A Method for Estimating Zero-Flow Pressure and Intracranial Pressure

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Abstract

Background—It has been hypothesized that critical closing pressure of cerebral circulation, or zero-flow pressure (ZFP), can estimate intracranial pressure (ICP). One ZFP estimation method employs extrapolation of arterial blood pressure versus blood-flow velocity. The aim of this study is to improve ICP predictions.

Methods—Two revisions are considered: 1) The linear model employed for extrapolation is extended to a nonlinear equation, and 2) the parameters of the model are estimated by an alternative criterion (not least-squares). The method is applied to data on transcranial Doppler measurements of blood-flow velocity, arterial blood pressure, and ICP, from 104 patients suffering from closed traumatic brain injury, sampled across the United States and England.

Results—The revisions lead to qualitative (e.g., precluding negative ICP) and quantitative improvements in ICP prediction. In going from the original to the revised method, the ±2 standard deviation of error is reduced from 33 to 24 mm Hg; the root-mean-squared error (RMSE) is reduced from 11 to 8.2 mm Hg. The distribution of RMSE is tighter as well; for the revised

method the 25th and 75th percentiles are 4.1 and 13.7 mm Hg, respectively, as compared to 5.1 and 18.8 mm Hg for the original method.

Conclusions—Proposed alterations to a procedure for estimating ZFP lead to more accurate and more precise estimates of ICP, thereby offering improved means of estimating it noninvasively. The quality of the estimates is inadequate for many applications, but further work is proposed which may lead to clinically useful results.

Keywords

blood flow; brain; head injury; intracranial pressure; noninvasive

Monitoring and manipulation of intracranial pressure (ICP) aids patient management and may improve clinical outcome after trauma as well as other conditions.[1-12] Increased ICP impairs neural function by reducing blood flow (causing ischemia) as well as by direct mechanical compression or herniation of brain tissue. Measurements of intracranial pressure require placement of a pressure sensor within the cranium. The invasiveness of this procedure has motivated a variety of non-invasive approaches. One class of approaches uses transcranial Doppler (TCD) and arterial blood pressure (ABP) measurements.[13-15] Another class is based on imaging and analysis of various compartments of the eye, in particular, the ophthalmic artery or the optic nerve sheath diameter.[16-22] In the present study, blood flow velocity (FV) in the middle cerebral artery, derived from TCD, and ABP, are used to develop an alternative approach to the estimation of ICP.

Burton[23] offered analysis showing that arterial critical closing pressure (CCP) may approximate both ICP and a force resulting from the tension of arterial walls' smooth muscles. Aaslid[24] and colleagues[25] examined several methods for estimating CCP, comparing the results with a "gold standard," measured during induced ventricular fibrillation. Michel et al.[26] and Kottenberg-Assenmacher et al.[27] have employed physics-based models to address CCP measurements, and how it may aid in estimating ICP noninvasively. Another study, more focused on haemodynamics in pregnancy[28], has examined the connection between CCP and ICP. The role played by the cerebrovascular wall tension in the CCP-ICP connection has been examined as well.[29]

A simple method for estimating CCP involves fitting a least-squares line through ABP versus FV. Specifically, one first considers the scatterplot of ABP versus FV when the two have been aligned to have comparable phase (i.e., maximum correlation). If the scatterplot displays a linear relationship between ABP and FV, the y-intercept of a line fitting the scatterplot defines an estimate of CCP. This method is simple because the alternatives generally consider smoothing or filtering based on Fourier analysis of the various time series; e.g., Aaslid et al.[25] Preprocessing of this type adds complexity to the analysis, and for this reason, the CCP estimation method considered here is a variation of the simple, extrapolation method. The main goal of the study here is not to improve on the estimation of CCP itself, but rather to develop alternative models of CCP estimation which better correlate with ICP.

