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Hybrid Method of Non-invasive Intracranial Pressure Measurement Using Autoencoder Neural Network Algorithm

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Both short-term and long-term intracranial pressure (ICP) monitoring is indicated for a number of neurological pathologies. The clinical gold standard for ICP monitoring is invasive and involves inserting a pressure sensor into the brain tissue or cerebral spinal fluid space. Such sensors can only be used for a limited time due to the risk of infection and sensor degradation. Our aim was to develop a method for long-term non-invasive ICP monitoring after the removal of invasive ICP sensor. Arterial blood pressure (ABP) and cerebral blood flow velocity (FV) signals were used as inputs to an artificial autoencoder neural network. The network was trained with invasively measured ICP. Following the training phase, the network's outputs were used for estimating ICP based on ABP and FV only. The method was verified on clinical data from 98 traumatic brain injury patients. The proposed procedure managed to recover ICP using FV and ABP measurements. The median value of the Pearson correlation between the recovered and the reference ICP signals was 0.7, and the root mean square error was 3.9 mmHg with an interquartile range of less than 5 mmHg. An additional feature of our algorithm is that it not only outputs an ICP estimate, but also provides a confidence level.

topics: artificial neural networks (ANN), autoencoder, biomedical signal processing, intracranial pressure

1. Introduction

Intracranial pressure (ICP) is an important parameter used for diagnosing numerous neurological disorders. Some acute pathologies require ICP to be monitored continuously, either for a short or for a longer time. During short-term monitoring, it is often the case that the rapid changes in ICP or the occurrence of some abnormal waveforms within this signal call for an immediate medical intervention. On the other hand, the results of the long-term monitoring could be used to appropriately adapt the doses of medication. In both cases, the availability of an exact and reliable method of measuring ICP is important.

The standard clinical method of measuring ICP consists of introducing a pressure sensor into the patient's cranium. It is obviously an invasive measurement procedure, which comes with associated risks. Invasive ICP measurement uncertainty is just a few mmHg, but it does not allow for truly long-term monitoring. After a few days, the patient's infection risk rises, and the sensor itself may exhibit zero drift and should be removed or replaced.

Many non-invasive ICP estimation methods have been proposed in the past. All of them have two important drawbacks. Firstly, their accuracy is not as good as invasive methods, especially within a highly heterogeneous group of patients. The second drawback is that known non-invasive methods provide completely wrong values of ICP, which are not

related to the real pressure waveforms, for a significant part of patients. One could speculate that the reason behind this weakness lies in the total incompatibility of the mathematical model with the specific features characteristic of the individual patient's physiology [1]. As a consequence, the degree of confidence among the medical personnel in non-invasive ICP measurement methods is typically relatively low. An experiment carried out by authors in [2] shows that initial calibration based on individual patient significantly improves non-invasive ICP estimation accuracy.

Our study attempts to formulate a hybrid method that combines features of invasive and non-invasive methods. During the first phase, called the training phase, the proposed algorithm utilizes the results of ICP measurements obtained with the conventional invasive method. Based on this data, the algorithm adapts its underlying mathematical model to the specific features of the individual patient. The learning phase is continued as long as the ICP sensors remain within the patient's cranium and do not degrade. At the end of the learning phase, the algorithm is able to compute some quantitative measures that provide reliable information on whether the quality of the identification of the mathematical model mentioned above is sufficient. If this is the case, then the algorithm switches to the non-invasive ICP measurement mode and is able to continue working in this mode for many days. If not, it refrains from estimating the ICP of a given patient. The clinical scenario for the proposed method assumes the presence of the inherent learning phase based on invasive ICP measurements. Although this requirement is somewhat limiting for the potential areas of application, it results in precise adaptation to the specific features of individual patient and, in consequence, provides significantly lower measurement uncertainty in the non-invasive mode than the competitive, non-invasive only methods. The availability of quantitative measures of the quality of outcomes should notably increase the confidence of the medical personnel in the measurements made in the non-invasive mode. Furthermore, the proposed algorithm, even while working in the non-invasive mode, still has some abilities to automatically detect the inferior quality of the measured ICP and provide the personnel with such information.

