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An Experimental Study of Relationship Between Magnetic Induction Phase Shift and Brain Parenchyma Volume With Brain Edema in Traumatic Brain Injury

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ABSTRACT As a very common secondary disease after traumatic brain injury (TBI), brain edema can lead to increased intracranial water content and elevated intracranial pressure (ICP), which makes the patient suffer a less favorable prognosis outcome such as hemiplegia, aphasia, dysgnosia, and even death. Its real-time monitoring is of great significance for improving the therapeutic condition of TBI and reducing the mortality and disability rate. Magnetic induction phase shift (MIPS) has the advantages of non-invasive, non-contact, strong penetration, and real-time bedside monitoring. In this work, 34 rabbits divided into the experimental group (n = 26) and control group (n = 8) were used to carry out 24-h MIPS monitoring in brain edema. Meanwhile, ICP and brain water content (BWC) were chosen as references. The MIPS of rabbits in the experimental group decreased continuously in 24 h, while the ICP and BWC increased. Furthermore, MIPS detection sensitivity became lower and lower within the development of brain edema. The weights of ICP and BWC estimated by MIPS in three different stages were calculated to get the index of brain edema severity (BESI), which can evaluate the severity of brain edema. The BESI of rabbits in the experimental group increased over time, ranging from 0 to 1. The 0 represents normal, and the 1 represents severe brain edema. The first stage of BESI changed from 0 to 0.43, the second stage from 0.43 to 0.917, and the third stage from 0.917 to 1. The BESI of rabbits in the control group did not increase obviously within time. There were significant differences among them. Through the comparative experimental study of MIPS, ICP, and BWC on rabbits with brain edema, a more effective and direct parameter was found, which can promote the application value of MIPS in the real-time bedside monitoring of brain edema.

INDEX TERMS Cerebral edema, magnetic induction, intracranial pressure, brain water content.

I. INTRODUCTION

Traumatic brain injury (TBI) is one of the leading causes of death and disability worldwide [1]. TBI serious enough can result in hospitalization or death and is projected to affect 10 million people annually, plus an estimated 57 million individuals previously hospitalized with two or more TBIs [2].

When the integrity of blood-brain barrier is damaged by TBI, the intercellular junction of brain tissue is destroyed, and the increase of capillary permeability leads to a large amount of water exudation, which accumulates around blood vessels and between nerve cells. Meanwhile, some plasma or proteins also permeate into extracellular fluid with water, which increases the osmotic pressure of extracellular fluid, resulting in abnormal increase of water leakage from vascular wall and edema formation. Some clinical studies demonstrate that the...
presence of brain edema is a significant independent prognostic factor in TBI [3]–[5]. This suggests that brain edema may lead to secondary damage, which disposes the patient to a less favorable outcome [6], [7]. Therefore, real-time monitoring of edema is of great significance for improving the therapeutic condition of TBI and reducing the mortality and disability rate.

At present, invasive ICP monitoring and imaging methods are two ways commonly used for the detection of brain edema. Although invasive ICP monitoring can do real-time observation of the development of edema, it will cause additional pain even infection which aggravates the condition. Imaging methods such as MRI, CT and PET can get rich information about the edema by craniocerebral imaging without invasion. However, these kinds of imaging equipment which are too large and usually set fixed, cannot do real-time monitoring and have low detection time resolution, thus running the risk of delay in diagnosis.