Czosnyka et al.[30] examined several methods for estimating CCP, and also studied the correlation between CCP and ICP. Using a data set involving 98 patients, they report a correlation coefficient of 0.41 between ICP and CCP. They also report that ICP can be predicted from CCP to within ±27 mm Hg (95% confidence level). Thees et al.[31] found a correlation of 0.91, based on 70 patients (no predictive error bar is reported). On a data set involving 20 patients, Buhre and colleagues[32] used a method developed by Weyland and collaborators[33], and reported a correlation coefficient of 0.93, and a 2 standard deviation (i.e., approximately 95.5% confidence interval) of ±15.2 mm Hg. In the work done by these

authors, CCP is often referred to as the zero-flow pressure (ZFP), and so we define the "ZFP hypothesis" as the hypothesis that ICP can be estimated from some estimate of ZFP (or CCP).

In the current paper, two revisions to the extrapolation method are examined, both aimed at improving the estimation of ICP. The revisions involve 1) relaxing the linearity of the equation/model used for extrapolation, and 2) employing an alternative criterion (not least squares) for estimating the parameters of the model. The first revision ensures that the ICP predictions are physical (i.e., non-negative), and the second revision eliminates the need to align FV and ABP – a necessary step in the original extrapolation method. In addition to these qualitative improvements, the revised method also leads to more accurate and precise estimates of ICP.

Material and Methods

Patients

Patient data for this pre-clinical study were collected from a variety of hospitals in the USA, following a study at the University of Washington led by Dr. Mourad, as well as from Addenbrooke's Hospital, Cambridge, England, led by Dr. Czosnyka.

The core contributing hospitals within the United States were Harborview Medical Center (Seattle, Washington), Columbia University Medical College (New York City, New York) and the University of Texas Medical School at Houston, Texas. Data from 59 patients (49 males, 10 females) with mean age 34 years (range: 13-81) and mean Glasgow Coma Score 5 (range: 3-11). Studies there met the following inclusion criteria: 1) All patients experienced closed head injury; 2) No patients received neurosurgical intervention other than placement of an invasive ICP monitor; 3) All patients had an ABP catheter in place at the time of study; 4) All patients could tolerate a TCD exam; 5) All patients were eight years old or older; and 6) Informed consent was obtained from all patients or their families. These criteria were also followed at Addenbrooke's Hospital, except that patients regardless of age could consent into the study and, where in addition, all patients were intubated. Finally, for both centers, all patients were monitored and treated following the specifications of the Brain Trauma Foundation.[9,10]

Fig. 1 shows the distribution of 59 patients' mean invasive ICP (in black) collected by the team at the University of Washington. Additionally, 45 patients from Cambridge England were chosen from over 300 anonymous cases collected by that institution, in order to "fill in" the gaps in the ICP distribution of data collected at the University of Washington. These gaps are on the high-ICP side of the distribution. However, in order to avoid a situation where all high-ICP patients are from Cambridge, low-ICP patients from Cambridge were also included in the analysis. The distribution of ICP for the Cambridge patients is shown in red in Fig. 1. Schmidt et al.[13] described the circumstances under which this data were collected, including the fact that TCD recording was a part of routine daily examination of cerebral haemodynamics, and anonymous use of these recordings for further retrospective methodological studies was approved by local Neurocitical Care Users Committee.

Data

For each patient, ABP, ICP, and maximum blood-flow velocity within the middle cerebral artery (or Flow Velocity – FV) Doppler time series were acquired via clinically approved TCD units and processed via custom software so as to provide synchronized ABP, ICP, and FV data. Data acquisition lengths varied from 5 to 30 minutes, obtained anywhere from 0-11 days after placement of an ICP sensor. ICP was monitored using a ventricular catheter (Integra Lifesciences Corporation or Camino Laboratories) where cerebral spinal fluid

drains were closed and supervised during data capture. ICP was also monitored with a Camino parenchymal catheter (Integra Lifesciences Corporation) or Codman parenchymal ICP microsensor (Codman Neuroscience). Blood pressure was acquired invasively from an arterial line placed in the radial, femoral, brachial or ulnar artery. All patients from Cambridge were sedated, paralysed, and ventilated to maintain adequate oxygenation and mild hypocapnia. All patients from the University of Washington cohort experienced the same treatment, except for one patient who was no longer under ventilation when this study was performed.

All retrospective data processing and analysis was conducted at the Applied Physics Laboratory (APL), University of Washington. Data collected via APL's hospital cohort were digitized at 125 Hz while data collected in Cambridge were digitized at 40 Hz. To place the data sets on the same footing, the APL data sets were down-sampled to 40 Hz. A fixed duration (5 minutes) was selected from each of the 104 patients for statistical analysis.

