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ORIGINAL RESEARCH PAPER

Impact of gaze deviation on the optic nerve sheath diameter metric: A prospective interventional study

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ABSTRACT

Background: Optic nerve sheath diameter (ONSD) is a widely used non-invasive surrogate marker of intracranial pressure. Current recommendations state that measurements should be obtained with a neutral gaze. However, the effect of gaze deviation on ONSD has never been investigated. We aimed to evaluate the reliability of ONSD in case of gaze deviation and quantify the associated measurement error. A secondary aim was to assess whether bed inclination has a significant effect on ONSD values.

Methods: We conducted a prospective interventional study on 44 healthy volunteers during routine ocular ultrasound training. ONSD was measured bilaterally along the horizontal and vertical axes at 45° head-of-bed elevation in neutral and deviated gaze. After repositioning the bed to 0° and a 2-minute stabilization period, horizontal measurements were repeated. Measurements were performed according to current consensus recommendations and ALARA principles. Nonparametric analyses were used to analyse the results.

Results: Gaze deviation significantly reduced ONSD values across all axes and both eyes, with a consistent median difference of 0.8–1.0 mm (all $p < 0.001$) and large effect sizes. In contrast, no significant differences were observed between measurements obtained at 45° and 0° ($p > 0.05$).

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Conclusions: Gaze deviation induces a predictable "stretching" effect on the optic nerve sheath, resulting in clinically relevant ONSD reduction. If confirmed in neurocritical populations, this systematic difference may allow estimation of neutral-gaze ONSD in non compliant patients and could form the basis for a dynamic test that estimates optic nerve sheath compliance.

Key words: ONSD, Point of Care Ultrasound, Neurocritical care, gaze, ocular ultrasound, ONSD stretch, 30-degree test.

Introduction

Optic nerve sheath diameter (ONSD) measurement is considered as a non-invasive surrogate marker of elevated intracranial pressure (ICP) and is widely used in clinical practice worldwide (1). It is particularly valuable in the evaluation of patients with acute brain injury, especially in low-resource settings, when invasive ICP monitoring is unavailable or not indicated, and as an initial screening tool in patients with suspected intracranial hypertension.

Current consensus statements and methodological recommendations for ONSD assessment (2) emphasize that measurements should be obtained with the patient's gaze in a neutral position in order to ensure accuracy and reproducibility. However, despite this recommendation, the specific effect of gaze deviation on ONSD measurements has not been systematically investigated or quantified in the available literature. As a result, the degree to which eye position may influence ONSD values and measurement reliability remains uncertain. In addition, patient positioning—particularly head-of-bed elevation—has been suggested as another potential source of variability in ONSD measurements, but its impact has not been fully clarified.

At the same time, automated and semi-automated techniques for ONSD detection are emerging, including approaches based on artificial intelligence (3). These tools may help mitigate operator-dependent variability and could potentially compensate for non-ideal acquisition conditions, such as gaze deviation or non-standard bed inclination, by estimating measurement error and providing corrected values. This capability may be especially relevant in uncooperative patients and in emergency or triage settings, where strict control of gaze direction and patient positioning is often not feasible.

The primary aim of this study was to evaluate the reliability of ONSD measurements in the presence of gaze deviation and to quantify the associated measurement error. The secondary aim was to assess whether bed inclination has a significant effect on ONSD values.

Material and methods

We conducted a prospective interventional study on healthy volunteers enrolled during routine educational sessions on ONSD measurement. The enrolment was done during courses held between January and February 2026. All participants provided written informed consent prior to inclusion. This work was approved by the Bioethical committee of the University of Pisa with the n. 56/2025 the 28th of July 2025. Inclusion criteria were: age ≥18 years, signed informed consent, and participation in scheduled hands-on ultrasound training sessions. Exclusion criteria included previously reported neurological disease, severe ocular pathology (including prior ocular surgery or known anatomical abnormalities affecting the orbit or optic nerve), and pregnancy.

Ultrasound protocol

All ONSD measurements were obtained by three expert operators (GM, GCo, GCu) as part of a standardized teaching protocol using ocular ultrasound. Examinations were performed in accordance with the most recent international consensus recommendations for ONSD assessment and following the ALARA (As Low As Reasonably Achievable) safety principles (2) using the Vivid S5® US machine (GE HealthCare, Chicago, Illinois, USA). A single operator acquired the image and performed the measurement in real time. The results of the measurements were transcribed into the database during the exam by another operator. When images were not clear and the operator was not satisfied with the quality of the image (i.e. uncertain of the measurement), data were not collected.