Magnetic induction phase shift (MIPS) is a new method to detect the dielectric properties of biological tissues, which is to use the excitation signal of a certain frequency generated by an excitation coil to generate a main magnetic field in the biological tissue, which will produce an eddy current in the tissues and form a disturbing magnetic field [8]. The intensity of the disturbing magnetic field is related to the structure and physiological state of biological tissues. MIPS with advantages of non-invasiveness, non-contact, strong penetration and small size is expected to become an effective method for continuously bedside monitoring of brain edema. However, due to low dielectric properties of biological tissues, MIPS detection suffers from low sensitivity and poor stability. In the preliminary research process, our research team has been working hard to improve this situation. Based on the symmetrical structure of the left and right hemispheres of the brain, Gui Jin designed a contra-lateral hemisphere cancellation sensor in 2013; this method is more effective for eliminating most of the interference of the main magnetic field, thus significantly improving the detection sensitivity of MIPS [9]. A broadband MIPS detection system was designed and completed by Pan et al. [10] in 2015, by which the sensitivity of MIPS in detecting cerebral hemorrhage was further enhanced. Yan et al. [11] designed a square coil sensor, by analyzing the experimental results of cerebral ischemia and cerebral hemorrhage in rabbits, made preliminary exploration of the feasibility of early identification of two types of stroke (ischemic and hemorrhagic) by MIPS. In the same year, Gen Li designed a set of MIPS brain edema real-time continuously monitoring system, which has high sensitivity and good stability. The 24-hour brain edema monitoring experiment in rabbits showed that MIPS technology could effectively monitor brain edema [12], [13]. However, due to lack of effective references, MIPS cannot classify and identify the severity of brain edema. For different individuals, the progression of brain edema after TBI is not the same. This study also did not expound the relationship between brain parenchyma enlargement and MIPS, which is the direct pathological reaction of brain edema. As an engineering physical quantity, MIPS is intricate for clinician to evaluate the severity of brain edema. More convenient monitoring indicator to reflect the changes of brain parenchymal volume directly need to be proposed.

As a direct quantitative index reflecting the changes of brain parenchyma water content, BWC has been widely used to evaluate the severity of brain edema in clinical and experimental studies [14]. The expansion of the brain parenchyma volume induced by brain edema can directly lead to the raise of ICP. In this work, based on MIPS real-time monitoring system for brain edema constructed by our research group before, ICP and BWC were used as the reference to carry out in-depth experimental study on the rabbit brain edema monitoring. The relationship between brain parenchyma volume changes and MIPS was explored by investigating the relationship between MIPS, ICP and BWC. Finally, a new index which can monitor the severity of brain edema effectively was proposed.

![Figure 1: Consist of MIPS real-time continuous monitoring system for brain edema.](image-url)

**II. MATERIALS AND METHODS**

**A. MIPS REAL-TIME MONITORING SYSTEM FOR BRAIN EDEMA**

MIPS brain edema real-time continuously monitoring system is composed of magnetic induction brain monitor, two coils and real-time continuously monitoring software of brain edema. For observing conveniently, a liquid crystal display is usually added. The equivalent circuit of this system was shown in figure 1. The magnetic induction brain monitor which includes a source, a signal separation module, two receivers, a signal processing module and a display module is the center of the monitoring system. The source can output a stable wide-band signal continuously, and through the signal separation module, two signals within the same amplitude, phase, and frequency range are formed. The one acts as an excitation signal outputs by port 1 and generates the main magnetic field (B) via the excitation coil. The main magnetic field (B) causes an induced current in the brain and forms a disturbing magnetic field (∆B). The detecting coil receives the superimposed magnetic field (∆B+B) and transmits it.
to the receiver 2 through the port 2. The other is used as a reference signal and received directly by the receiver 2. The signal processing module is responsible for processing the detection signal and reference signal independently acquired by the two receivers and calculates the phase difference ($\Delta \theta$) between the two signals, that is, MIPS. Finally, the MIPS is displayed on the screen.

$$\text{MIPS} = \Delta \theta = \theta_{det} - \theta_{ref}$$ (1)

$\theta_{det}$ is the phase of the detection signal, $\theta_{ref}$ is the phase of the reference signal. According to Griffiths et al. [15], when the frequency of the excitation signal is constant, the size of the MIPS is proportional to the amount of change in the overall average conductivity of the brain. Under normal conditions, the brain parenchyma, cerebrospinal fluid (CSF) and cerebral blood flow (CBF) form a dynamic balance of cranial contents. As the increasing of brain parenchyma volume induced by brain edema, CSF first compensates to maintain this balance. When the volume of brain parenchyma is further increased, the compensatory capacity of CSF reaches its limit, and the nervous system maintains balance by regulating CBF. After that, the volume of cranial contents will expand with the continued development of brain edema. Because the conductivities of CSF, CBF and brain parenchyma are different, the changes of cranial contents components and volume can lead to the change of the overall average brain conductivity [12]. Therefore, MIPS can monitor the development of brain edema in real-time.