Data Processing and Statistical Analysis

In this study, the methodology of Weyland et al.[33] and Buhre et al.[32] (hence forth, the *WB method)* is revised. The revised method involves two specific alterations: 1) The linear model/equation in the WB method is replaced with a nonlinear equation, and 2) the least-squares criterion for estimating the parameters of the model is replaced with an alternative criterion which does not have a common name; we shall refer to it as the *SD criterion*. These revisions are further described in the Appendix. The main purpose of the first revision is to prevent negative ICP predictions that arise in the WB method. The primary benefit of the second revision is to preclude the preprocessing step of aligning the FV and ABP time series. This alignment is necessary for the least-squares criterion method, and requires the specification of quantities which add to its complexity. For example, given that the alignment procedure is an optimization problem, one must specify the quantity being optimized; the correlation or the covariance between the two series are common choices, but can lead to different results. The duration of the two time series over which the alignment is performed is another quantity which can affect the results. In addition to these benefits, the revised methodology (involving both revisions) leads to higher quality ICP predictions as compared to those of the WB method. The goodness of the ICP estimates is assessed in terms of the bias, standard deviation, and root-mean-square of the errors (RMSE).

In order to demonstrate the ingredients of the WB method, consider the data from a single patient. The top panel in Fig. 2 shows the time series for FV (solid curve) and ABP (dashed line) for one patient, for a duration of 2.5 seconds (i.e., 100 data points displayed at 40 Hz). The middle panel displays the scatterplot of ABP versus FV (circles), after they have been aligned. The two lines are based on the least-squares criterion (dotted), and the SD criterion (solid); their equations are $y = 14.1 + 0.70x$, and $y = 13.0 + 0.73x$, respectively. The ZFP hypothesis asserts that the y-intercept of the least-squares line approximates mean ICP. The mean of the observed ICP for this patient is 13.5 mm Hg, marked with an arrow along the y-axis. Evidently, the y-intercept of the least-squares line agrees with this patient's mean ICP, supporting the ZFP hypothesis for this patient. In this case, the lines according to the two criteria are nearly identical, and so, they lead to approximately equal estimates of mean ICP.

As mentioned above, a utility of the SD criterion is that it does not require an alignment of the ABP and FV time series. This is demonstrated in the bottom panel in Fig. 2, where the scatterplot of ABP versus FV is shown without any alignment. Also shown are the lines corresponding to the least-squares and the SD criteria; their equations are $y = 29.7 + 0.50x$ and $y = 13.0 + 0.73x$, respectively. Whereas the y-intercept of the former deviates considerably from the mean ICP of 13.5 mm Hg, that of the latter does not. Indeed, the SD line for the non-aligned data is identical to that of the aligned data. This feature is not a

coincidence, and is explained in the Appendix. The SD line is unaffected by any phase difference between the ABP and FV time series. Using the SD line, therefore, simplifies the WB method by eliminating the alignment procedure.

Our paper compares the WB method to the revised method developed here. Each method is applied to a segment of the ABP and FV time series 7.5 seconds (i.e., 300 data points) in duration. This duration was selected because it is sufficiently long to cover several respiratory cycles (2 to 4, depending on the patient), but is also sufficiently short to be unaffected by slow waves in ICP. Although the results are relatively insensitive to the length of the time series, very short time segments do not produce sufficient cases for an adequate estimation of the fit. On the other hand, recall that the ZFP as estimated from the ABP and FV observed over a time segment is expected to approximate the **mean** of ICP over that same time segment. As such, results obtained from very long time segments are likely to be confounded by slow changes in ICP.

In order to utilize the information in the time series more fully (i.e., beyond only one time segment 7.5 seconds in duration), 200 different segments of the time series are sampled randomly. Each of these 200 trials yields an estimate of mean ICP. This sampling of the time series is important because any given time segment may, or may not, confirm the ZFP hypothesis. Only the aggregate of all the 200 estimates legitimately assesses the validity of the hypothesis and its statistical significance.