2. Methods

The proposed hybrid algorithm in non-invasive ICP mode estimates the ICP signal on the basis of two other readily available physiological signals: arterial blood pressure (ABP) and cerebral blood flow velocity (FV). The rationale behind this approach is that many existing mathematical models of the cerebrospinal system closely relate these three signals (ICP, ABP, and FV). Moreover, the measurements of ABP (either using an arterial catheter or the plethysmographic sensor [3]) and FV (e.g., by the ultrasonic transcranial Doppler flowmeter [4, 5]) are already routinely applied for patient monitoring and are considered as minimally invasive [6].

Most published models of the cerebrospinal system comprise multiple non-linear and time-variant models that involve many parameters. These parameters either have arbitrarily assigned fixed values [7, 8] (limiting the applicability of the model to different patients) or are estimated from the measurements using complicated methods, which are not strongly legitimated (as they are mostly heuristic) [9]. Therefore, we decided to use a universal "black-box" model in the form of an *artificial neural network* (ANN) [10], more precisely, an autoencoder network.

The inputs of the ANN are fed with the values of ABP and FV signals. The neural network has three outputs, which estimate the values of the desired intracranial pressure signal ($\widehat{ICP}$), as well as the recreated versions of both input signals: the arterial blood pressure ($\widehat{ABP}$) ($\widehat{ABP}$) and the flow velocity ($\widehat{FV}$). During the learning phase, when the invasively measured ICP signal is available as a reference, the parameters of the ANN (i.e., the weights and biases of all the neurons) are optimized to recreate all three signals ($\widehat{ICP}$, $\widehat{ABP}$, and $\widehat{FV}$). The optimization criterion for each of the outputs consists not only of the mean square error of the reconstructed signal with respect to the original (measured) one, but also of the correlation between the reconstructed and measured signals.

If (and only if) during the learning phase the neural network was able to achieve an adequate quality of the reconstruction of all three signals, then the network is allowed to be used in the non-invasive ICP measurement mode. In this mode of operation, the inputs of the network are still supplied with the non-invasively measured ABP and FV signals, and the $\widehat{ICP}$ output is used as the non-invasively recreated intracranial pressure signal. At the same time, the $\widehat{ABP}$ and $\widehat{FV}$ outputs of the network are utilized for the real-time assessment of the correctness of the behaviour of the network by comparing them with real ABP and FV signals. Poor quality of reconstruction of the latter (measured) signals by the former (recreated) ones is obvious evidence of the unreliable $\widehat{ICP}$ estimation.

The authors support the view that even if the exact mathematical model relating the ICP, ABP, and FV signals is very complicated, highly non-linear, and time-variant, it still can be formulated with adequate accuracy by just a few fundamental laws of the cerebrospinal system's physiology. This fundamental assumption led to the choice of the applied structure of the artificial neural network. The authors resorted to a modified form of

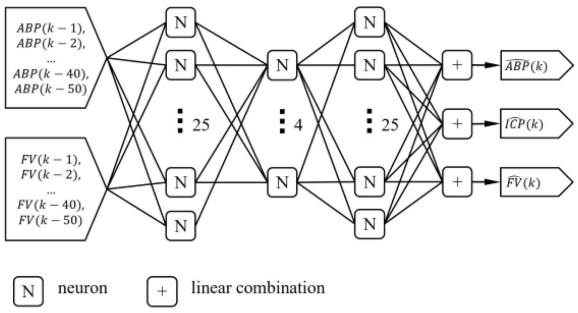

Fig. 1. Autoencoder neural network structure. On the left are inputs — ABP and FV samples from the past. In the middle are three layers of neurons. On the right are the outputs, namely $\widehat{ABP}$, $\widehat{FV}$, and $\widehat{ICP}$ samples, which represent estimates of current ABP, FV, and ICP, respectively.

an autoencoder [11], featuring just a few neurons in the hidden layer. This relatively low number of intermediate neurons (actually, just four neurons were used) forces the network to learn the features of ABP and FV necessary to reconstruct ICP.