Participants were initially positioned with the head of the bed elevated at 45°. ONSD measurements were acquired for both eyes along the horizontal and vertical axes. Measurements were performed with the gaze in a neutral position and then repeated during gaze deviation. Specifically, participants were instructed to direct their gaze medially for horizontal-axis measurements and downward for vertical-axis measurements. The direction of gaze deviation was selected according to the anatomical course of the optic nerve in order to maximize optic nerve stretching (Figure 1).

After completion of the measurements at 45° head elevation, the bed position was changed to 0°. After a 2-minute stabilization period, additional ONSD measurements were obtained along the horizontal axis for both the left and right eyes. The interval between changes in bed inclination and subsequent

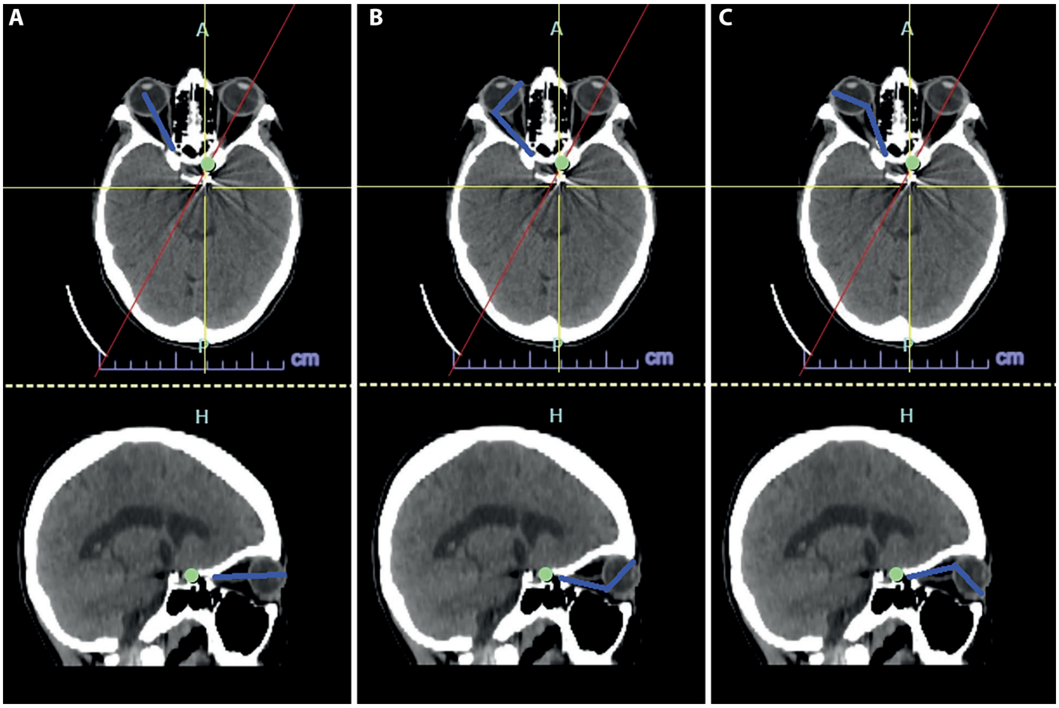
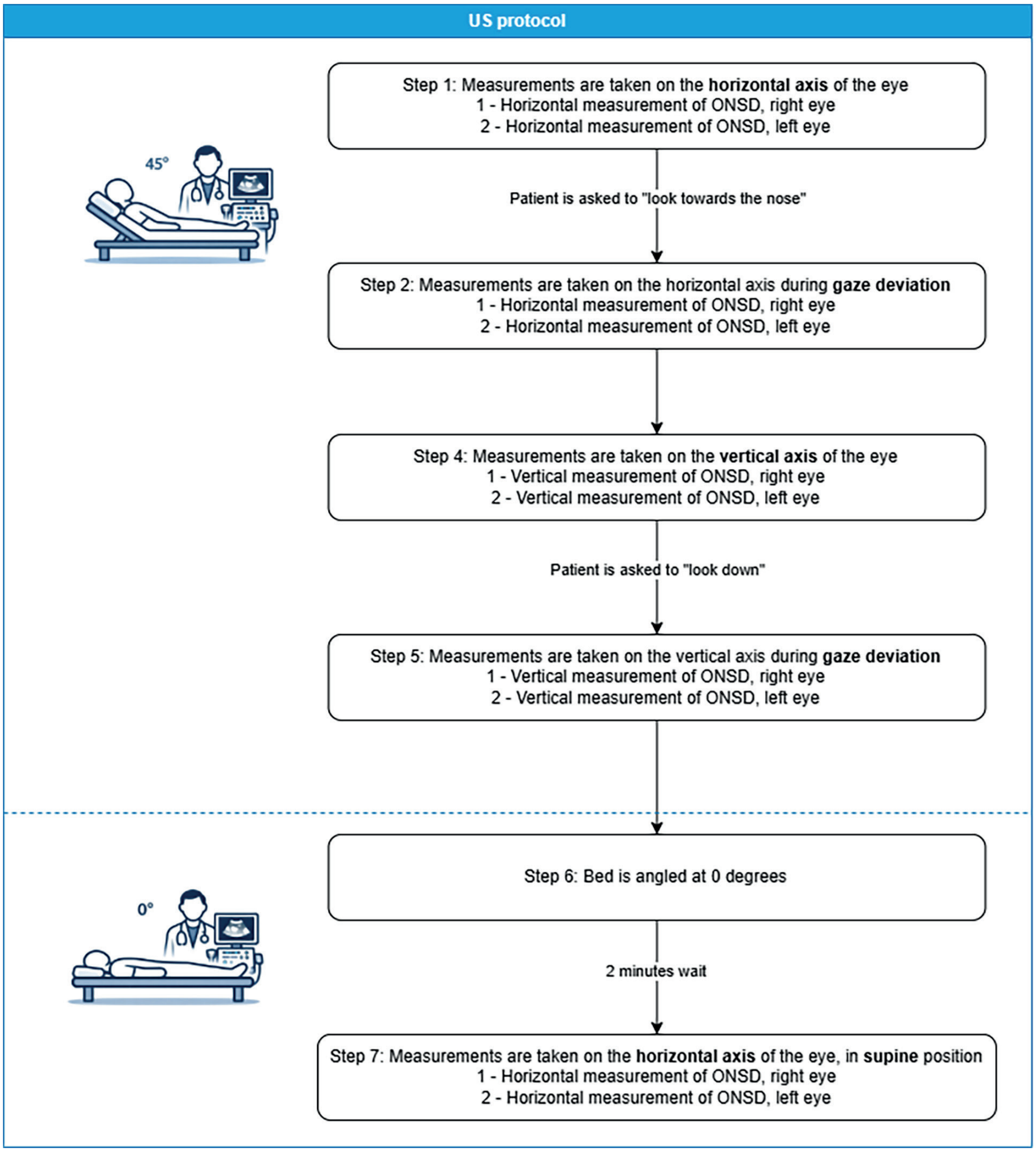