All analysis is performed using a statistical analysis software called R.[34]

Results

Fig. 3 shows the scatterplot of the observed ICP versus ZFP (i.e., the estimated ICP) for all 104 patients, for the WB method (top) and the revised method (bottom). Each cluster/color in the figures corresponds to a patient, and so each cluster contains 200 points associated with the aforementioned 200 trials. The vertical and horizontal lines denote the grand mean of observed ICP across all patients. The diagonal line has slope of 1 and a 0 y-intercept. If the estimates were perfect, all the points in scatterplot would reside on this diagonal line. On the other hand, if the ZFP hypothesis did not hold at all, the points would be randomly distributed (at best, about the vertical line). Without performing any quantitative analysis, it is quite evident from these scatterplots that the ZFP hypothesis does hold in the WB method (top panel) because that procedure produces negative (unphysical) ZFP values. By contrast, the revised method (bottom panel) does not. The revised method also produce a "tighter" scatterplot, suggesting higher-quality predictions, further discussed below.

Instead of a scatterplot of ICP vs. ZFP, many studies consider the Bland-Altman plot, i.e., the plot of the errors (ICP - ZFP) versus the average of ICP and ZFP. The top panel in Fig. 4 shows such a plot for the WB method . The three dashed lines show the average of the errors (i.e., bias) ± 2 standard deviations; in this case, they are at -4 ± 33 mm Hg. The fact that the average of the errors is below zero, indicates that the estimates are (positively) biased, i.e., ZFP is generally larger than the observed ICP. Furthermore, the average of ICP and ZFP takes on negative values as a consequence of ZFP itself taking negative values. In order to eliminate these negative values, it may be tempting to simply shift all ZFP by some positive amount; but this further increases the bias. Similarly, shifting ZFP by some negative amount decreases the bias, but only at the cost of increasing the incidents of negative ZFP.

The results from the revised method are shown in the bottom panel of Fig. 4. The average ± 2 standard deviation of the errors are now at 0 ± 24 mm Hg. The ± 2 standard deviation of the errors is reduced, from 33 to 24 mm Hg. In short, the revised method leads to estimates that

are non-negative (i.e., physical) and more precise than for the WB method. The average error in the revised method is nearly zero, as a consequence of setting γ in Eq. (4) to 17.5 mm Hg . The reason for this choice is discussed in the next section.

Table 1 shows quantiles of the distribution of the errors for the two methods. It is evident that the revised method is superior to the WB method in terms of both the median (50th percentile) and the spread of the distribution of errors. The distribution of RMSE values is also shown. The median RMSE for the two methods are 11.1 and 8.2 mm Hg respectively; the revised method has the narrower of the two distributions, thereby leading to more precise estimates of ICP.

A direct comparison of the WB method and the revised method is presented in the form of a Bland-Altman plot, showing the difference between the two estimates of ZFP as a function of their average (Fig. 5). Evidently, the two estimates can differ significantly, depending on the patient. For some patients, the difference between the two estimates is small (±5 mm Hg) and centered about zero. For other patients, the two estimates can differ as much as ±20 mm Hg. For some patients, the revised estimates of ZFP are consistently higher than the WB estimates, while for other patients that comparison is reversed. Moreover, the nonlinear pattern (across patients) shown in Fig. 5 implies that the two estimates are nonlinearly related; this nonlinearity is a direct consequence of the nonlinearity of Eq. (4). In short, the relationship between the two estimates is complex, and varies between patients.

Discussion

The "ZFP hypothesis" asserts that the ZFP approximates ICP. Although many groups have contributed to testing this hypothesis, one of the simplest methods estimates ZFP by extrapolation using a least-squares, straight-line fit of ABP versus FV, after the two time series have been aligned. Here several revisions to that method (called the "WB method") are proposed: First, instead of a straight line fit, a nonlinear equation is used. Second, instead of the least-squares criterion for estimating the parameters of the fit, the SD criterion is employed. These revisions preclude negative ICP predictions, and eliminate the least-squares requirement of maximally correlating the FV and ABP data. Moreover, it is shown that these revisions improve the estimates of ICP in terms of their bias (accuracy) and standard deviation (precision), as well as their RMSE. The mean ± 2 standard deviation of the errors for the revised model is about 0 ± 24 mm Hg, in contrast with -4 ± 33 mm Hg as obtained by applying the WB method to our data set. The median RMSE for the revised model is 8.2 mm Hg, compared with 11.1 mm Hg for the WB method.