The network structure proposed in the paper differs from the conventional autoencoder (possessing the same number of input and output signals) by an extra channel for recreating intracranial pressure. The rationale behind such an approach is based on the assumption that ICP is closely related to ABP and FV. Therefore, the accurate reconstruction of the two latter signals should result in the good reconstruction of the former one as well.

Another important difference between the conventional autoencoder and the proposed structure was motivated by the need to take into account multiple time horizons of the input signals. To achieve this, the ABP and FV inputs of the network consist not only of the scalar values of the most current samples of both signals (averaged over the heartbeat), but rather of the vectors of appropriately chosen past samples of these signals. The samples are taken non-uniformly, i.e., densely in the near past and sparsely in the longer time horizon (up to 50 heartbeats ago), to cover all clinically relevant spectral components. The $\widehat{ABP}$ and $\widehat{FV}$ outputs of the network are vectors as well to make them readily comparable with the inputs of the network during the recreation quality assessment.

The structure of the proposed autoencoder resulting from the above considerations is shown in Fig. 1. The neurons in each layer use the most common bipolar sigmoidal activation function and the extra bias term, added to the linear combination of the inputs.

During the learning phase, the conventional error backpropagation algorithm is used [12]. However, at the same time, many (at least 10) independent neural networks are being trained in parallel, each one with differently randomized initial values of the neuron weights. The concurrent training of multiple networks, although computationally demanding, is not a problem nowadays due to the broad availability of massively multicore platforms such as *graphics processing units* (GPUs). Near the end of the learning phase, the input signals are used to verify whether the given network has not been overtrained. Among all networks that pass this test, we choose the one that recreates in its outputs all three signals under consideration with the best quality. If that quality seems adequate for clinical use, the network switches to the non-invasive ICP measurement mode.

3. Results

The data used for validation of the proposed algorithm originates from a database of neuro-intensive care recordings that have been collected for more than 20 years at Cambridge University Hospital in United Kindom (Addenbrooke's Hospital). The database encompasses ICP, ABP, and FV, as well as other clinical recordings of several hundred patients after traumatic head injury. Signals were recorded based on a clinical need to daily assess the autoregulation of cerebral blood flow during the stay of the patients in the neuro-critical care unit. The local Neurocritical Care Unit (NCCU) Users' Committee and then the local Research Ethics Committee approved the use of anonymized data for future validation of methodological projects. For our research, we have discarded recordings shorter than half an hour (2000 heartbeats). These recordings do not fit into the assumed clinical scenario, according to which the data should be long enough to be used to train the neural network and then verify its performance. For the sake of clarity, we have also discarded recordings in which any artifacts were identified (data corruption, sensor failure, and misleading data due to specific medical treatment). Recordings concerning the same patient, but separated with a time interval longer than 2 h, were considered separately (as if they came from different patients). Another criterion used for abandoning the neural network learning procedure was the narrow range of the recorded ICP values, as there is no way for a neural network to guess what changes in FV and ABP signals would coincide with significant changes in ICP signal if no such changes appeared in the learning phase. As a rule, we have thus discarded the recordings with an ICP range (in the recording fragment used for neural network learning) narrower than 12 mmHg. The total number of recordings meeting the above criteria was 193 recordings of 98 patients. There were 21 females and 72 males, with a mean age of 31. The mean Glasgow Coma Score was 6.35, and the median outcome was moderate disability (with a 22% mortality rate). A total

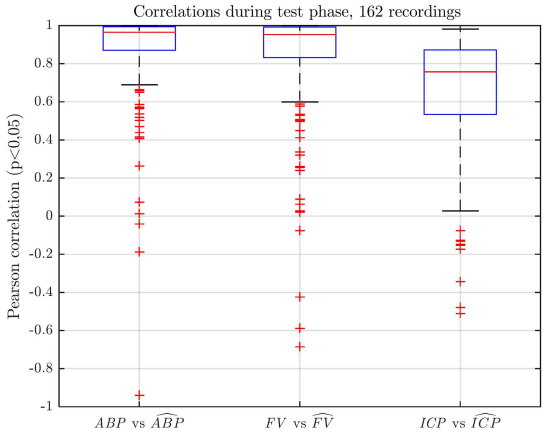

Fig. 2. Correlation between measured signals ABP, FV, ICP and their counterparts computed by the neural network. The correlation has been computed on 162 blocks of test data.