Figure 1. CT scan volumetric reconstruction. In the image above (panel A, axial plane, neutral gaze) the optic nerve points towards the lateral side of the orbit. In the image below (panel A, sagittal plane, neutral gaze) the optic nerve is centred into the orbit without major deviations. In panel B and C is illustrated with blue lines the hypothetical effect of gaze deviation on the optic nerve and bulb structures. This image explains why medial gaze deviation maximises the angling of the optic nerve producing a maximum "stretch". Regarding the vertical axis we conventionally chose the downward gaze deviation being the easiest and therefore the most reliable measurement to acquire (due to the smoother zygomatic arch bone profile). The green dot in the image represents the pivot point on which we aligned and reconstructed the image using volumetric reconstruction of the CT scan software**.**

ONSD measurement was intentionally kept short in order to explore the potential for rapid changes in optic nerve sheath dynamics. The selected time frame corresponded to the minimum practical duration required to reposition the patient, adjust the ultrasound settings, and perform the examination under standardized conditions. A complete detailed flowchart of the US protocol applied is shown in Figure 2.

Statistical analysis

ONSD measurements were checked for normality using Shapiro-Wilk test and QQ plots. After normality checking, ONSD differences were compared using parametric or non-parametric statistical methods for paired samples as appropriate. Descriptive statistics are reported as median and interquartile range [IQR] or mean (SD) as appropriate. Sample size was not



Step 1: Measurements are taken on the **horizontal axis** of the eye
1 - Horizontal measurement of ONSD, right eye
2 - Horizontal measurement of ONSD, left eye

Patient is asked to "look towards the nose"

Step 2: Measurements are taken on the horizontal axis during **gaze deviation**
1 - Horizontal measurement of ONSD, right eye
2 - Horizontal measurement of ONSD, left eye

Step 4: Measurements are taken on the **vertical axis** of the eye
1 - Vertical measurement of ONSD, right eye
2 - Vertical measurement of ONSD, left eye

Patient is asked to "look down"