The development on the magnetic induction detection of biological tissue initially is on the basis of the coaxial-coil. To obtain more universal applicability and value, the traditional coaxial-coil was adopted in this work. Two coils were formed by winding the AWG32 copper-lacquered wire with diameter of 1 mm at both ends of the Plexiglas’s tube, one of which acted as excitation coil and the other as detection coil, with turns of 10. Both the excitation coil and the detection coil had the same radius ($R1 = R2 = 5.2$ cm) and the distance was 10 cm. They were connected to the magnetic induction brain monitor through the high frequency coaxial line [12].

The real-time continuously monitoring software of brain edema can not only help the entire monitoring system complete the automatic setting of MIPS measurement parameters, but also continuously read the MIPS real-time data at any frequency of the excitation signal and display it as a real-time dynamic waveform. Brain edema usually occurs slowly and lasts for several days. This software made the whole monitoring system meet the requirements of real-time monitoring of brain edema in long time.

### B. EXPERIMENTAL METHOD

All the animal experiments involved were approved by the Animal Experimental Ethics Committee of the Army Medical University. The experiment was carried out in accordance with the Helsinki Declaration and IASP guidelines, respecting animal life, reducing animal stress, pain and injury, and euthanasia was adopted after the experiment.

Forty rabbits were divided into experimental group (n=34) and control group (n=6), each weighing 2.2-2.8 kg and averaging 2.5±0.3 kg. Firstly, 25% of 5ml/kg solution was injected into the ear vein to anesthetize the rabbits in the experimental group. Next, the 4.5cm incision was performed along the epidermis of the midline of the cranial roof, exposing the front halogen and the “cross gap”. Referring to the brain atlas of Sawyer rabbits, the intersection points of the “cross suture” was taken as the base point, 6 mm to the right along the coronal suture, and 1 mm backward along the sagittal suture. A bone window about 5 mm in diameter was drilled here to expose the dura mater. Soak in a liquid nitrogen tank for a long time to freeze the pen vertically into the bone window. After freezing, the bone window was sealed with a mixture of dental cement and glue.

Camino invasive ICP monitor was used as a reference. The sagittal suture was used as the axial symmetry position of the lateral ventricle burried tube. The skull was drilled with a drill, which was carried in Camino toolkit. The Camino intracranial pressure fiber probe was then inserted into the ventricle slowly at a depth of about 7 mm and fixed with a bolt (the bolt was self-contained). The rabbits in the control group underwent the same operation with the experimental group but did not freeze.

After operative procedure, the rabbits were lying on the bench, abdomen facing down, limbs facing out, head in the excitation coil and the detection coil axis offset the lower position, about 2.2 cm; frozen position from the excitation coil 3 cm. As shown in figure 2, the rabbit, the ICP monitor and the MIPS brain edema real-time monitoring system were placed reasonably. The excitation signal frequency was set to 64.14396 MHz and the sampling rate of MIPS was 60 times per hour by the real-time continuous monitoring software of brain edema. The ICP sampling rate was set to 60 times per hour to achieve the purpose of synchronous monitoring with MIPS. When the breath rate of rabbits was regular, the real-time and synchronous monitoring of ICP and MIPS was started, and the data of ICP and MIPS were continuously recorded.

The rabbits in the experimental group were divided into four different monitoring time lengths to perform ICP and
MIPS synchronous continued monitoring for 2 hours (n=8), 6 hours (n=8), 12 hours (n=8) and 24 hours (n=10) respectively. When each monitoring process was over, the rabbits were killed immediately by air injection. Then the brain was quickly removed from the cortical surface of the pie mater, cerebellum, brain stem, and placed on an electronic balance to weigh the brain wet weight (BWW), and then placed in a 100° thermostat, baked 72 hours later, and then put on an electronic balance to weigh the brain dry weight (BDW). Finally, BWC was calculated according to the following formula [17].

\[
\text{BWC} = \left[\left(\text{BWW} - \text{BDW}\right)/\text{BWW}\right] \times 100\%
\]

In the control group, the rabbits underwent 24-hour ICP and MIPS real-time synchronous monitoring. BWW and BDW were weighed by the same way, and BWC was calculated as control.