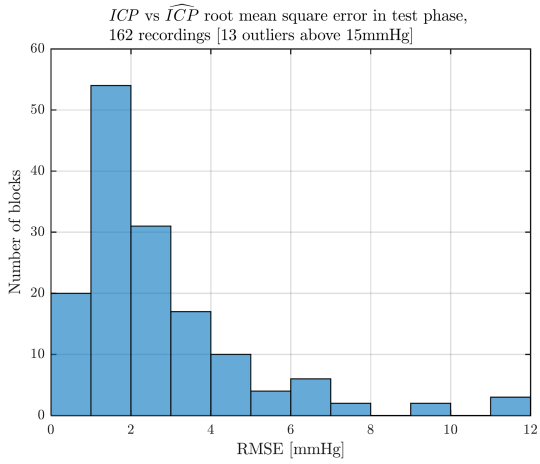

Fig. 3. *Root mean square* (RMS) value of ICP recovery error. The box plot is based on 162 signal blocks. Thirteen outliers bigger than 15 mmHg are not shown in the plot.

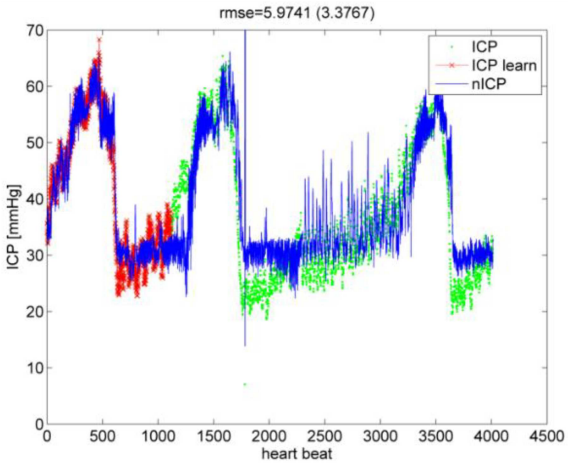

Fig. 4. The ICP (blue) and $\widehat{ICP}$ (ICP learn (red) is ICP computed in learning phase, $nICP$ (green) is ICP computed in test phase) signals — Case A.

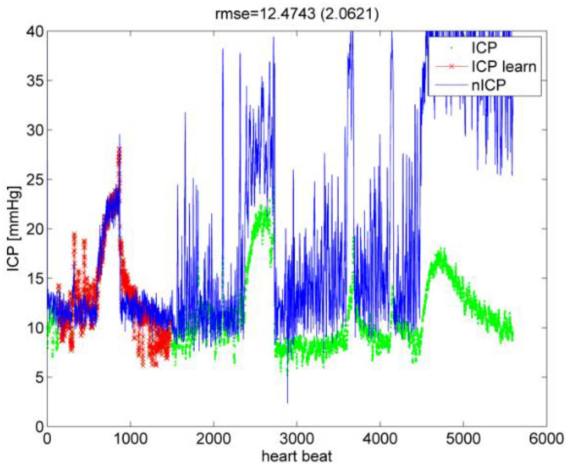

Fig. 5. The ICP (blue) and $\widehat{ICP}$ (ICP learn (red) is ICP computed in learning phase, $nICP$ (green) is ICP computed in test phase) signals — Case B.

of 31 recordings were rejected from the testing phase because all networks trained on a validation subset of data have an ICP estimation error above 6 mmHg or Pearson correlation coefficient less than 0.6. In the testing phase, the neural network was computing estimates of $\widehat{ABP}$, $\widehat{FV}$, and $\widehat{ICP}$ in the same way as during the training stage but for a different set of data.

In Fig. 2, the performance of the neural network is presented in terms of the Pearson correlation between acquired signals (test data) and their recovered counterparts. The correlations have been computed for 162 signal blocks that had not been discarded during the preprocessing stage or validation. For each of these blocks, the correlation coefficient was found to be statistically significant as the corresponding p-value was smaller than 0.05.