Step 5: Measurements are taken on the vertical axis during **gaze deviation**
1 - Vertical measurement of ONSD, right eye
2 - Vertical measurement of ONSD, left eye

Step 6: Bed is angled at 0 degrees

2 minutes wait

Step 7: Measurements are taken on the **horizontal axis** of the eye, in **supine** position
1 - Horizontal measurement of ONSD, right eye
2 - Horizontal measurement of ONSD, left eye

Figure 2. Ultrasound protocol used to acquire the measurements of the ONSD. US: ultrasound. ONSD: optic nerve sheath diameter.

calculated a priori as no previous literature exists. We aimed to have a minimum sample of 40 volunteers and calculated effect sizes. Mean differences and their corresponding confidence intervals were reported. When data were missing for one of the paired measures, that pair was excluded from analysis.

Graphical representations were generated using violin plots with paired lines. A two-sided p value < 0.05 was considered statistically significant. All statistical analyses and figures were produced using R Studio (4).

Results

We enrolled a total of 44 healthy volunteers during four 3-hour sessions about ONSD training. All the volunteers were enrolled and gave their consent to participate. Median age was 49 years [28-62]. Females were 19 (43%), and males were 25 (57%). A detailed workflow of the enrolment of participants is shown in Figure 3.

Normality check of distributions performed with Shapiro Wilk test and QQ plots revealed that not all the data were normally distributed. Due to the non-normal distribution observed in several variables, the Wilcoxon Signed-Rank test was used for all paired comparisons to ensure a consistent and robust statistical approach.

Regarding the quality of images and availability of measurements, operators judged the images of sufficient quality to take the measure in almost all the cases. Nevertheless, in the vertical plane images were more difficult to obtain in some cases due to the bone prominence in respect to the eye (i.e. superior margin of the orbit and zygomatic arch). Specifically, in cases of sunken eyes or prominent bone structures, the optic nerve insertion shifted beyond the probe's contact area, making it difficult to maintain an adequate acoustic window. The overall availability of images for each axis and type of gaze is reported in Table 1.

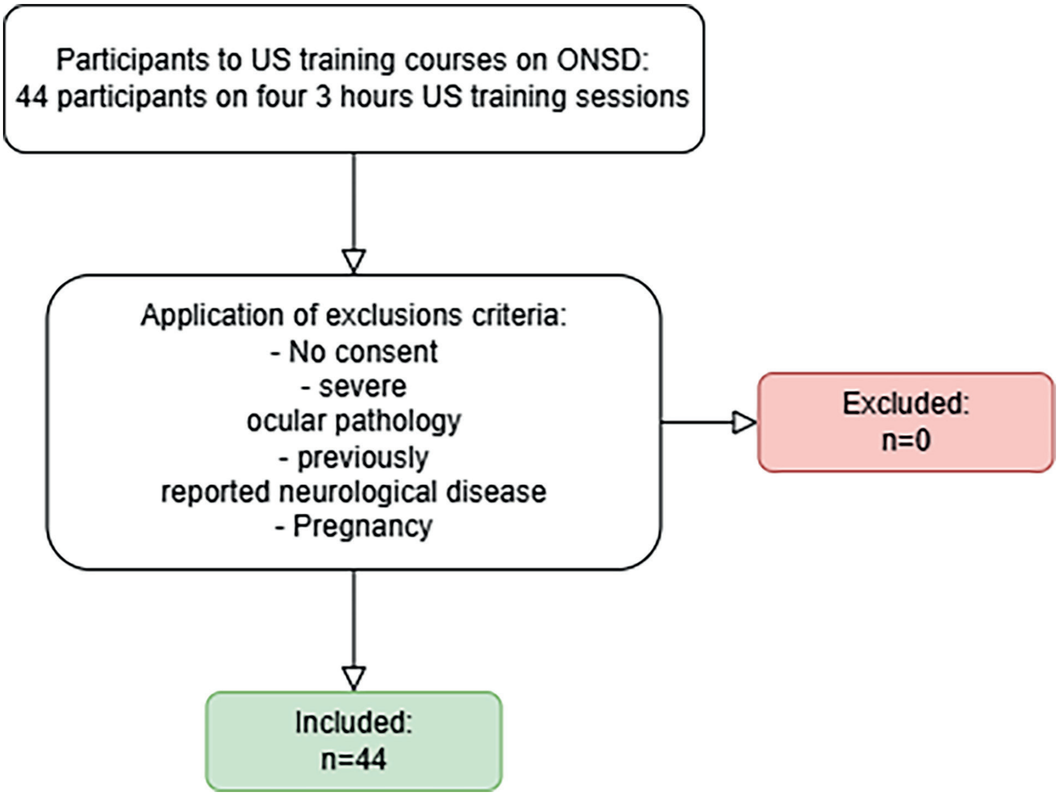


Figure 3. Inclusion and exclusion process workflow.

