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# Forecasting Intracranial Pressure Elevation Using Pulse Waveform Morphology

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*Abstract* – **Management of intracranial pressure (ICP) following a traumatic brain injury (TBI) is an essential aspect of minimizing such secondary brain injuries as intracranial hypertension and cerebral hypoxia. Currently, ICU management of ICP elevations is reactive in nature; we propose a quantitative method to predict potentially harmful elevations in ICP.**

**Methods - Continuous intracranial pressure measurements were obtained from 37 patients at the UCLA Medical Center. Intracranial hypertension (IH) episodes were identified along with slow wave segments (used for control sets). Four, five minute segments were then constructed from the IH episode: one from the onset of ICP elevation (pre-IH #0) along with sets 5, 20, and 35 minutes prior to the elevation (pre-IH #5, #20, #35 respectively). Quantification and recognition of the three ICP sub peaks was performed using our group's algorithm termed Morphological Clustering and Analysis of Intracranial Pressure (MOCAIP). Furthermore, a quadratic classifier (QDC) was used to determine the metrics with the greatest predictive power. These metrics were then used to compare the control data set to the data sets described previously.**

**Results – From the ten most frequently selected metrics each of the four pre- intracranial hypertension (pre-IH) segments were compared with the control. Sensitivity (SEN), specificity (SPE), and accuracy (AC) were determined for each set with a SEN and SPE for the data set five minutes prior to ICP elevation of 90% and 75% respectively.**

**Conclusion - Combining the MOCAIP analysis, QDC classification, and bootstrap method of statistical sampling, our analysis has the potential to predict an ICP elevation event 20 minutes prior to the event onset.**

## I. Introduction

Nearly 1.5 million cases of traumatic brain injury (TBI) are reported annually in the United States. Management of intracranial pressure (ICP) is a key component in minimizing secondary brain injury; intracranial hypertension may result in brain herniation, cerebral hypoxia, and cerebral ischemia [1]-[3]. The contents of the skull, tissue, cerebrospinal fluid (CSF), and blood are maintained at a constant volume within the rigid bone case enclosing the brain. In general, ICP is the sum of the pressures exerted within the system, including the cranium and the vertebral column [3].

First described by Lundberg *et al.* in 1965, the ICP waveform may be broken down into the following categories: A, B, and C waves. "A" or "plateau" waves are defined by an abrupt increase in ICP to peaks of 50-80 mmHg for the duration of greater than five minutes. These ICP plateau waves are generally considered ischemic pathological events that can be associated with secondary brain injury. Moreover, semi-periodic increases in ICP defined as "B" waves have an elevation of 20-30 mmHg. These "B" waves need to be accurately differentiated from the malignant plateau waves as 'over-treatment' may result. Lundberg also described a "C" wave that occurs with maximum amplitude of 20 mmHg and a frequency of 4-8 per minute [4].

Clinically, ICP management has experienced a delayed maturation over the past 40 years. The fundamentals of the ICP pulse waveform have been known for decades; however, precise quantitative relationships and physiological explanations are still predominantly based on assumptions and not sound scientific proof. We propose a method to differentiate pathological ICP elevations (plateau waves) from potentially benign elevations. Identification and intervention of the pathological ICP elevations at the moment of onset, or ideally prior to the event, may improve.

## II. Methods

*Patient Data*

During monitoring at UCLA Medical Center, continuous intracranial pressure measurements were obtained from 37 patients admitted for the following reasons:

1. Diagnostic evaluation for possible normal pressure hydrocephalus
2. Headache evaluation in patients with suspected idiopathic intracranial hypertension or shunt malfunction
3. Management of adult slit ventricle syndrome

All measurements and procedures were approved by the UCLA Medical Center Institutional Review Board (IRB) committee.

Intracranial hypertension episodes defined as an elevated ICP of greater than 20 mmHg for longer than five minutes

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were manually identified by an experienced observer. Furthermore, slow waves or B waves were also manually segmented. From the 125 slow wave segments, 63 samples were selected at random for use as controls.

*MOCAIP Algorithm*

A detailed description of the MOCAIP algorithm may be found in previous publications [5]. In general, the MOCAIP algorithm is comprised of five signal processing blocks: Pulse Detection, Pulse Clustering, Legitimate Pulse Recognition, Peak Detection, and Peak Designation. The MOCAIP algorithm also utilizes a reference library of legitimate ICP pulses.

### *A. Pulse Detection*

Pulse detection in the MOCAIP algorithm is utilized by using conventional ECG QRS detection with adaptive interval constraints as proposed in [6].

### *B. Pulse Clustering*

A clustering algorithm is then used to group individual pulses based on the Euclidian distance for a short segment of signals. The average pulse of the largest cluster is then retained for further analysis, which is termed as the dominant pulse. The length of the ICP segment used for each pulse was one minute.