Buhre et al.[32] report a value of 15.2 mm Hg for the ± 2 standard deviation of the errors when they apply the WB method to their data set, nearly half of the value found here (33 mm Hg) when the WB method is applied to the current data set. A few explanations for the discrepancy are as follows: One difference between the two studies is in the mean ICP across all patients; Buhre et al. report a mean ICP of 34.7 mm Hg for their data set, as opposed to 20 mm Hg for the current data set. So, their patients have generally higher ICP than those analyzed here. Therefore, it may be that the ZFP hypothesis works better at higher ICP values. Another difference is in the size of the sample; the data set analyzed by Buhre et al. consists of 20 patients, much smaller than the 104 patients in the data set analyzed here. Furthermore, they report that the median number of measurements taken from each patient is about 7, resulting in a total of 180 measurements. The number of measurements taken from each patient in the current data set is 200, resulting in a total of 20,800 measurements. The larger number of patients, and the larger number of measurements per patient, together are likely to lead to the larger errors found on the current data set.

It is important to explain why the mean of the errors from the revised method is nearly 0 mm Hg. The revised method is based on a model (Eq. 4), which in addition to the intercept and slope parameters (α, β), also has another parameter (γ) which effectively controls the mean of the errors (i.e., the bias of the ICP predictions). Whereas the former parameters vary between patients, the latter is a constant for all patients. Given that it controls bias, it can be set to a value which in turn renders the predictions bias-free. For the current data set, that value is 17.5 mm Hg. Assuming the 104 patients in the data set are a random sample from the population of interest, then $\gamma = 17.5$ mm Hg should give bias-free predictions for all "future" patients not included in the current data. To test that expectation, a resampling method[35] was employed for the purpose of estimating the sampling variability of bias, when $\gamma = 17.5$ mm Hg. (Only bias was considered because it is the facet of performance most affected by γ.) Specifically, the proposed model (with $\gamma = 17.5$ mm Hg) was applied to half of the 104 patients, randomly selected, and the bias of the predictions was recorded. This re-sampling procedure was repeated 10 times, each time taking a different random sample of 52 patients and computing the bias of the predictions. The mean ±2 standard deviation across the 10 trials was found to be 0.9 ±2.0 mm Hg, well within the bounds of observational and instrumental error. In other words, the bias-free nature of the predictions on the current data set (as assured by $\gamma = 17.5$ mm Hg) is likely to be insensitive to sampling variations.

Also, note that **only the mean** of the observed values of ICP is employed in determining this value of γ because bias is simply the difference between the mean of the observed and predicted ICP. This observation offers another explanation for why the choice of $\gamma = 17.5$ mm Hg is likely to be generalizable to the population at large. It is also possible to set $\gamma = 0$, in which case observed mean of ICP is not used at all at any stage in the development of the revised model. The result (not shown here) is that the revised method still outperforms the WB method in terms of the percentiles of the errors and the RMSE, although the bias of the errors is no longer zero.

A visual examination of Fig. 3 suggests that although there is a correlation between ICP and ZFP "between patients," the correlation "within patient" is less clear. For some patients, the 200 points are tightly clustered around a line (implying a strong within-patient correlation), but for other patients no such correlation is evident. We are currently investigating characteristics of the patients (e.g., the location of the ABP gauge) that may distinguish between these types of patients. The decomposition of variance (into between patient and within patient) may also improve the estimates of ICP through the development of mixed-effects models.[36]

In all of the analysis performed here, the quantity called ZFP has served only as a predictor of ICP; it has been assumed that this ZFP is an accurate measure of the "true" ZFP. Indeed, even the quantity called ABP has been assumed to be an accurate estimate of the true ABP. The first assumption has been addressed by Aaslid et al.[25], wherein it appears that examining the first harmonics of the time series for ABP and FV may lead to more accurate estimates of the true ZFP. Kalmar et al.[37] have also considered alternative measures of ZFP. Hsu, Chen and Hu[38] examine the effects of more accurate measures of the true arterial blood pressure in assessing the true ZFP. It is, therefore, possible that the ICP predictions from our method can be further improved by invoking more accurate measures of the true ZFP and ABP.

