# Analysis of intracranial pressure during acute intracranial hypertension using Lempel-Ziv complexity: further evidence 

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#### Abstract

We analyzed intracranial pressure (ICP) signals during periods of acute intracranial hypertension (ICH) using the Lempel-Ziv ( $L Z$ ) complexity measure. Our results indicate the $L Z$ complexity of ICP decreases during periods of ICH. The mean $L Z$ complexity before ICH was $0.20 \pm 0.04$, while the mean $L Z$ complexity during ICH was $0.16 \pm 0.03(p<0.05)$. The mean decrease of the $L Z$ complexity values during the ICH episodes was $19.5 \%$. Additionally, we present preliminary evidence suggesting that periods of ICH may be detectable from non-invasive signals coupled with ICP, such as pulse oximetry ( SpO 2 ).


Keywords Lempel-Ziv complexity • Intracranial hypertension • Intracranial pressure irregularity • Approximate entropy • Traumatic brain injury

## Abbreviations

| ApEn | Approximate entropy |
| :--- | :--- |
| ABP | Arterial blood pressure |
| CAR | Cerebral auto-regulation |
| HRV | Heart rate variability |
| ICH | Intracranial hypertension |
| ICP | Intracranial pressure |
| $L Z$ | Lempel-Ziv |

[^0]TBI Traumatic brain injury
SpO 2 Pulse oximetry

## 1 Introduction

Intracranial pressure (ICP) monitoring and management has substantially improved the outcome of patients with traumatic brain injury (TBI). TBI is one of the leading causes of death and disability in the United States [6]. Periods of intracranial hypertension (ICH) following TBI often result in secondary injury due to decreased cerebral perfusion pressure and cerebral ischemia [6]. Current ICP therapy is based predominantly on the mean ICP and the ICP pulse morphology. Generally, intervention to lower mean ICP is undertaken when it surpasses a certain threshold (usually 20 mmHg ) [10]. Taken alone, however, the mean ICP offers insufficient insight regarding the underlying physiological mechanisms that drive brain compliance and cerebral autoregulation (CAR) [3, 12] and determining ways to obtain such knowledge remains a significant research goal. Several researchers have developed indices derived from the ICP pulse morphology [2, 4, 5, 12].

This study provides further evidence suggesting that measures of ICP complexity decrease during acute episodes of ICH. Previous results showed that Approximate Entropy (ApEn) decreases during ICH [7, 8]. We analyzed ICP signals during ICH periods using the Lempel-Ziv ( $L Z$ ) complexity measure. $L Z$ complexity is a nonparametric measure of complexity for one-dimensional signals related to the number of distinct substrings (i.e. patterns) and the rate of their occurrence along a given sequence [9, 11].

This metric of complexity was originally designed to evaluate the randomness of finite sequences, and has been extensively used to solve information theoretic problems such as coding and lossless data compression. In recent years, $L Z$ complexity has been applied extensively in biomedical signal analysis as a metric to estimate the complexity of discrete-time physiologic signals [13-17]. Additionally, we report preliminary results suggesting that periods of ICH may be detected by analysis of other noninvasive physiologic signals coupled with ICP, such as pulse oximetry ( SpO 2 ).

## 2 Materials and methods

### 2.1 Signals

This study included 14 ICP signals containing ICH episodes obtained from seven patients with brain injury admitted to the Intensive Care Unit at Doernbecher Children's Hospital. All the signals were acquired using a Philips Merlin monitor. $L Z$ complexity was applied to 12 of the 14 ICP signals. In the other two signals the period of ICH was analyzed by applying $L Z$ complexity to SpO 2 signals recorded simultaneously with the ICP signals, since these ICP signals contained regions of artefacts where part of the ICP signal was lost due to saturation (i.e. the signal was clipped), and was not available for direct analysis. The requirement for informed consent was waived. Patient management guidelines and criteria for ICH detection have been previously reported [8].

### 2.2 Lempel-Ziv ( $L Z$ ) complexity

$L Z$ complexity analysis is based on a coarse-graining of the measurements. Before calculating the $L Z$ complexity measure $c(n)$, the signal must be transformed into a finite symbol sequence. In the context of biomedical signal analysis, typically the discrete-time biomedical signal $x(n)$ is converted into a binary sequence. By comparison with a threshold $T_{d}$, the original signal samples are converted into a $0-1$ sequence $P=s(1), s(2), \ldots, s(n)$, with $s(i)$ defined by:
$s(i)= \begin{cases}0 & \text { if } x(i)<T_{d} \\ 1 & \text { if } x(i) \geq T_{d}\end{cases}$
We used the median as the threshold $T_{d}$ because of its robustness to outliers [11]. Previous studies [13, 16, 17] have shown that $0-1$ conversion is adequate to estimate the $L Z$ complexity in biomedical signals.

To compute $L Z$ complexity, the sequence $P$ has to be scanned from left to right and a complexity counter $c(n)$ is increased by one unit every time a new subsequence of
consecutive characters is encountered. The detailed algorithm to estimate $c(n)$ can be found in [1, 16, 17].

In order to obtain a complexity measure which is independent of the sequence length, $c(n)$ should be normalized. In the case of a $0-1$ sequence, $c(n)$ can be normalized as follows [16]:
$C(n)=\frac{c(n)}{\frac{n}{\log _{2}(n)}}$
$C(n)$, the normalized $L Z$ complexity, reflects the arising rate of new patterns along with the sequence, capturing its temporal structure. Larger values correspond to more complexity in the sequence.