### *C. Legitimate Pulse Recognition*

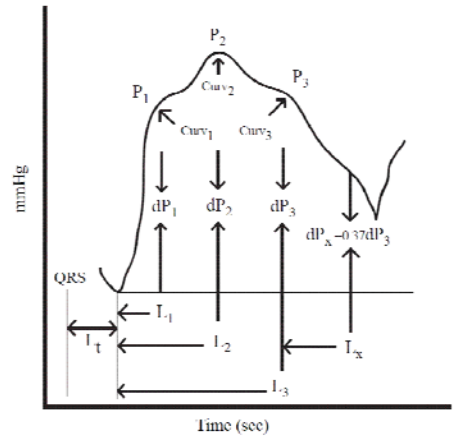
Raw ICP pulse waves are particularly sensitive to transient disturbances such as coughing or patient movement; the averaging reduces noise and effectively isolates the representative pulse for a given segment. Possibly, a given one-minute segment could contain only noise; therefore, the dominant pulse would render useless. Using the legitimate pulse library such illegitimate dominant pulses are removed.

### *D. Peak Detection & Peak Designation*

Normally, the ICP pulse waveform contains three characteristic peaks, each having a physiological source [1]. Through peak detection, each legitimate dominant pulse is analyzed and a set of 24 MOCAIP metrics are generated for each dominant pulse (Table 1). Finally, the peak designation process is executed to optimally designate the three well established ICP peaks for each legitimate dominant pulse. More detailed descriptions of this algorithm may be found in previous publications [5].

*Determination of Sensitivity and Specificity of the Identified Precursors of ICP Elevation*

Using a two-step classification experiment and conventional measures of sensitivity (SEN) and specificity (SPE), we test our current hypothesis: that ICP waveform morphology is fundamentally different and can be quantitatively differentiated between an Intracranial Hypertension segment (termed pre-IH segment) and a normal ICP waveform (termed normal segment).




| MOCAIP Metric Group | | Metrics |
|---|---|---|
| Amplitude | Absolute | mICP, $dP_1$, $dP_2$, $dP_3$, diasICP |
| | Ratio | $dP_2/ dP_1(dP_{12})$, $dP_3/ dP_1(dP_{13})$, $dP_3/ dP_2(dP_{23})$ |
| Time Interval | Absolute | $L_T$, $L_1$, $L_2$, $L_3$ |
| | Relative | $L_2 - L_1(L_{12})$, $L_3 - L_1(L_{13})$, $L_3 - L_2(L_{23})$ |
| Pulse Curvature | Absolute | $Curv_1$, $Curv_2$, $Curv_3$, $Curv_m$ |
| | Ratio | $Curv_2/ Curv_1(Curv_{12})$, $Curv_3/ Curv_1(Curv_{13})$, $Curv_3/ Curv_2(Curv_{23})$ |
| Slope | | $(P_1$- diasICP$)/ L_1 (k_1)$ |
| Decay time constant | | $L_x$ where $dP_x = 0.37\ dP_3$ |

Table. 1. Illustration of ICP related metrics that can be extracted by the current MOCAIP algorithm.

Step 1: Determination of the Predictive power of each MOCAIP metrics.

We previously defined 24 MOCAIP metrics (Table 1), of which any combination may be used as the feature vector input to our simple quadratic classifier (QDC) with the exception of mean and diastolic ICP along with onset latency ($L_t$). The exclusion of mean and diastolic ICP were deemed necessary to further challenge the identification of elevated ICP. In general the QDC uses the feature vector of n MOCAIP metrics and outputs a decision of either positive or negative for the given case. Due to the large amount of possible MOCAIP metrics combinations, any could be used in the feature vector. An efficient global random search strategy called Particle Swarm Optimization (PSO) was implemented to improve the chance of locating the optimal combination of metrics. More specifically, the process of finding the optimal combination of metrics was executed as follows:

1. Using the manually tagged starting position of the ICP elevation four datasets of five minutes were built. The datasets correspond to different time locations during and prior to the ICP elevation event. Dataset #0 contains a five minute segment directly following ICP elevation. Datasets #5, #20, and #35 include five minute segments 5, 20, and 35 minutes prior to ICP elevation respectively (Fig. 1).
2. Using the 125 representative slow wave episodes along with the 63 randomly selected baseline segments a control dataset was constructed.

3. For the control data set along with one of the four pre-IH datasets the following procedures were performed:
   a. Data from both the control and pre IH data set were combined. Each segment was identified as negative or positive respectively.
   b. The following bootstrap procedures were run for 200 independent repetitions.
      i. A training set was built by randomly sampling the positive and negative cases while maintaining the initial distribution.
      ii. The PSO algorithm was applied and the optimal MOCAIP metric combination was calculated and saved. It is important to note that this combination differed for each repetition.
4. Based on the frequency of selection, the optimal MOCAIP metrics are saved.

