In silico identification of cerebral vasospasm biomarkers

INSIGNEO
Institute for *in silico* Medicine

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Background

Cerebral vasospasm (CVS) is the progressive narrowing of intracranial arteries following brain hæmorrhage [1]. Currently, the diagnosis process relies on transcranial Doppler (TCD) monitoring of mean blood velocity. This velocity “biomarker” is capable of detecting CVS in the case of TCD measurements directly performed on the narrowing vessel. In the case of peripheral narrowing, the velocity biomarker prediction ability is lost and the CVS is not detected until the condition becomes severe.

Methods

A mechanistic 1D model of the cerebral circulation was developed to study the influence of vessel narrowing on pulse waveforms (Figure 1). A sensitivity analysis empowered by Gaussian process (GP) emulation [2] was performed to identify those waveform features that are most sensitive to vessel narrowing indicative of CVS. The use of GP emulators reduced the computational cost of the analysis by 95% compared to a full Monte Carlo analysis.

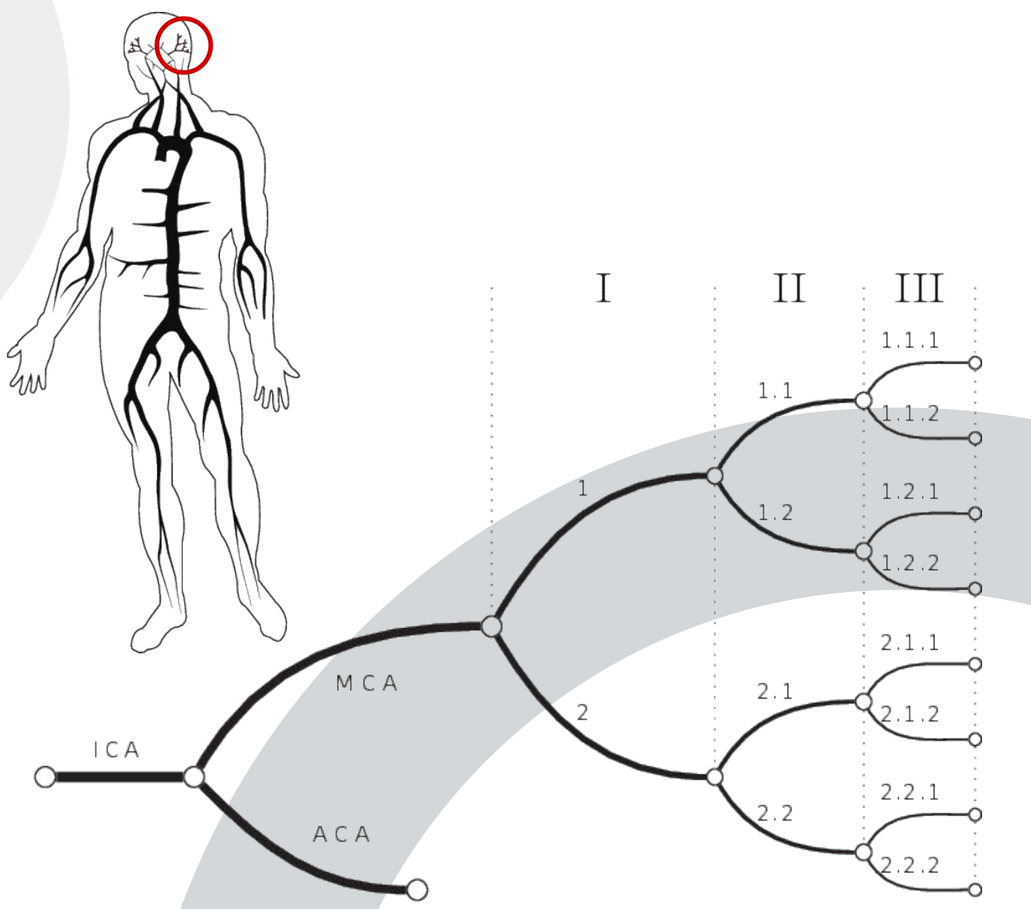

Figure 1. Diagram of the whole cardiovascular system and (red circle) vascular network used in the study.