## 3 Results and discussion

Figure 1 shows the results of the $L Z$ complexity evaluated on detrended ICP signals using a moving window of 10 s with $90 \%$ overlap for 4 of the 12 analyzed episodes. The ICP signals were high-pass filtered with a cut-off frequency of 0.5 Hz to eliminate the mean (i.e. trend) prior to the computation of $L Z$ complexity. Generally, the $L Z$ complexity of ICP decreased as subjects progressed from a stable state of normal ICP to a state of acutely elevated ICP. We estimated the average $L Z$ complexity before ICH and during ICH in the 12 episodes. The mean $L Z$ complexity before ICH was $0.20 \pm 0.04$, while the mean $L Z$ complexity during ICH was $0.16 \pm 0.03$. To take into account the correction for multiple samples from the same patients, we calculated the mean $L Z$ complexity value of ICP before and during ICH episodes from each of the seven patients. Then, we applied the Student's $t$ test, which showed that the decrease in $L Z$ complexity of ICP during the ICH episodes was significant ( $p<0.05$ ). Moreover, the average decrease of the $L Z$ complexity values during the ICH episodes was $19.5 \%$.

Our results provide further evidence to indicate that decreased complexity of ICP coincides with episodes of ICH in TBI. Furthermore, these results are consistent with those of our previously published study involving the analysis of ICP during ICH using $A p E n[7,8]$. The average normalized $A p E n$ before ICH was $0.52 \pm 0.01$, while the mean normalized $A p E n$ during ICH was $0.39 \pm 0.08$. The average decrease of ApEn during the ICH episodes was $25 \%$. Both ApEn and $L Z$ complexity decreased significantly during ICH episodes, although the reduction was higher with ApEn. Thus, these results show that the decreased complexity and irregularity of ICP signals coincide with periods of ICH.

These findings suggest that the complex regulatory mechanisms that govern ICP are disrupted during acute


Fig. 1 Representative results showing four ICP signals and the corresponding $L Z$ complexity during periods of ICH. These results indicate that decreased $L Z$ complexity of ICP coincides with ICH episodes in TBI
rises in ICP. Acute ICH is a result of failure of normal cerebral autoregulatory mechanisms to compensate for overwhelming changes in cerebral volume (haemorrhage or oedema), external pressure (depressed skull fractures), cerebral blood volume (cerebral hyperperfusion), or cerebral spinal fluid (obstructive hydrocephalus). Thus, we can speculate that, similar to sepsis, the ICP waveform exhibits diminished complexity and increased regularity during periods of ICH when CAR has failed. Conversely, when CAR is intact, the ICP is more complex and irregular. However, further work must be carried out to check if $L Z$ complexity and ApEn of the ICP waveform might provide an indirect measure of CAR.

Decreased complexity during ICH has very important implications, since there are several physiologic signals closely coupled with the ICP signal where decreased $L Z$ complexity may also be detectable. Consequently, it may be possible to estimate the mean ICP or detect periods of ICH by monitoring the $L Z$ complexity of other physiologic signals such as arterial blood pressure (ABP) and, potentially, SpO2. Figure 2 shows two ICP signals, the corresponding SpO 2 signals recorded simultaneously with each ICP signal, and the $L Z$ complexity calculated on each SpO 2 signal. Note that the $L Z$ complexity evaluated from the SpO 2 signal decreases during periods of ICH. This result has tremendous significance and practical consequences, since it suggests that it may be possible to manage ICP based on noninvasive signals such as SpO 2 in situations where the ICP signal cannot be obtained.

In Fig. 2b the result is particularly promising, since it is impossible to detect any changes in the SpO 2 signal by visual inspection or basic signal analysis. Decreases in $L Z$ complexity during ICH might correspond to a decrease in the stochastic variability of the cardiac component, or a decrease in heart rate variability (HRV).

Based on our simulation studies involving $L Z$ complexity, in the case of pressure signals such as ICP, ABP, and SpO 2 , the $L Z$ complexity measure can be interpreted as a metric that quantifies the bandwidth of the signal harmonics [1]. Thus, decreases in $L Z$ complexity during ICH may correspond to a decrease in the stochastic variability of the cardiac component, or a decrease in HRV. Based on our simulation study [1] and the present work, we conclude that values of $L Z$ complexity in pressure signals typically range from 0.05 to 0.3 . A value close to 1 corresponds to a signal with full bandwidth (i.e. an uncorrelated stochastic process). Values of $L Z$ complexity around 0.05 correspond to periodic signals, and values around 0.2 correspond to quasi-periodic signals with variable harmonics [1]. The results of this study serve to provide further evidence to previous published results involving ApEn analysis of ICP during ICH , and as preliminary results suggesting the


Fig. 2 a, b Preliminary results showing that the $L Z$ complexity evaluated on SpO 2 decreases during periods of ICH. These results suggest that it may be possible to detect periods of ICH by monitoring the $L Z$ complexity of noninvasive signals such as SpO 2
possibility of detection of ICH episodes by monitoring the $L Z$ complexity of noninvasive signals such as SpO 2 . However, the full development of an ICH detection algorithm based on analysis of SpO 2 signals still requires further research.

Future lines of research involve the collection of a large database containing simultaneously recorded ICP and SpO 2 signals free of artefacts during periods of increased ICP and ICH, and the replication of this study to scientifically assess the feasibility of these preliminary results.

## 4 Conclusions

We studied episodes of acute ICH in subjects with brain injury and found that the $L Z$ complexity of ICP decreases during ICH. This result agrees with previous research involving ApEn analysis of ICP during periods of ICH. Furthermore, we reported promising preliminary results that suggest that it may be possible to detect periods of ICH
by monitoring the $L Z$ complexity of noninvasive signals such as SpO 2 . This finding has relevant implications and should be further investigated.

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