An important limitation of our study centers on our use of arterial blood pressure (ABP) data. Specifically the height difference between the point of ABP measurement and point of TCD measurement was not reported with the data collected at Addenbrooke's Hospital. We therefore did not reduce the peripherally measured ABP by an amount proportional to this

height difference to create a proxy for cerebral ABP at the middle cerebral artery. This may have introduced a systematic overestimation of cerebral ABP, and therefore a shift in the scatterplots to the right with systematical errors of ZFP and consequently of γ. This potential source of error would, however, contribute equally to both the WB method and the SD method, leaving the conclusion of this paper intact, namely the advantage of the SD method relative to the WB method. Future work will consider correction to the measured ABP based upon the potential height difference between the point of measurements of ABP and blood flow in the brain, which may further improve the results.

Conclusion

Proposed revisions to a methodology for estimating ICP from ZFP, via FV and ABP, are shown to lead to improved predictions of invasively measured values of ICP. Although the ±2 standard deviation of errors is reduced from 33 to 24 mm Hg, the quality of the predictions remains mostly unacceptable, at least clinically, because most applications would require a prediction error of 10 mm Hg or less. Further work, including those suggested here, is necessary before this approach can yield a clinically useful predictor for ICP.

Acknowledgments

Appendix

Appendix:

For data on *(x,y)*, the WB method calls for a straight line fit

$$y=\alpha+\beta x \quad (1)$$

where the parameters α, β are estimated via the least-squares criterion from data on $x = \text{FV}$ and $y = \text{ABP}$, i.e.,

$$\alpha = mean\,(ABP) - mean\,(FV) * \beta, \quad \beta = \frac{r * sd\,(ABP)}{sd\,(FV)}, \quad (2)$$

and *r* is Pearson's correlation coefficient between ABP and FV. The ZFP hypothesis asserts that the least-squares estimate of α (i.e., the y-intercept) approximates ICP. The *SD criterion* is based on the standard deviation of *x* and *y* (hence the "SD" in the name). The line according to the SD criterion is defined as the line that goes through the point defined by the mean of *x* and mean of *y*, with a slope given by the ratio *sd(y)/sd(x)*, where *sd* denotes standard deviation.[39] In short, the equation of an SD line for ABP versus FV is that given in Eq. (1), but with

$$\alpha = mean\,(ABP) - mean\,(FV) * \beta, \quad \beta = \frac{sd\,(ABP)}{sd\,(FV)}, \quad (3)$$

Note that the only difference is that the correlation coefficient does not enter into the latter. This is the reason why the SD line is unaffected by the alignment of *x* and *y*. The geometry underlying the SD criterion is in many ways more intuitive than that of the least-squares criterion, in spite of the popularity of the latter. For example, if a scatterplot displays a cigar-shaped or elliptical pattern, then the SD line coincides with the major axis of the ellipse,

while the least-squares line has a slope generally smaller than that of the SD line.[39] Note that, in Eq. (2), as r approaches 1, then the estimates of α and β according to the least-squares criterion coincide with the estimates given by the SD criterion in Eq. (3). Said differently, the SD line and the least-squares line coincide when *x* and *y* are aligned.

The structure of the fit in Eq. (1) does not preclude negative values of the y-intercept. In order to disallow such unphysical values of ICP, we propose the following fit