Table 1. Feasibility of insonation of the ONSD along the vertical and horizontal axis, with different gaze and bed elevation. Images were considered not reliable when the operators judged them of low quality and were uncertain about the measurement taken.

Bed elevation	**ONSD metric**	N	Feasibility
45 degrees	Right, horizontal axis, neutral gaze	44/44	100.0%
	Right, vertical axis, neutral gaze	43/44	97.7%
	Left, horizontal axis, neutral gaze	44/44	100.0%
	Left, vertical axis, neutral gaze	43/44	97.7%
	Right, horizontal axis, deviated gaze	43/44	97.7%
	Left, horizontal axis, deviated gaze	43/44	97.7%
	Right, vertical axis, deviated gaze	35/44	79.5%
	Left, vertical axis, deviated gaze	35/44	79.5%
0 degrees	Right, horizontal axis	43/44	97.7%
	Left, horizontal axis	43/44	97.7%

Effect of gaze deviation on ONSD measurements

A statistically significant reduction in ONSD values was observed during gaze deviation compared with the neutral gaze position across all measurement axes and for both eyes (Table 2, Figure 4).

For the right eye along the horizontal axis, median ONSD decreased from 5.20 mm [4.90–5.40] in the neutral position to 4.10 mm [3.80–4.60] during gaze deviation, with a median difference of 0.9 mm (95% CI 0.75–1.1; $p < 0.001$; effect size −0.866).

Similarly, for the left eye along the horizontal axis, median ONSD decreased from 5.10 mm [4.90–5.40] to 4.10 mm [3.90–4.55], corresponding to a median difference of 0.95 mm (95% CI 0.75–1.05; $p < 0.001$; effect size −0.956).

Along the vertical axis, the right eye showed a reduction from 5.10 mm [4.85–5.20] in the neutral position to 4.00 mm [3.75–4.40] during deviation, with a median difference of 0.95 mm (95% CI 0.8–1.1; $p < 0.001$; effect size −0.993).

The left eye demonstrated comparable findings, with median ONSD decreasing from 5.10 mm [4.80–5.30] to 4.10 mm [3.95–4.50], yielding a median difference of 0.95 mm (95% CI 0.8–1.05; $p < 0.001$; effect size −1.000).

Across all comparisons, gaze deviation was associated with a consistent reduction of approximately 0.9–1.0 mm in ONSD measurements, with large effect sizes, indicating a substantial and systematic measurement bias.

Effect of bed inclination on ONSD measurements

No statistically significant differences were observed between measurements obtained at 45° head-of-bed elevation and those obtained at 0° (Table 2, Figure 5).

For the right eye (horizontal axis), median ONSD was 5.10 mm [4.90–5.40] at 45° and 5.10 mm [4.85–5.35] at 0°, with a median difference of 0.05 mm (95% CI −0.15 to 0.2; $p = 0.606$; effect size −0.097).

For the left eye (horizontal axis), median ONSD was 5.00 mm [4.90–5.40] at 45° and 5.20 mm [4.80–5.50] at 0°, corresponding to a median difference of −0.05 mm (95% CI −0.25 to 0.1; $p = 0.581$; effect size 0.103).

These findings suggest that, in contrast to gaze deviation, head-of-bed elevation from 0° to 45° does not significantly influence ONSD measurements under the conditions of this study.

Discussion

We performed a prospective interventional study on 44 volunteers demonstrating that gaze deviation

Table 2. Main results of the study reporting the differences between the measurements before and after the gaze deviation (stretching of the nerve) and with bed elevation at 45° vs 0°. CI: confidence interval.

Comparison	**Neutral gaze**	**Deviated gaze**	**Median Difference [CI]**	**Effect size**	***p* value**	**N**
Right horizontal — Neutral vs Deviated	5.20 [4.90–5.40]	4.10 [3.80–4.60]	0.9 [0.75–1.1]	-0.866	<0.001	43
Left horizontal — Neutral vs Deviated	5.10 [4.90–5.40]	4.10 [3.90–4.55]	0.95 [0.75–1.05]	-0.956	<0.001	43
Right vertical — Neutral vs Deviated	5.10 [4.85–5.20]	4.00 [3.75–4.40]	0.95 [0.8–1.1]	-0.993	<0,001	35
Left vertical — Neutral vs Deviated	5.10 [4.80–5.30]	4.10 [3.95–4.50]	0.95 [0.8–1.05]	-1	<0.001	35
Comparison	Bed 45°	Bed 0°	Median Difference [CI]	Effect size	*p* value	N
Right horizontal — 45° vs 0°	5.10 [4.90–5.40]	5.10 [4.85–5.35]	0.05 [-0.15–0.2]	-0.097	0.606	43
Left horizontal — 45° vs 0°	5.00 [4.90–5.40]	5.20 [4.80–5.50]	-0.05 [-0.25–0.1]	0.103	0.581	43