Results

A CVS occurring at the measurement location caused an increase (more than 450%) of the velocity biomarker. However, when the CVS occurred more peripherally, the velocity biomarker was only marginally affected by the vessel lumen reduction (Figure 2). The maximum gradient of the pressure waveform was sensitive to CVS in both proximal and distal arteries. Increase (up to 150%) of this biomarker occurred for all the CVS configurations tested.

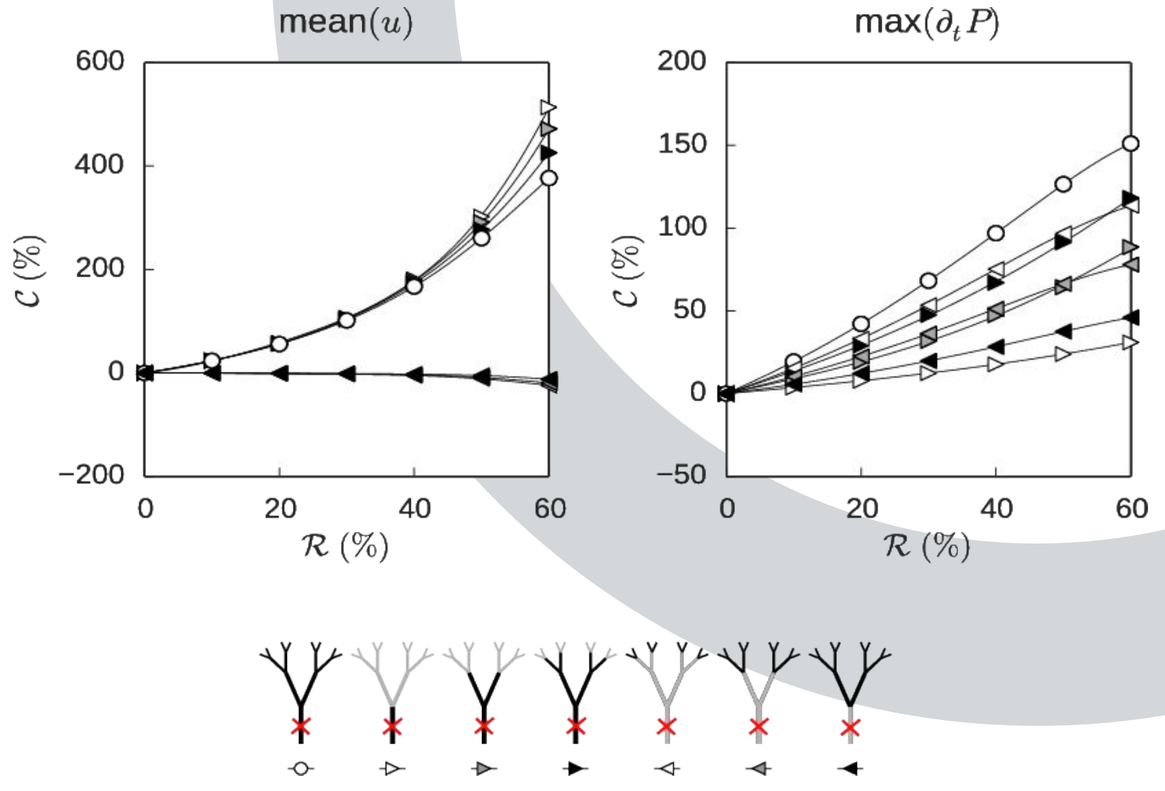

Figure 2. (left) Velocity and (right) pressure biomarkers change with respect to baseline value for different CVS configurations (bottom).

Conclusions

The proposed mechanistic model was used to describe pressure waveforms in cerebral circulation affected by cerebral vasospasm. This model was used to identify more sensitive cerebral vasospasm biomarker than those currently used in clinical practice. A further improvement of the numerical model would consist in the development of a larger vascular network, including the whole circle of Willis, both sides of the cerebral circulation, and a representation of the auto-regulation mechanism. In addition, the newly found biomarker will be tested on patient specific measurements.

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[2] A. Melis, R. H. Clayton, and A. Marzo. Bayesian sensitivity analysis of a 1D vascular model with gaussian process emulators. *International Journal for Numerical Methods in Biomedical Engineering,* 2017. cnm.2882.

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