$$(y - y)^{1/2} = \alpha + \beta x \quad (4)$$

where γ is a fixed non-negative constant. Then, the ZFP is given by γ + α², and so cannot be negative. Structures involving the exponential have also been tested, but with no noticeable difference.
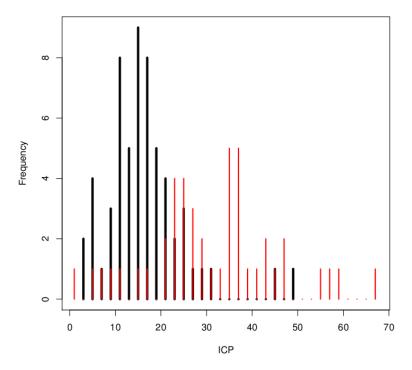
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Figure 1.
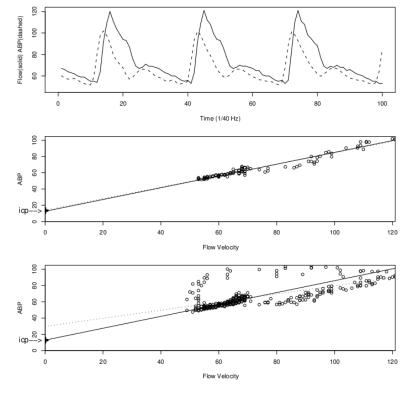Distribution of ICP for the University of Washington patients (black), and for the Cambridge patients (red).

Figure 2.
Top panel: The time series of FV (solid line) and ABP (dashed line) for one patient. Middle panel: Scatterplot of ABP versus FV (circles), the least-squares fit (dotted line), and the SD line (solid line). The mean ICP for this patient is labeled along the y-axis with an arrow. Bottom panel: same as middle panel, but prior to alignment of the two time series.
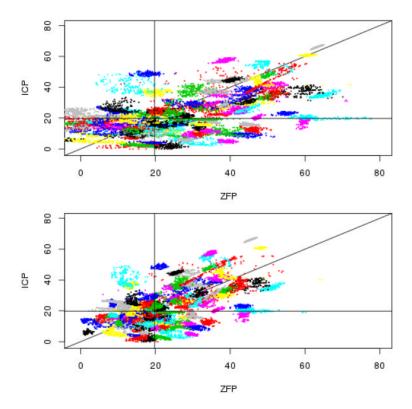
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Figure 3.
The scatterplot of observed ICP versus ZFP (i.e., estimated ICP), for all 104 patients (clusters in different colors), according to the WB method (top) and the revised method (bottom). Each cluster contains 200 points corresponding to 200 different time segments of the time series for that patient. The vertical and horizontal lines denote the grand mean of the observed ICP across all patients. The diagonal line is a line with slope equal to 1 and y-intercept equal to 0.
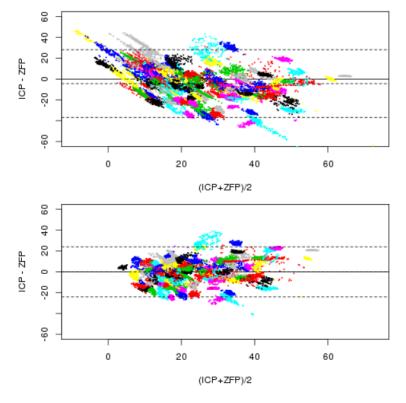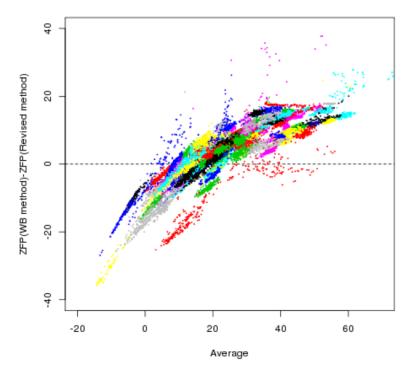
J Neurosurg Anesthesiol. Author manuscript; available in PMC 2014 January 01.

Figure 4.
Comparison of ICP and ZFP for the WB method (top) and the revised method (bottom). The dashed horizontal lines denote the mean, and mean ± 2 standard deviation; They are −4 ± 33 mm Hg, and 0 ± 24 mm Hg, respectively.

Figure 5.
A Bland-Altman plot showing the difference between the ZFP estimated by the two methods (WB and revised) as a function of their average. The two estimates appear to have a nonlinear and complex relationship which varies across patients.

Table 1

The percentiles of the distribution of errors, and of RMSE, for the two methods.

| | Percentiles of Error | | | | | | Percentiles of RMSE | | | | | |
	0th	25th	50th	75th	100th	0th	25th	50th	75th	100th
WB Method	−67.4	−14.9	−4.8	5.5	46.6	0.0	5.1	11.1	18.8	67.4
Revised Method	−41.2	−8.4	0.1	8.1	39.2	0.0	4.1	8.2	13.7	41.2