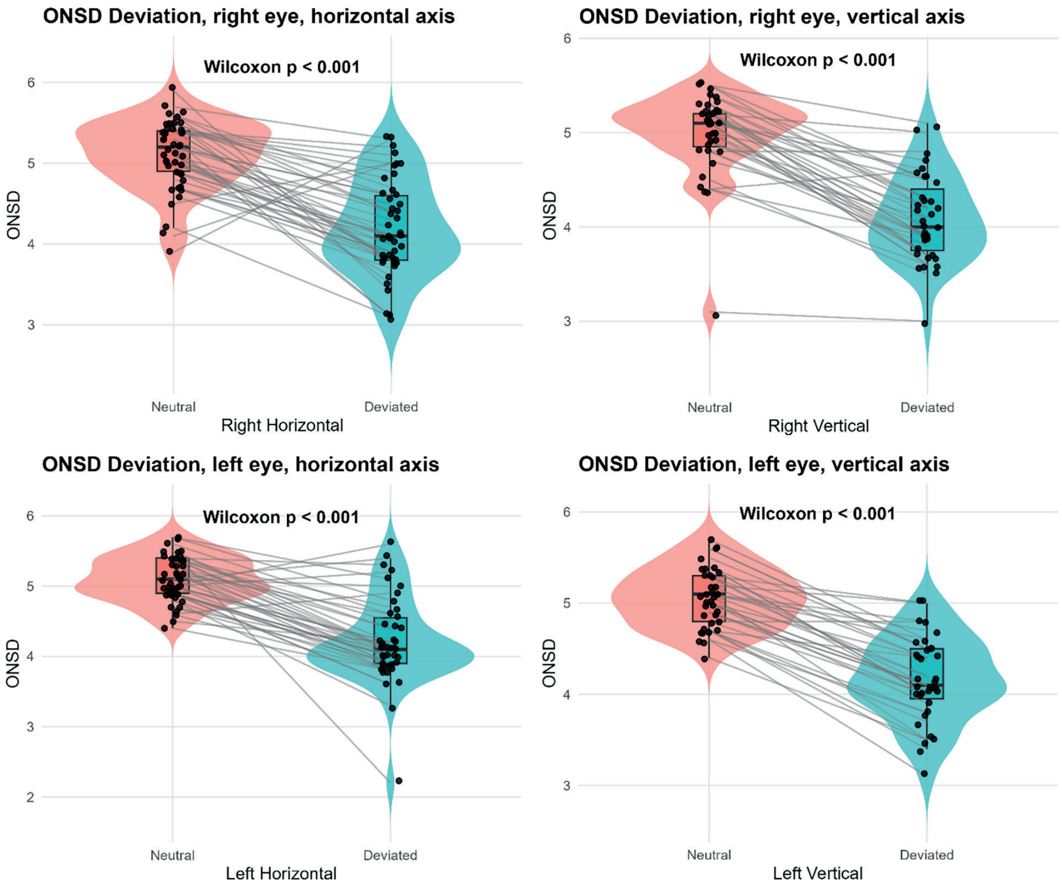


Figure 4. Violin plots with paired lines showing the effect of the gaze deviation on the ONSD metric for both eyes and axis of insonation.

