positions behind the eye. The nerve can be clearly distinguished from its surrounding CSF sheath, which itself is bordered by the nerve sheath. Diameters of the optic nerve and its sheath are summarized in Table 1. MRI yielded mean optic nerve diameters of 3.23 mm at a position 5 mm behind the eye and dropped to 2.67 mm at a position 15 mm behind the eye. The same applied to its sheath, with diameters declining from 5.72 to 3.98 mm, respectively. Compared with MRI readings, ultrasonography consistently yielded smaller diameters. In the A-scan mode, diameters were 2.31 mm for the retrobulbar optic nerve and 4.08 mm for the sheath. Slightly larger diameters of the optic nerve and its sheath were obtained in the B-scan mode. In straight gaze, the optic nerve diameters were 2.60 mm and 4.16 mm for the sheath, and in abduction they were 2.60 mm and 4.09 mm, respectively. Mean diameters of the optic nerve and sheath obtained with all three methods (A-scan, B-scan, MRI) differed statistically significantly (P < 0.05) and were normally distributed. In comparisons of straight gaze and abduction, the nerve and sheath diameters obtained with B-scan ultrasonography did not differ significantly.
DISCUSSION

Apart from our recent pilot study, this is the first systematic application of HASTE sequences to investigate the dimensions of the orbital optic nerve. HASTE clearly demonstrated a narrowing of the nerve and its sheath as they approached the orbital apex. In addition to the high contrast between CSF and the nerve and between 2% and 6% for the sheath, A-scan ultrasonography yielded CVs of 13% for the nerve and 9% for its sheath. B-scan ultrasonography was slightly more precise with CVs of approximately 8% for both the nerve and the sheath. CVs for A-scan and B-scan ultrasonography did not differ significantly (P > 0.05). However, CVs for MRI were significantly lower than those for the ultrasonographic methods (P < 0.001).

When a second radiologist remeasured the optic nerve diameters in the original scans, the CVs among readers ranged between 4% anteriorly and 7% posteriorly. For the sheath they varied between 5% and 7%, respectively. When the whole MRI procedure was repeated in a subset of subjects, the CVs were similar and ranged between 5% and 6% for the nerve and between 2% and 6% for the sheath. A-scan ultrasonography yielded CVs of 13% for the nerve and 9% for its sheath. B-scan ultrasonography was slightly more precise with CVs of approximately 8% for both the nerve and the sheath. CVs for A-scan and B-scan ultrasonography did not differ significantly (P > 0.05). However, CVs for MRI were significantly lower than those for the ultrasonographic methods (P < 0.001).
phase-encoding direction, enabling precise measurements for the inner and outer diameters of the CSF sheath. In HASTE images, other tissues may be blurred; however, in the present study, their respective signals had almost vanished because of the high TE and, hence, did not affect quantification. In fact, we took advantage of this high contrast between bright CSF and dark adjacent tissues. Common clinical TSE protocols have echo train durations of approximately 150 ms, whereas tissues under observation have $T_2$ relaxation times shorter than 100 ms. Therefore, such routine TSE sequences have worse point spread functions for CSF than HASTE sequences.

Several histomorphometric studies have focused on the composition of optic nerve tissue in normal, healthy human nerves\(^{50-52}\) and in glaucomatous human nerves.\(^{40,41}\) However, only Karim et al.\(^{50}\) examined differences in tissue composition along the entire intraorbital course of the nerve. Indeed, they found a relative decrease in connective tissue volume compared with an unchanged volume of axonal tissue as the nerve extended from the eye toward the orbital apex. These findings are based on Masson trichrome–stained sections from 2 to 16 mm behind the globe, showing that the percentage of connective tissue decreased from 30% behind the globe to 20% in the orbital apex while the percentage of axonal tissue remained constant.

Although our MRI measurements and those reported in the literature yield consistent diameters, sonographic measurements of the optic nerve and its sheath vary greatly. With A-scan ultrasonography, retrobulbar optic nerve diameters have been quantified as 2.8 to 3.1 mm,\(^{42,43}\) 3.5 ± 0.5 mm,\(^{45}\) 2.8 to 3.4 mm,\(^{21}\) or 3.6 mm.\(^{44}\) For the sheath, diameters of 3.8 to 5.5 mm\(^{42}\) and 4.0 to 5.3 mm\(^{43}\) have been reported. The present measurements range below those reported in the other studies and in our own MRI study. With B-scan ultrasonography, the literature reports optic nerve diameters of 1.9 ± 0.1 mm,\(^{26}\) 2.86 ± 0.46 mm,\(^{10}\) and 3.0 mm ± 0.3 mm.\(^{8}\) Sheath diameters of 4.8 ± 0.6 mm,\(^{26}\) 2.9 to 4.3 mm,\(^{6,7}\) 4.5 mm,\(^{45}\) and 2.4 to 4.7 mm\(^{43}\) have been published. Factors contributing to this tremendous variation are differences in examiner experience, uncertainty in finding the right cutting plane along the nerve, limited spatial resolution, and the inability to achieve perpendicular ultrasonic penetration of the optic nerve.\(^{25}\)

The spectrum of methods for retrobulbar imaging has changed over the years from sonography to more precise MRI. This is likely a logical consequence of the rapid developments in MR technology. However, one has to be aware that this trend has led to higher costs and logistic complexity. Ultrasonography and MRI have their own advantages and disadvantages. Nevertheless, in our study, MRI yielded higher precision. The low variance and short data acquisition time documented herein indicate that HASTE sequences may be particularly practical compared with other MRI sequences in evaluating the optic nerve and its sheath.

**References**


**Erratum**


In Materials and Methods, in the fourth paragraph of the “Image Acquisition” section, the eighth sentence should read, “These sectors were named according to their locations as temporal (T; 311–40°), superotemporal (ST; 41–80°), superonasal (SN; 81–120°), nasal (N; 121–230°), inferonasal (IN; 231–270°), and inferotemporal (IT; 271–310°).”

In the “Statistical Analysis” section, the equation should read:

\[
t = (r_{AB} - r_{AC}) \cdot \sqrt{[(N - 1) \cdot (1 + r_{BC})]/[(2(N - 1)/(N - 3))] \cdot |R|} + \left[ (r_{AB} + r_{AC})/2 \right]^2 \cdot [(1 - r_{BC})^3]
\]

where \( R = (1 - r_{AB}^2 - r_{AC}^2 - r_{BC}^2) + (2 \cdot r_{AB} \cdot r_{AC} \cdot r_{BC}) \), and \( N \) is the sample size.