Author’s response to reviews

Title: Reproducibility and accuracy of optic nerve sheath diameter assessment using ultrasound compared to magnetic resonance imaging

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Author’s response to reviews: see over
Sirs,

Thank you for the positive review of our manuscript, ID MS: 1003167386941617, entitled “Reproducibility and accuracy of optic nerve sheath diameter assessment using ultrasound compared to magnetic resonance imaging”. We have changed the manuscript according to the reviewers’ comments which, as we believe, very much ameliorated the paper.

Let me address all of the reviewers’ comments point-by-point:

Reviewer 1

I have however some major comments that need to be addressed.

1. The statistical method for inter and intra-observer variability study is probably not sufficient. A method using the Kappa coefficient would be of interest, and give additional information.

We thank reviewer 1 for suggesting this analysis, as it improves the interpretation of our data. We added this analysis in the result section.

2. The limits of agreements can be regarded as being large for ONSD when exceeding 0.3-0.4 mm. This is the case in the majority of the comparisons. This should be discussed more profoundly in the discussion section as a limit of the method.

The limits of agreement for intra- and interobserver variability at a depth of 3 mm comply with the range you suggest. With regard to the scan-rescan variability the wider limits of agreement may reflect intra-individual fluctuations of the ONSD over the time. Since we found good intra-rater variability this observation is rather physiological than a methodical inaccuracy. We added this point in the discussion section.

3. The main limit of this study is that only healthy volunteers has been studied. These subjects are very unlikely to have abnormal ICP. The results of this study can therefore only be applied to subjects with normal ICP. Having patients with intracranial hypertension or hypotension would be of major interest to study the variability of the measurement in such conditions. This should be discussed.

Thank you for this important remark. We added this issue in the discussion section.

“Our study is limited by the fact that intracranial pressure was presumed to be normal by taking history. Otherwise intracranial masses were ruled out by MRI. Furthermore, the results of this investigation can only be applied on healthy adults. In patients with intracranial hyper- or hypotension sonographic ONSD depiction may be altered leading to deferring test variabilities. This should be the focus of further investigations.”

4. The figure 1, panel A and B are not clear to the reviewer. For the panel A, the external border of the hypochoogenic area can be regarded as an artifact (acoustic shadow) as already described by Copetti (Intensive Care Med). A better example of ONSD measurement using ocular sonography could probably be presented in the Panel A.

We replaced Panel A and think the updated figure shows the borders of the optic nerve sheath more clearly now.

5. The Panel B shows ONSD measurement in several axes. However in the method section, only the coronal section is mentioned to be used for ONSD measurement using MRI. Please precise.

This information has been provided already in the method section:

“Two different variants of a T2-weighted turbo spin echo (TSE) sequence were employed [10, 14, 15]: (1) A fast T2-weighted overview TSE which provides good soft tissue contrast and morphological data for planning: TR = 4000 ms, TE = 130 ms, echo train length = 25, bandwidth = 120 Hz/pixel, ‘weak’ chemical fat saturation. The sequence was applied twice
with nine contiguous slices in sagittal (FOV = 21 x 21 cm², Matrix = 448 x 448) and transversal (FOV = 21 x 18 cm², Matrix = 448 x 392) orientation leading to a nominal spatial resolution of 0.47 x 0.47 mm² with slice thickness = 3 mm. The acquisition time was 1:06 min (transversal) and 1:10 min (sagittal), respectively (Fig. 1)."

6. If I understand well the following sentences : « For calculation of inter-observer variability, observer 2 quantified ONSD in two volunteers at the first visit and in 8 volunteers at the second visit. » the inter-observer variability has been evaluated in only 10 measurement for ultrasound ONSD, correct ? This is probably a limit of the study

The five remaining individuals were examined by both investigators at a third visit as described in the method section:
“For calculation of inter-observer variability, observer 2 quantified ONSD in two volunteers at the first visit and in 8 volunteers at the second visit. Five individuals were measured on a third visit by both sonographers."

7. The fact that ONSD measurement was performed using ultrasound only in one plane (transversal) should be discussed, as previous studies have used several axis to determine ONSD.

In our study we used the sonographic approach published by K. Helmke and H.C. Hansen (Pediatr Radiology, 1996). They used only the axial plane and recommended repeated measurements to control the variability of the scanning procedure. Since the optic nerve sheath can be seen as fluid filled tube one should not expect differing results by adding another plane to the assessment. Probably, our examination protocol may reduce the duration of sonographic insonation of the eye ball. Therefore, we investigated the ONSD in an axial plane.
Since both methods are commonly used in ONSD literature without any evidence that one procedure is beneficial, we take the liberty not to discuss this issue in our paper.

Reviewer 2

1. interesting results between correlation echo diameter of optique nerve and MRI mesures and clinical application.

2. But little sample (only 15 healthy volunteers)

We discussed this limitation in the manuscript:
“Additionally, the results may be limited by the small number of study participants. Nevertheless, we found similar test variabilities than Steinborn et al. [11] documented in 65 children.

3. In my experience the measurement depth is 5 mm behind the papilla and not 3 mm (anatomical reason)

K. Helmke and H.C. Hansen (Pediatr Radiology, 1996) found in there experimental study on the ONSD that maximal diameter fluctuations could be expected 3 mm behind the papilla and thus recommended this depth for ONSD measurements.

Kind regards
Jochen Bäuerle