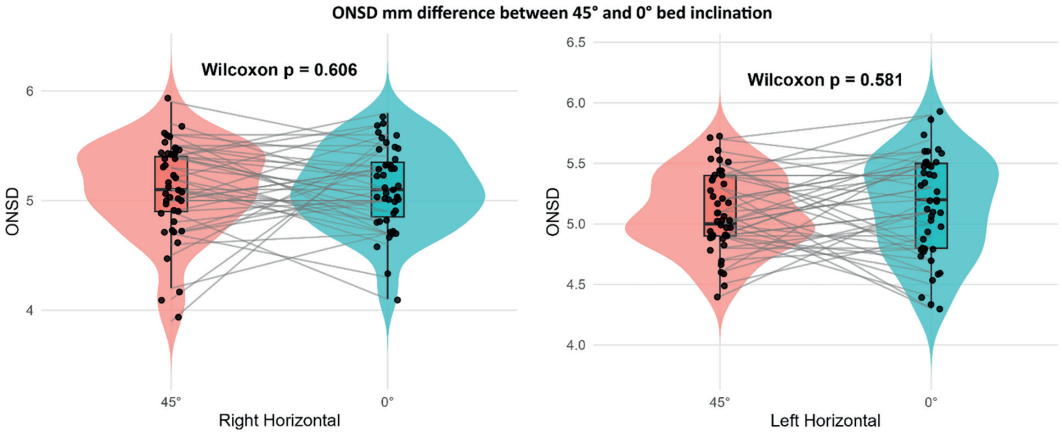


Figure 5. Difference of the ONSD metrics with changes in the bed elevation (45 vs 0° angle). No statistical difference were noticed.

has a significant impact on the ONSD measurement, that ranges around 0.75–1.1 mm of median difference. In addition, bed inclination between 45 and 0° seemed to have no impact on the final ONSD measurement.

No previous study has specifically investigated the impact of gaze deviation on ONSD measurement. While current consensus recommendations clearly state that measurements should be obtained with the eye in a neutral position (2), the consequences of deviating from this condition have not been formally quantified. From a technical standpoint, gaze deviation alters the sonographic appearance of the optic nerve sheath, particularly by partially blurring the margins of the dura mater–arachnoid interface (5). Despite this, we did not encounter substantial technical difficulties in acquiring the measurements. The outer contour of the optic nerve sheath remained clearly identifiable, and ONSD measurements during gaze deviation were feasible and reproducible within the study protocol.

However, the absence of reference values for ONSD obtained during gaze deviation represents a relevant clinical issue. Our data demonstrate that the difference between neutral and deviated gaze measurements consistently ranges between 0.9-0.95 mm [0.75-1.1 95% CI]. If future studies confirm these findings in neurocritically ill populations, the systematic and predictable magnitude of the observed difference may allow clinicians to approximate the expected neutral-gaze ONSD even in the presence of gaze deviation, potentially improving the interpretability of measurements obtained under non-standardized conditions such as in uncooperative or uncooperative patients (altered consciousness, agitation, or severe neurological impairment). Based on these results, it may also be inferred that ONSD measurements obtained during gaze deviation could still provide clinically meaningful information. For instance, very low ONSD values measured in deviated gaze (e.g., approximately 3–4 mm) might represent a reliable negative predictor of elevated intracranial pressure, whereas values that would already be considered borderline or high in neutral gaze (e.g., around 5.5–6 mm) when measured during gaze deviation could suggest a high likelihood of increased intracranial pressure. Future studies might investigate if a cutoff for intracranial hypertension in case of gaze deviation is identifiable, or the possibility to have a correction factor for the angle of the gaze.

Emerging automated and artificial intelligence–based systems for automatic ONSD assessment may offer potential solutions (3,6). Several studies evaluating automated ONSD detection have shown that measurement accuracy and agreement with manual assessment depend strongly on correct alignment and optimal visualization of the optic nerve sheath. Reduced alignment quality has been associated with lower accuracy and diminished ability to discriminate elevated ICP (7). This suggests that algorithm-based measurements may also be vulnerable to gaze-induced geometric distortion and US artifacts (8), potentially amplifying measurement error in non-neutral eye positions (5). Future systems may need to incorporate eye-position recognition and correction algorithms capable of interpreting both neutral and deviated gaze configurations or even integrating measurements from multiple gaze positions. Anyway, the possibility of applying correction factors for gaze deviation requires careful development and represents a research challenge.

Beyond measurement bias, the difference between neutral and deviated gaze may have physiological implications. Straight and deviated gaze positions could theoretically function as a dynamic stress test of optic nerve sheath compliance. In ophthalmologic practice, the so-called “30-degree test,” performed using standardized A-scan ultrasonography, is employed in chronic intracranial hypertension to assess optic nerve sheath compliance (9). The underlying assumption is that chronically elevated ICP induces fibrotic remodelling of the sheath, reducing its elasticity; consequently, sheath diameter changes less with gaze deviation in chronically stressed nerves. To the best of our knowledge, the applicability of a similar dynamic maneuver in neurocritical care has not been explored. Nevertheless, a study by Le et al. examined human optic nerve sheaths from donors aged 4-93 years and found significant age-related changes (10). The sheath was increased in thickness and showed a bilaminar rather that unilaminar structure, with a denser, more compact collagen in the inner layer. In addition, the density of the elastin (that predominates in the inner layer) and the sheath thickness was increased with age significantly. Other studies described ageing related changes of the optic nerve structures, and confirmed the increase in collagen types I, III and IV suggesting inter-individual differences (11). In relation to these studies, some older patients, even in absence of chronic ICP elevation, might exhibit limited ONSD dilation even in case of acute ICP elevations (i.e. be false negatives). In this subgroup of patients, the dynamic stress test could explain the false negative result. The stress test could inform then about the reliability of the ONSD metric and could be an essential test especially in older adults. Further studies aiming to assess the influence of the age and sex on the dynamic stress test might be useful to determine the influence of these covariates in the nerve compliance.

