## **Transmantle pressure**

The pressure gradient between the ventricles and the subarachnoid space (transmantle pressure) is crucial for understanding cerebrospinal fluid circulation and certain neurodegenerative disease pathogenesis. This pressure can be approximated by the pressure difference across theaqueduct ( $\Delta P$ ).

## Prospective observational studies with a technical development focus

No dedicated platform exists for quantifying  $\Delta P$ , and no research has been conducted on the impact of breathing on  $\Delta P$ . This study aims to develop a post-processing platform that balances accuracy and ease of use to quantify aqueduct resistance and, in combination with real-time phase contrast MRI, quantify  $\Delta P$  driven by free breathing and cardiac activities.

Thirty-four healthy participants underwent 3D balanced fast field echo (BFFE) sequence and real-time phase contrast (RT-PC) imaging on a 3T scanner. We used the developed post-processing platform to analyze the BFFE images to quantify the aqueduct morphological parameters such as resistance. RT-PC data were then processed to quantify peak flow rates driven by cardiac and free breathing activity (Qc and Qb) in both directions. By multiplying this Q by resistance,  $\Delta P$  driven by cardiac and breathing activity was obtained ( $\Delta Pc$  and  $\Delta Pb$ ). The relationships between aqueduct resistance and flow rates and  $\Delta P$  driven by cardiac and breathing activity were analyzed, including a sex difference analysis.

The aqueduct resistance was 78 ± 51 mPa·s/mm<sup>3</sup>. The peak-to-peak cardiac-driven  $\Delta P$  (Sum of  $\Delta Pc+$  and  $\Delta Pc-$ ) was 24.2 ± 11.4 Pa, i.e., 0.18 ± 0.09 mmHg. The peak-to-peak breath-driven  $\Delta P$  was 19 ± 14.4 Pa, i.e., 0.14 ± 0.11 mmHg. Males had a longer aqueduct than females (17.9 ± 3.1 mm vs. 15 ± 2.5 mm, p < 0.01) and a larger average diameter (2.0 ± 0.2 mm vs. 1.8 ± 0.3 mm, p = 0.024), but there was no gender difference in resistance values (p = 0.25). Aqueduct resistance was negatively correlated with stroke volume and the peak cardiac-driven flow (p < 0.05); however, there was no correlation between aqueduct resistance and breath-driven peak flow rate.

The highly automated post-processing software developed in this study effectively balances ease of use and accuracy for quantifying aqueduct resistance, providing technical support for future research on cerebral circulation physiology and exploring new clinical diagnostic methods. By integrating real-time phase contrast MRI, this study is the first to quantify the aqueduct pressure difference under the influence of free breathing. This provides an important physiological reference for further studies on the impact of breathing on transmantle pressure and cerebral circulation mechanisms <sup>1)</sup>

While the findings are promising, they are preliminary, and further studies with larger sample sizes, disease populations, and longer follow-up periods are needed to validate these results and explore their clinical implications. The lack of a detailed description of the software's algorithms and technical specifications also limits the broader applicability of the approach, and future papers should provide more transparency in this area to ensure reproducibility and robustness. Nevertheless, this research opens the door to a better understanding CSF circulation and its potential role in neurodegenerative diseases.

## 1)

Liu P, Owashi K, Monnier H, Metanbou S, Capel C, Balédent O. Transmantle pressure under the influence of free breathing: non-invasive quantification of the aqueduct pressure gradient in healthy adults. Fluids Barriers CNS. 2025 Jan 3;22(1):1. doi: 10.1186/s12987-024-00612-x. PMID: 39754238.

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