C. MIPS SIGNAL PROCESSING

The sampling rate of MIPS signal is 60 times / time, and the frequency of overall trend change of MIPS is concentrated in the low frequency band. In this experiment, wavelet transform is used to process the MIPS signal. The discrete wavelet decomposition is 8-layer Daubechies wavelet (5th order). The original signal is decomposed into low-frequency A1-A8 according to the frequency band from high to low. The seven layers of A1-A7 are removed, the remaining A8-layer sequence is restored, and the wavelet weight is carried out. The resulting signal is equivalent to removing most of the interference. After filtering, the MIPS signal is re-sampled with the ICP signal at intervals of 30 minutes, and 49 synchronous discrete variables of MIPS and ICP are obtained for further analysis.

D. BESI EXTRACTION METHOD

According to the theory relationship between MIPS and BWC, the sensitivity of MIPS to detect BWC was higher in the early stage, but decreased gradually in the later stage, while ICP was lower in the early stage and higher in the later stage because of intracranial compensation. Because brain edema is a complex pathological process, the relationship between BWC and ICP and MIPS was studied to establish an effective index for evaluating the severity of brain edema (BESI).

After studying the relationship between MIPS and BWC, MIPS and ICP, estimated values of BWC and ICP were obtained. To eliminate the influence of dimension, the estimated values of BWC and ICP were normalized to get \( BWC_{one} \) and \( ICP_{one} \). Then principal component analysis (PCA) was carried out according to the normalized values of BWC and ICP. The formula was as follows:

\[
a = \frac{|\text{Coefficient}_{BWC}|}{|\text{Coefficient}_{BWC}| + |\text{Coefficient}_{ICP}|}
\]

\[
b = \frac{|\text{Coefficient}_{ICP}|}{|\text{Coefficient}_{BWC}| + |\text{Coefficient}_{ICP}|}
\]

Combining the weights and values of the two methods, the severity index (Brain Edema Serious Index, BESI), which can be used to evaluate the severity of brain edema, was obtained. The specific calculation methods were as follows:

\[
\text{BESI} = a \times BWC_{one} + b \times ICP_{one}
\]

E. STATISTICAL ANALYSIS

All of the data were expressed as the mean ± standard deviation from six independent experiments at least. In order to describe the relationship between MIPS and ICP, the MIPS mean of rabbits in the experimental group was taken as independent variable, the ICP mean was taken as dependent variable, and the exponential decay function was selected to carry out the non-linear regression analysis in Origin 9.1 (Origin Lab, Massachusetts, MA, USA). The values of all regression coefficients were determined, and the variance significance F test was carried out. The significance level was set at \( p < 0.05 \). Finally, functional relation between MIPS and ICP was obtained. For researching the relationship between MIPS and BWC, quadratic function was chosen to perform similar nonlinear regression analysis of BWC and MIPS with significance level of 0.05.

In SPSS software version 19.0 (SPSS Inc., Chicago, IL, USA), BESI in different state was tested by multiple independent samples Kruskal-Wallis. The significance level was set at \( p < 0.05 \).

III. RESULTS

A. MIPS&ICP SYNCHRONOUS MONITORING

Figure 3 (a) & (b) showed the mean ± standard deviation (SD) of MIPS and ICP in the experimental group \( n=10 \) and the control group \( n=6 \) within 24 hours, respectively. The MIPS signal in experimental group showed a continuous downward trend with minimum value of -21.097 ± 6.164° at 24th hour, while ICP increased gradually and changed to 36.8 ± 3.458mmHg. The MIPS and ICP of the control group did not increase or decrease obviously within 24 hours, only with small fluctuations around the initial value. The rabbits in the control group underwent the same operation as those in the experimental group only without freezing. Although there may be slight bleeding, both CSF and CBF were in...
normal circulation. As a result, the changes of MIPS in control group were very low. There was no significant change in the control data compared with the experimental group. The results showed that freezing-induced brain edema was the cause of the significant difference between experimental & control group.