With regard to bed inclination, we did not observe a significant difference between measurements obtained at 45° and 0°. This finding may be explained by the short interval (2 minutes) between repositioning and measurement acquisition. Previous studies reporting significant differences often allowed a longer (several hours) equilibration period before reassessment (12,13). Our findings may therefore reflect the short-term biomechanical behaviour of the optic nerve sheath, which appears sufficiently rigid to buffer brief variations in ICP within the physiological range. This “dampening” effect may limit the capacity of ONSD to reflect rapid or minor ICP fluctuations and supports the concept that ONSD should not be interpreted as a direct surrogate of absolute ICP values, but rather as a marker of sustained or clinically relevant intracranial hypertension (14,15).

Several limitations should be acknowledged to this study. Standardization of the degree of gaze deviation and quantification of the exact angle of ocular deviation across participants was not feasible. As patients needed to be with their eyes closed during examination, the ability to regulate and control the degree of gaze deviation was also impossible. For this reason, we asked for their maximal gaze deviation during the examination. Nevertheless, considering the very small magnitude of the changes observed in our study (approximately 1 mm across the full range of gaze excursion), detecting systematic differences related to smaller variations in gaze angle may be challenging without the use of magnification techniques or automated image analysis software. Future studies could specifically aim to quantify the angle of ocular deviation and investigate whether different degrees of gaze excursion produce measurable differences in optic nerve sheath diameter (ONSD).

Another limitation of our study is that measurements were not repeated by different operators; therefore, intra- and inter-rater reliability were not assessed. However, each participant was assessed by the same operator at both time points. In this paired design, the intra-observer standard error of measurement (SEM) can be considered constant, minimizing inter-observer variability and systematic bias. As a result, the observed differences (Δ values) are more likely to reflect true physiological changes rather than measurement variability. Inter-rater reliability was not assessed but limited by the fact that the three operators are part of the same working group and used a consistent validated method to measure ONSD.

In addition, this was a single-center study, which may limit the generalizability of the findings. Second, the study population consisted exclusively of healthy volunteers, and generalizability of results to critically ill patients or individuals with intracranial pathology must be made with caution. Further investigations in neurocritical care populations are warranted to confirm these findings and to explore their clinical implications.

Conclusions

In this prospective interventional study, gaze deviation was associated with a consistent and clinically relevant reduction in ONSD measurements of approximately 0.9–0.95 mm using B-mode US. Short-term changes in bed inclination between 45° and 0° did not significantly affect ONSD values. This suggests that gaze deviation does not simply introduce random measurement error, but rather induces a predictable "stretching" effect. The dynamic change in ONSD may represent a potential functional test of optic nerve sheath compliance, conceptually analogous to the 30-degree test described in ophthalmologic practice. Future studies should investigate whether this "stretching test" could provide additional information about optic nerve compliance, differentiating patients with altered sheath elasticity (i.e. false negatives).

Competing interests: The authors declare no conflict of interests.

Ethics approval and consent to participate: This work was approved by the "Bioethical committee" of the University of Pisa with the n. 56/2025 the 28th of July 2025. All the volunteers gave their consent to participate to the study. This study has been conducted in accordance with the Declaration of Helsinki (https://www.wma.net/wp-content/uploads/2016/11/DoH-Oct2008.pdf).

Declaration on the use of AI: Large language models were used in order to draft some parts of the text or revise/improve the paragraphs. The content was fully suggested to the model by the authors, and the authors reviewed and approved the parts edited with AI.

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Authors' contributions: GCu: Conceptualization, Data curation, Formal analysis, Methodology, Visualization, Writing – original draft, Validation, Writing – review & editing. GM, GCo: Data curation, Validation, Writing – review & editing. FDM, FF, Supervision, Validation, Writing – review & editing. FC: Methodology, Supervision, Validation, Writing – review & editing. All the authors approved the final version of the manuscript.

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