The histogram shown in Fig. 3 illustrates the root mean square error of ICP signal recovery. The plot was constructed from 162 samples, where each sample represents a signal block of various lengths. The ICP root mean square error has an upper quartile (75% of recordings) of 3.9 mmHg (95% CI 3.5 to 4.9 mmHg) and a median (50% of recordings) of 2.2 mmHg (95% CI 1.9 to 2.6 mmHg), where CI is confidence interval. In the case of 13 recordings (11 patients) — the outliers in Fig. 3 — our algorithm has failed to estimate ICP with an error above 15 mmHg.

In Figs. 4 and 5, the performance of the constructed neural network is presented for two different patients. In both patients, the autoencoder networks have been trained so that the errors between

ICP and $\widehat{ICP}$ are relatively small. This error stays at the low level in Case A, illustrated in Fig. 4. Such a good performance of the network was possible because the dynamics and range of ICP signal changes during the training stage were similar to those in the testing phase. For Case B, illustrated in Fig. 5, the situation is quite different. Despite this, it was possible to achieve a small recovery error during the training stage; the difference between the recovered and the measured ICP signals is quite big. The reason for such undesired behaviour of the constructed network in some of the cases requires further research that would need more exhaustive data on each case, e.g., information on patient treatment and recovery.

4. Discussion

For many years, clinical neuroscientists have tried to find an accurate, non-invasive or less invasive method for measuring ICP. A number of such methods are described in the literature, as listed in review paper [13]. In [14], the authors propose a "black box" system which attempts to convert arterial blood pressure (ABP) and transcranial Doppler blood flow velocity (FV) waveforms using linear regression analysis. The results are promising; the mean of the absolute values of the differences between measured and predicted ICP is 4.0 mmHg with a 95% confidence interval (95% CI) 2.2 to 5.8 mmHg), but based on a very small group of patients (11 for training, 10 for testing) and short measurement time of 100 seconds. An improved method presented in [15] studied a much larger group (145 patients, 197 recordings). It achieved an ICP error of 6.0 mmHg (95% CI 4.9 to 6.9 mmHg), but only for 50% of recordings. For 75% of recordings, the ICP estimation error was 9.1 mmHg (95% CI 8.1 to 10.5 mmHg) and for 90% of recordings, the ICP estimation error was 14.4 mmHg (95% CI 12.5 to 18.1 mmHg). Another innovative method of non-invasive ICP measurement is presented in [16] using 57 patients. The authors show that it is possible to measure absolute (without learning or intracranial reference measurement) ICP with 0.9 mmHg (95% CI $\pm$12 mmHg) mean difference between invasive and non-invasive method. The method is based on a two-depth transcranial Doppler (TCD) technique for absolute intracranial pressure (aICP) and external absolute pressure (aPe) comparison using the ophthalmic artery (EA) as natural "balance". The main drawback is highly customized equipment installed on the patient's eye. Another approach is shown in [9], where authors used a simplified Ursino and Lodi model [7] with only two parameters (brain arterial compliance and resistance to blood flow, changing with each heartbeat) to estimate ICP . These results are promising but require further validation on larger patient cohorts. In [17], the authors present a highly advanced approach based on nonlinear regression analysis that gives 6.0 mmHg (upper 95% CI 7.61 mmHg) ICP estimation error, but their research is based on a small group of 23 patients.

Our study validates the concept of non-invasive estimation of ICP using TCD and arterial blood pressure using autoencoder neural networks. Initial results obtained using retrospective analysis of pre-recorded clinical data are promising. In clinical practice, this method may be applied after the end of invasive ICP monitoring in cases where knowledge of non-invasive ICP is still valuable. This includes ICP monitoring after weaning from mechanical ventilation when the ICP sensor is removed but patients still are unconscious or semi-conscious.

5. Conclusions

In our view, the hybrid algorithm proposed in the paper, which utilizes invasive ICP measurements during the learning phase and then passes into the non-invasive measurement mode, can be applied in many practical clinical treatment scenarios. Autoencoder neural network, after a relatively short period of training, is able to non-invasively estimate ICP with the accuracy that seems to be clinically feasible. Further prospective clinical studies are needed.

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