Figure 4 (a) showed the average rate of change in terms of MIPS and ICP. On account of the strong intracranial compensatory effect, the change rate of MIPS was much higher than that of ICP from 0th to 2th hour. Next, the change rate of MIPS gradually decreased while ICP gradually increased with the decrease of compensatory effect from 2th to 6th hour. Thereafter, the change rate of MIPS basically remained stable from 6th to 18th hour. At this time, the volume of brain parenchyma continued to expand, accompanied by ICP increasing. Still, the change rate of ICP gradually decreased due to the limited brain volume and intracranial space in rabbits. From 18th to 24th hour, the intracranial space was almost completely occupied by swelled brain parenchyma, and the change rate of MIPS and ICP decreased to the lowest level. Therefore, the pathological process of ICP elevation induced by brain edema can be divided into three stages: compensatory stage, decompensated stage and last stage. Figure 4 (b) showed the changes of MIPS and ICP in these three stages. In the compensatory period, the change range of MIPS was higher than that of ICP, especially in 0-2 hours. In the decompensated period, ICP reversely changed more promptly than MIPS. Eventually, in the last stage, both MIPS and ICP showed a tiny change.

Increased ICP is directly associated with increased brain parenchymal volume as a result of brain edema. Cushing et al. have shown an exponential relationship between ICP and increased intracranial volume [18]. Therefore, the exponential decay function model can better describe the relationship between MIPS and ICP. Thus, this model was used to analyze the three stages of ICP elevation caused by brain edema (Figure 5 (a) (b) (c)). In those three stages, $R^2$ was 0.998, 0.998 and 0.962 respectively, indicating that the fitting effect is extremely reliable.

The non-linear regression analysis of MIPS and ICP showed that in the process of ICP elevation caused by brain edema, the increase of ICP increased exponentially with the exponential attenuation of the decline of MIPS.

**B. RELATIONSHIP BETWEEN MIPS AND BRAIN PARENCHYMA VOLUME**

Figure 6 showed the trend of MIPS and BWC (mean ± SD) in 24h. With the increase of BWC, MIPS showed a continuously descending trend, which was consistent with the physical experiment results by Flores et al. [19]. The enlargement of brain parenchyma volume directly triggered the increase of BWC. The mean value of BWC increased from $(77.215 \pm 0.326\%)$ to $(81.839 \pm 0.296\%)$. Combined with the results of MIPS and ICP simultaneous monitoring experiments, it can be concluded that MIPS constantly declined
thanks to the continuous expansion of brain parenchymal volume.

As shown in Figure 7, the BWC detection sensitivity of MIPS gradually decreased at each stage. The changes of CSF and cerebral blood flow (CBF) in the early stage led to the rapid change in MIPS in the first stage. Afterwards, the MIPS change slowed down. Literally, MIPS contained the information of relative volume change of the cranial contents in addition to the increase in BWC [20]. That is, during the 24-hour monitoring of brain edema, the sensitivity of MIPS to detect brain parenchymal enlargement fell down progressively, and the relationship between MIPS & BWC was not linear.

The quadratic function was used for nonlinear fitting between MIPS and BWC (Figure 8). The fitting result indicated that the $R^2$ practically approaches 1. According to the relationship between BWC and MIPS, it is found that the normal state of BWC was 77.164% before brain edema took place. Along with the development of brain edema, BWC quadratically rose in pace with the decline of MIPS.

### C. BESI

Through the study of the relationship between MIPS & ICP as well as MIPS & BWC, it was found that the MIPS sensitivity to detect the volume changes of brain parenchyma gradually decreased during the development of brain edema. In addition, MIPS is not suitable for medical staff to perform diagnosis as it’s an indirect monitoring parameter. Therefore, this work searched for a more effective monitoring parameter to conduct direct evaluation.

BWC and ICP in each stage of ICP elevation were normalized by principal component analysis. Moreover, the first stage was further divided into two stages: pre-compensatory stage (0-2h) and post-compensatory stage (2-6h). According to the scoring coefficients of BWC and ICP components in each stage (Table 1), the weights of BWC and ICP in each stage can be obtained.

<table>
<thead>
<tr>
<th>Period</th>
<th>Parameters</th>
<th>Component score coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2h</td>
<td>BWC</td>
<td>3.525</td>
</tr>
<tr>
<td></td>
<td>ICP</td>
<td>-2.813</td>
</tr>
<tr>
<td>2-6h</td>
<td>BWC</td>
<td>-2.885</td>
</tr>
<tr>
<td></td>
<td>ICP</td>
<td>3.596</td>
</tr>
<tr>
<td>6-18h</td>
<td>BWC</td>
<td>-129.519</td>
</tr>
<tr>
<td></td>
<td>ICP</td>
<td>130.226</td>
</tr>
<tr>
<td>18-24h</td>
<td>BWC</td>
<td>-2.091</td>
</tr>
<tr>
<td></td>
<td>ICP</td>
<td>2.806</td>
</tr>
</tbody>
</table>