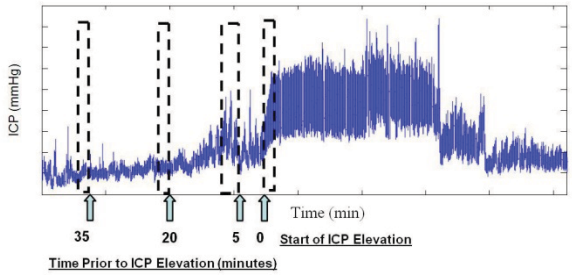



Fig. 1. Illustration of constructing pre-intracranial hypertension segments at different time intervals relative to the start of ICP elevation for an episode of ICP plateau wave.

Step 2: Estimation of the sensitivity and specificity of using top MOCAIP metrics to classify normal control ICP waveforms from those associated with ICP elevation.

Through the same bootstrapping method described above the SEN and SPE were estimated. In general, the bootstrapping method estimates given properties from an approximate distribution. The method randomly samples the population and then estimates the properties from the given distribution. Unbiased estimates of SEN and SPE are calculated for each repetition. Again the following procedures were performed for both the control data set along with each of the pre IH datasets.

1. Records were combined into mixed data set.
2. Control segments and pre-IH segments were identified as negative and positive respectively.
3. The following steps were independently repeated 200 times
   a. A training set was built by randomly sampling (with repetition) the positive and negative cases while maintaining their empirical distribution.
   b. Based on the training set, a QDC was calculated based on the ten MOCAIP metrics of highest predictive power.
   c. This classifier was evaluated on both the training set and the original dataset with respect to the SEN, SEP, and AC.

$$SEN = \frac{TP}{TP+FN} \qquad SPE = \frac{TN}{TP+FN} \qquad AC = \frac{TP+TN}{N},$$

where TP represents the number of true positive cases, TN represents the number of true negative cases, and N is the total number of cases.

   d. The difference between the pre-IH datasets and the original datasets were then calculated.

$$\Delta SEN_i = tSEN_i - oSEN_i$$
$$\Delta SPE_i = tSPE_i - oSPE$$
$$\Delta AC_i = tAC_i - oAC,$$

where i represents the current iteration of the 200 bootstrap repatriations, t represents the performance metrics from the training dataset, o represents those from the original dataset.

4. A QDC was derived and tested using the original dataset.
5. The final estimate for SEN, SPE, and AC are given below:

$$aSEN = SEN - \overline{\Delta SEN_i}$$
$$aSPE = SPE - \overline{\Delta SPE_i}$$
$$aAC = AC - \overline{\Delta AC_i},$$

where $\overline{\Delta SEN_i}$ is the average of the $\Delta SEN_i$ from the 200 iterations of the bootstrap method. *SEN* is the sensitivity obtained from the previous step that uses the original dataset for both building and testing the classifier, and finally *aSEN* represents the adjusted sensitivity.

In summary, we were able to quantitatively describe the predicative power of the MOCAIP metrics for each of the four pre-IH segments.

## III. RESULTS

The predictive power of each MOCAIP metric was defined by the frequency at which it was chosen. For each of the four pre-IH segments, Table 2 lists the MOCAIP metrics chosen with the highest frequency. From the 21 total metrics considered 14 were chosen at least once; however, the six latency related metrics and curvature of the first peak were never selected.

| Pre IH | Top 10 most predictive MOCAIP metrics | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 0 | $Curv_3$ | $dP_{12}$ | $dP_{13}$ | $dP_1$ | $Curv_{12}$ | $dP_3$ | Slope | $dP_{23}$ | $Curv_m$ | $L_x$ |
| 5 | $Curv_2$ | $Curv_3$ | $L_x$ | $dP_3$ | $dP_{12}$ | $Curv_m$ | $dP_2$ | $dP_{23}$ | $dP_{13}$ | $dP_1$ |
| 20 | $Curv_2$ | $dP_{23}$ | $Curv_3$ | $dP_{13}$ | $L_x$ | $dP_{12}$ | $Curv_{12}$ | $dP_1$ | Slope | $dP_2$ |
| 35 | $Curv_3$ | $Curv_2$ | $Curv_m$ | $Curv_{13}$ | $Curv_{23}$ | $dP_{23}$ | $dP_{13}$ | $dP_1$ | $L_x$ | $dP_{12}$ |

Table 2. List of top 10 most predictive MOCAIP metrics for differentiating pre-intracranial hypertension segments from normal ones.

