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Supplemental material

Fully automated, real-time, calibration-free, continuous noninvasive estimation of intracranial pressure in children
Fanelli et al.
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Mathematical Formulation of Estimation Problem

As described in Kashif et al.\textsuperscript{1}, the circuit model representation shown in Figure 1a of the relevant cerebrovascular physiology is mathematically described by the first-order differential equation

\[ CBFV(t) = \frac{ABP(t) - ICP}{R} + C \frac{d}{dt} [ABP(t) - ICP] \]  \hspace{1cm} (1)

where \( CBFV(t) \) is the cerebral blood flow velocity waveform at the middle cerebral artery (MCA); \( ABP(t) \) is the corresponding arterial blood pressure waveform; \( C \) is the lumped cerebrovascular and brain tissue compliance; \( R \) is the resistance to blood flow through the MCA territory, and \( ICP \) is the intracranial pressure. Equation (1) imposes a mathematical constraint between the model parameters \( R, C, \) and \( ICP \) on the one hand and the measurable waveforms \( CBFV(t) \) and \( ABP(t) \) on the other hand. To estimate \( nICP \), we record the MCA CBFV and the radial ABP waveforms and solve Equation (1) to obtain estimates of \( R, C, \) and \( ICP \). Rather than solving Equation (1) for each cardiac cycle, we assume that \( R, C, \) and \( ICP \) are constant for the duration of 60 beats (estimation window) and estimate one value for \( R, C, \) and \( ICP \) for each 60-beat estimation window.

To arrive at an \( nICP \) estimate, we decompose the estimation problem by first estimating \( C \) during the early ejection period when the rate of change in ABP is largest and flow into the MCA territory is predominantly stored in the expansion of the elastic arteries. Assuming the flow through the resistance is negligible during the ejection period, Equation (1) can be approximated as

\[ [ABP(t_1) - ABP(t_2)] \cdot C \approx \int_{t_1}^{t_2} CBFV(t') dt' \]  \hspace{1cm} (2)

where \( t_1 \) and \( t_2 \) are the onset and end of the sharp systolic upslope in the \( ABP \) wavelet. Equation (2) can be formulated for each beat in the estimation window, and the resultant set of equations can then be solved in a least-square manner to arrive at the compliance estimate \( \hat{C} \). With \( \hat{C} \) so estimated, the flow \( CBFV_R(t) \) through the resistive element can be approximated as

\[ CBFV_R(t) = CBFV(t) - \frac{\hat{C}}{dt} APB(t) \]  \hspace{1cm} (3)
Making use of the constitutive relation for flow through the resistive element, ICP was expressed as

\[ ICP = ABP(t) - R \cdot CBFV_R(t) \]  \hspace{1cm} (4)

and under the assumption of constant ICP over a beat and estimation window, the resistance \( R \) can be estimated by evaluating Equation (4) at two (or more) time points during a cardiac cycle and eliminating the constant \( ICP \):

\[ [CBFV_R(t_2) - CBFV_R(t_1)] \cdot \hat{R} = ABP(t_2) - ABP(t_1) \]  \hspace{1cm} (5)

The final estimate of \( ICP \) is then determined according to

\[ \overline{ICP} = \overline{ABP} - \hat{R} \cdot \overline{CBFV_R} \]  \hspace{1cm} (6)

where the overbars indicate beat-averaged values of \( ABP \) and \( CBFV_R \). Equations (5) and (6) are likewise evaluated for each beat in the 60-beat estimation window and solved in a least-square manner to arrive at one estimate \( \hat{R} \) and \( \overline{ICP} \) for each estimation window.

**Fine Signal Quality Assessment**

We evaluated the beat-by-beat ABP waveform quality by first computing, for each beat, the mean absolute sample-by-sample difference \( d_i = \text{mean}_j \in [n(i), n(i+1)-1] \| ABP(j) - ABP(j+1) \| \), where \( n(i) \) denotes the onset sample of the \( i \)-th beat, and the interval \([n(i), n(i+1)-1] \) spans all samples of the \( i \)-th beat. We computed a standardized score \( \hat{d}_i = \frac{\|d_i - \overline{d}_i\|}{\overline{d}_i} \) by subtracting and normalizing \( d_i \) by a running average of the past 20 mean absolute deviations \( \overline{d}_i = \frac{1}{20} (d_{i-1} + d_{i-2} + \cdots + d_{i-20}) \). This beat-by-beat, normalized, absolute deviation metric \( \hat{d}_i \) assumes large values in regions in which the waveform morphology is corrupted by noise and artifact. We chose an empirical threshold of 0.3 to identify beats of questionable signal quality and to binarize the beat-by-beat ABP signal quality metric (Supplemental Figure S1).

The beat-by-beat fine CBFV signal quality was determined by first computing the spectral correlation between the ABP and CBFV signals over a sliding window of 8 s in duration and then quantifying the deviation
of each CBFV wavelet from an adaptively updated wavelet template.\textsuperscript{2} Since the lower frequency components of the ABP and CBFV waveforms are dominated by the cardiac beating frequency and its harmonics, the power spectra of the two signals normally have dominant peaks at the same frequencies. During periods of significant noise and artifact in one of the signals, the strength of this spectral correlation declines. In a first step, regions of the CBFV signal were identified for rejection if – in the frequency range from 0.5 to 5.0 Hz – the correlation coefficient between the power spectral densities of the CBFV and ABP was below the empirical threshold of 0.5. Subsequently, a CBFV wavelet template was obtained on potentially acceptable beats by computing the median CBFV wavelet across all beats that had not been rejected. This template was then used to assess the quality of the CBFV waveform on a beat-by-beat basis and to identify beats that had a large normalized mean-squared error when referenced to the template.
Supplemental Figure S1 Fine Signal-Quality Assessment (SQA). Examples of applying our fine SQA filter to (a) the ABP and (b) the CBFV waveform. Regions of poor waveform morphology are flagged (marked here in blue). (c) Regions of the input data are flagged and excluded from further analysis if either the ABP or the CBFV fine SQA flags indicate poor waveform quality.
**Supplemental Figure S2 Beat-onset alignment.** Sample cross-correlation between the ABP and CBFV waveforms. The time lag associated with the peak of the cross-correlation identifies the starting delay between the waveforms. We correct for this delay by subtracting it from the CBFV time stamps to achieve alignment of corresponding ABP and CBFV wavelets.