### TABLE 2. BWC and ICP weights for the four periods.

<table>
<thead>
<tr>
<th>Period</th>
<th>The weights of BWC</th>
<th>The weights of ICP</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2h</td>
<td>0.56</td>
<td>0.44</td>
</tr>
<tr>
<td>2-6h</td>
<td>0.45</td>
<td>0.55</td>
</tr>
<tr>
<td>6-18h</td>
<td>0.50</td>
<td>0.50</td>
</tr>
<tr>
<td>18-24h</td>
<td>0.43</td>
<td>0.57</td>
</tr>
</tbody>
</table>

The weights of BWC and ICP in different stages were shown in Table 2. In the first stage (0-2h), BWC weighed heavier than ICP. In the second stage (2-6h), the weight of ICP significantly increased and BWC weighed lighter than ICP owing to the gradually weakened compensation effect. In the third stage, BWC and ICP shared equal weight. The last stage was at the end of compensation and ICP accounted for a larger proportion than BWC.
As shown in figure 9, BESI_T and BESI_C were respectively obtained from the mean MIPS values of rabbits in the experimental group (n=10) and control group (n=6). The value of BESI ranged from 0 to 1, for which 0 represented no brain edema state, and 1 stood for severe brain edema state. During 24 hours, BESI did not increase obviously in the control group, which merely fluctuated around 0. It is clear that no brain edema occurred in the control group. On the contrary, the BESI of experimental group changed from 0 to 0.2 (0-2h), 0.2 to 0.43 (2-6h), 0.43 to 0.917 (6-18h) and 0.917 to 1.0 (18-24h), stating that the severity of brain edema gradually worsened.

The multiple independent samples K-W test results of BESI in six states were shown in the figure 10. The six states were marked as follows: control group (Group 1), 2-hour monitoring group (Group 2), 6-hour group (Group 3), 12-hour monitoring group (Group 4), 18-hour monitoring group (Group 5) and 24-hour monitoring group (Group 6). The statistical value was 51.325 (degree of freedom: 5). The concomitant probability was below significant level. It can be concluded that there must be a certain connection between brain parenchymal volume and MIPS. Essentially, BWC and ICP can directly reflect the change of brain parenchyma volume. In the 24-hour brain edema monitoring experiment, the overall MIPS showed a downward trend along with the gradual increase of BWC & ICP, indicating that MIPS will decrease if brain parenchyma volume swells. In our previous studies, the MIPS signals contained a lot of noise due to somatic movements caused by various anesthesia depths [8]–[13]. Through signal processing method, most of the noise interference was filtered out in this work. Thus, the MIPS signal reflected only the volume change of the brain parenchyma. However, the sensitivity of MIPS detection is significantly affected by the relative position between the coil and objects. The traditional coaxial single excitation & single detection coil apparently have user-friendly limitations. Geometric and parametric optimization in terms of the MIPS detection sensor should be designed in further.

In neurosurgery departments, elevated ICP is an essential reference indicator. ICP monitoring has long been clinically regarded as an important means for brain edema diagnosis [25]. After establishment of freezing-induced brain edema
model in rabbits, ICP did not significantly increase in the early stage due to compensatory mechanism. Yet CSF and CBF have high conductivity so that the decrease of CSF & CBF volume triggered the rapid decrease of MIPS. In other words, MIPS has higher sensitivity than ICP in the early stage. Subsequently, a slight increase in brain parenchyma volume brought about a rapid increase in ICP amid the gradual exhaustion of intracranial compensation [26]. However, at the present time, the volume of CSF and CBF changed faintly and the decline rate of MIPS decelerated, which denoted that ICP and MIPS hold different characteristics in different stages of brain edema. The investigation on the relationship between brain parenchymal volume enlargement and MIPS should be carried out in each stage. The results of the 24-hour ICP monitoring of rabbits in the experimental group varied from each other to some extent, which was caused by the different intracranial compensatory capacity of different rabbits. Rabbits with strong compensatory ability maintained ICP unchanged or changed little over a long period of time, while ICP began to rise faster in those with weaker compensatory ability. According to the average results of simultaneous monitoring by MIPS and ICP, the intracranial compensatory ability gradually collapsed 2 hours after surgery and was basically exhausted at the 6th hour.