Comparison of the variance of a selected MOCAIP metric ($dP_3$) relative to the five groups tested (control, pre-IH #0, #5, #20, and #35) is shown in Fig. 2. Furthermore, if a given metric value was found to be statistically significant between

groups it is listed on the subplot. For example, the value of $dP_3$ was found to be statistically significant between five groups, meaning the control group could differentiated significantly from the pre-IH #0 and pre-IH #5 group, and the onset (pre IH #0) could be differentiated from the pre-IH #5, #20, and #35 group. Interestingly, even though $L_{23}$ was not selected in the top ten metrics for any of the pre-IH groups it was shown to be statistically significant in four cases (0-5, 0-20, 0-35, and 0-C, box plot not shown).

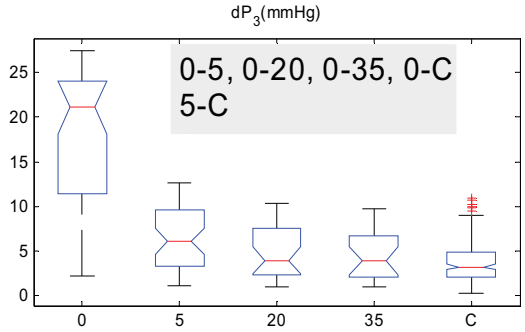



Fig. 2. Box-plot showing the distribution of one MOCAIP metrics ($dP_3$) among five different groups that include four pre-IH groups and one control group. By a proper multiple-comparison, we can detect, for each metric, the pairs of the groups that are statistically (corrected $p$ value <0.05) different.

Table 3 summarizes the adjusted performance metrics SEN, SPE, and AC for classifying pre-IH segments from the control dataset. Differentiating the pre-IH #0 group (onset of elevated ICP) not surprisingly showed the best results with a SEN of 93%, a SPE of 98%, and an overall AC of 97%. Even though these results are promising the overall goal of the work is to predict IH episodes before the event. Therefore, even though the results from the pre-IH #5 do not provide the same values for SEN, SPE, and AC the results are still promising, 90%, 75% and 77% respectively. From these values we can state that our algorithm could alert staff of an impending ICP plateau wave five minutes prior to its occurrence with 90% of those cases being a true plateau wave. Interestingly, a SPE value of 89% was found for the pre-IH #20 group, which is much higher than the 75% reported for the data five minutes prior to the event (pre-IH #5). With this prior exception, all other performance metrics decreased as the time from the elevated ICP event increased.

| Pre-IH | Sensitivity | Specificity | Accuracy |
|---|---|---|---|
| 0 | 0.93±0.04 | 0.98±0.01 | 0.97±0.01 |
| 5 | 0.90±0.05 | 0.75±0.03 | 0.77±0.03 |
| 20 | 0.77±0.08 | 0.89±0.02 | 0.88±0.02 |
| 35 | 0.76±0.10 | 0.71±0.02 | 0.72±0.02 |

Table 3. Adjusted performance metrics from using the top 10 most predictive MOCAIP metrics as feature vectors.

## IV. Discussion

Combining the MOCAIP analysis, QDC classification, and bootstrap method of statistical sampling, our analysis has the potential to predict an ICP elevation from 20 minutes before its onset; however, future work must be done to fully automate the process for clinical use. Furthermore, our current analysis does not completely address the mechanisms behind spontaneous ICP elevation, currently it is a purely data driven process.

Based on our control data set, we expect an increase in the specificity (SPE) for real-time running of the current algorithm. This estimation is based on the disproportionate amount of ICP slow waves segments included in the control dataset. The increase in ICP slow waves presents a more challenging case verses a baseline ICP segment that does not contain oscillatory ICP waves. Unfortunately, we do not expect an increase in the sensitivity (SEN); however the current SEN of 90% should be taken cautiously because of the small number of patients within the study and the result may be statistically biased due to the multiple contributions of ICP elevation segments from the same patient.

Despite the fact that ICP is rigorously controlled as commonly prescribed in brain injury patient management protocols, the experience in our neurocritical care unit shows that the percentage of time of elevated ICP can be still as high as 18%. This observation may be explained by many factors, one of which may result from the reactive nature of managing ICP. Reactive management of ICP depends on a timely capture of episodes of ICP elevation, which could potentially be delayed resulting in further delay of interventions whose efficacy on controlling ICP may also need time to take effect. Consequently, a reliable forecast of impending ICP elevation is very desirable to reduce the chance of missing ICP elevation and to provide additional time for interventions.

## V. Conclusion

The encouraging results we obtained in the present work may have significant clinical implications. The current reactive management practice for elevated ICP could be supplanted by a more proactive one where the moment of ICP elevation can be anticipated in a time window adequate for clinical interventions.

## References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