BWC is a direct quantitative index reflecting changes in intracranial water content. In clinical and experimental studies of brain edema, BWC is widely used to evaluate the severity of brain edema. Although the dry-wet weighing method is not a conventional clinical detection method, the BWC value can be precisely obtained [27]. At present, MRI is the most frequently used BWC detection method in clinical practice. Under normal circumstances, BWC is highly regulated. Once lesion occurs, pathological changes of BWC can easily be ascertained by MRI [27]. However, the MRI detection device is so bulky that is generally fixed in the department of radiology. Therefore, it is impossible to perform real-time continuously bedside monitoring for patients with brain edema. The increase of BWC will affect the overall average conductivity in brain, which will elicit changes in MIPS. Gonzalez et al. [28] also showed that MIPS change is correlated with the volume of intracranial water. The experimental results in this work revealed that, in the early stage of brain edema, the main reason for rapid change in MIPS is the decrease of CSF and CBF volume during intracranial compensatory process, after which the increase of BWC gradually dominates the development. In the compensatory stage, decompensated stage and final stage when brain edema leads to increased ICP, the sensitivity of MIPS to detect BWC decreased successively, indicating that the relationship between MIPS and BWC is nonlinear. It is reasonable to study the relationship between them through nonlinear regression analysis. However, limited by the small size of the rabbit skull and brain, BWC changed scarcely in a short period of time. Therefore, this experiment only measured the BWC at 5 time points including 2 hours, 6 hours, 12 hours, 24 hours after freezing in the experimental group and 24 hours in the control group. This rooted limitations for the in-depth study of the relationship between MIPS and BWC.

In follow-up studies, the monitoring time will be extended to 48 or 72 hours and the BWC with a large time interval will be measured.

For clinicians, MIPS is not suitable as a direct monitoring indicator of the severity of brain edema. Compared with the reported studies on brain edema detecting by magnetic induction method, this study was the first time to propose a magnetic induction monitoring index BESI which can directly reflect the changes of the brain edema severity. The MIPS sensitivity in detecting brain edema is at a high-level in the early stage and gradually decreases. Also, BWC gradually increases in the process of brain edema. Plus, ICP remains basically unchanged in the early stage and gradually increases in the later stages. Based on those facts, the development of brain edema was divided into different stages in this study and we established a simple and effective evaluation index of brain edema severity (BESI) by using the BWC and ICP estimates obtained by MIPS for objective weight analysis [29]. Before the principal component analysis, the estimation values of BWC and ICP were normalized to eliminate the impact caused by the dimensional difference between them. Compared with other objective weighting methods, the weight obtained through principal component analysis uses the idea of dimensionality reduction to explain most variables in the original data with smaller variables [30], [31]. Therefore, BESI established by the changing rules of BWC and ICP can effectively reflect the process of brain edema and distinguish its different severities. However, the researchers only adopted objective weight analysis and considered the results of principal component analysis merely. In next step, we will broaden the sample size and refer to the actual experience of clinical workers, combining subjectivity with objectivity to obtain more effective weights. In addition, imaging methods can clearly display intracranial images of patients with brain edema, and quantitative data of brain parenchymal volume changes, BWC changes, CSF volume changes and other pathological reactions can be obtained through corresponding technical means [32], [33]. Comparing the imaging method with BESI will enhance the reliability of BESI in the diagnosis and severity evaluation of brain edema.

V. CONCLUSION
In this work, MIPS and ICP synchronous monitoring and BWC measurements at different time points were performed to investigate the relationship between MIPS and brain parenchymal volume enlargement. The results indicated that with the enlargement of brain parenchymal, MIPS showed a continuous downward trend, but the change rate slowed down gradually. The relationship between MIPS and brain parenchymal volume was not linear. Based on the functional relations between MIPS, ICP and BWC, a qualitative and quantitative monitoring parameter-BESI was established, which is more effective and direct for brain edema. It is of great significance for the application of MIPS technology in...
non-invasive, non-contact, real-time bedside monitoring of brain edema.

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REFERENCES


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