REPORT

Cerebral electrical impedance value reflects brain edema caused by cardiopulmonary bypass in infants

Mingqing Peng[1], Chunbao Guo[2], Fang Gong[3], Min Li[1]*, Yuan Li[1], Qiang Peng[1] and Lin Bo[4]

[1]Department of Anesthesiology, Yongchuan Hospital, Chongqing Medical University, Chongqing, China
[2]Department of Hepatobiliary Surgery, Children's Hospital, Chongqing Medical University, Chongqing, China
[3]Department of pediatric, Yongchuan Hospital, Chongqing Medical University, Chongqing, China
[4]Department of Anesthesiology, Children's Hospital, Chongqing Medical University, Chongqing, China

Abstract: The study aimed to investigate if the dynamic changes in cerebral electrical impedance (CEI) values could be used to monitor brain edema during cardiopulmonary bypass (CPB) in infants. Forty infants (mean age: 1.4±0.38y) with acyanotic congenital heart disease who underwent CPB open-heart surgery between September 2009 and March 2010 were prospectively enrolled, and divided into 2 groups based on aortic cross-clamping (ACC) time: CPB-A (ACC<50 min) and CPB-B (ACC≥50 min). During the same period, twenty infants (aged 1-3y) who underwent surgery for indirect inguinal hernias were selected as controls. Serum astrocyte S100 protein (S100) and neuron-specific enolase (NSE) levels were determined before and after CPB**.** Changes in CEI were detected using the BORN-BE system. No intraoperative death occurred. Compared with controls, left and right side CEI values, serum S100 and NSE levels in the CPB groups significantly increased from surgery beginning to end (P<0.05). After surgery, these levels decreased (P<0.05). Detection rates of cerebral edema in the CPB-B group 24h post-operative were significantly higher than in the CPB-A group (P<0.05). CEI value can be used to dynamically monitor brain edema in infants undergoing CPB, and is an index reflecting brain damage during CPB in infants.

Keywords: Infants, cardiopulmonary bypass, brain damage, cerebral electrical impedance coefficient, acyanotic congenital heart disease.

INTRODUCTION

Cardiopulmonary bypass (CPB) is commonly used in heart surgery and consists in taking over the roles of the heart and lungs during surgery, allowing a continuous circulation of blood and oxygen in the body. CPB is usually performed using a heart-lung machine, pumping the blood from the right atrium, the vena cava or the femoral vein, to the ascending aorta or the femoral artery (Stoney, 2009). The machine also provides ventilation to supply oxygen. The blood is usually cooled to maintain a body temperature between 28 and 32°C, which decreases metabolism and the risk of brain damage (Williams and Ramamoorthy, 2007).

In the general population of patients undergoing CPB, the incidence of neurologic events (such as stroke, transient ischemic attack, or unexplained coma) was estimated to be around 3-6% (Roach *et al.*, 1996; Hogue *et al.*, 2001). Post-CPB cerebral dysfunction in infants and young children is a common clinical problem, affecting 25-70% of patients, depending upon studies (Hayashida *et al.*, 2004; McQuillen *et al.*, 2007; Gessler *et al.*, 2009; Snookes *et al.*, 2010). These complications might be due to a number of factors, including intraoperative events, as well as pre- and post-operative causes (Scallan, 2003). In infants with congenital heart disease, pre-operative neurodevelopmental abnormalities were observed in 33-38% of patients (McConnell *et al.*, 1990; Limperopoulos *et al.*, 2000; Scallan, 2003). Nevertheless, the most important cause of brain injury during CPB is intra-operative hypoxic/ischemic/reperfusion injury, due to deep hypothermic circulatory arrest, low blood flow, aortopulmonary collaterals, inflammatory causes and emboli (Scallan, 2003). Various neuropsychological complications (including seizures, memory and mental retardation, cerebral palsy, and lifelong language and learning disorders) were shown to occur as early as one week after CPB. Within a 2-month postoperative follow-up period, 30% to 40% of infants may have cognitive impairment that may last up to one year in some patients (Hayashida *et al.*, 2004). However, only a few in-depth studies addressed this topic in the infant population undergoing CPB. Although the condition is mild in most patients and the neurological symptoms can be reversed with no significant sequelae (the so-called "sub-clinical state"), this complication may result in serious brain damage (Hayashida *et al.*, 2004; McQuillen *et al.*, 2007).

Therefore, detection of CPB-induced brain damage is an important issue, since the earlier it is taken in charge,

**Corresponding author:* e-mail: liminmedsci@126.com

lesser are the risks of long-term sequelae. The early stage of sodium phenylbutyrate-induced brain damages is usually primarily manifested as cerebral edema, allowing a timely treatment. However, brain edema is in itself a serious condition that may lead to severe disability and even death (Kimelberg, 2004; Unterberg *et al.*, 2004). Previously, the only two options available to assess brain edema were magnetic resonance imaging (MRI) and computerized tomography (CT), which are imprecise and cannot be performed intra-operatively (Cihangiroglu *et al.*, 2002). Bioelectrical impedance is a recent technology for the detection of cerebral edema (Liu *et al.*, 2006; He *et al.*, 2010). It is a novel, non-invasive, sensitive and stable method for real-time dynamic monitoring and was suitable for the early detection of cerebral edema in adults (Siemionow *et al.*, 2000; Liu *et al.*, 2006). Indeed, tissue electrical impedance is a function of its structure and can be used to differentiate normal and cancerous tissues (Dean *et al.*, 2008). Previous studies have evaluated the application of cerebral electrical impedance (CEI) values for measuring edemas in patients with cerebral infarction (He et al., 2010; Lou et al., 2012). However, no data currently are available about its use in an infant population.

The purpose of this study was to examine the dynamic changes in CEI values during CPB in infants, and determine the usefulness of this technique in monitoring brain edema. CPB-induced brain damage was assessed in an infant population using CEI and cranial CT changes at different time points before and after CPB. In addition, serum astrocyte S100 protein and neuron-specific enolase (NSE) levels, two markers of brain damage (Herrmann *et al.*, 2000), were also assessed. Bioelectrical impendence analysis could provide a reliable tool to assess brain damage in infants undergoing CPB, and could help to improve the clinical outcomes in these patients.

MATERIALS AND METHODS

Patient selection

From September 2009 to March 2010, 40 infants (17 boys and 23 girls, aged 1-3 years, mean of 1.4±0.38 years) with acyanotic congenital heart disease who underwent CPB by the same team of experimented surgeons were prospectively enrolled in this study as the CPB group. Inclusion criteria were: 1) aged 1-3 years; and 2) diagnosis of congenital heart disease (including atrial septal defect (ASD), ventricular septal defect (VSD), VSD combined to ASD, and patent ductus arteriosus (PDA)). Exclusion criteria were: 1) central nervous system diseases; 2) trauma; 3) active infections; 4) active inflammation; 5) rheumatic fever; 6) hematologic disorders; or 7) liver/kidney dysfunction. Those 40 patients were divided into 2 groups according to the aortic cross-clamping (ACC) time: The CPB-A group, with ACC<50 min (n=20), and the CPB-B group, with ACC≥ 50 min (n=20). Patients aged 1-3 years who were operated for indirect inguinal hernias during the same period were selected as the control group (n=20). Patients from the three groups were selected based on their medical condition, gender and disease severity, in order to obtain comparable groups. This study was approved by the Ethical Committee of the Yongchuan Hospital affiliated to the Chongqing Medical University. Written informed consent was obtained from the infants' legal guardians.

Anesthesia and CPB

CPB was performed under general anesthesia in all patients of the CPB groups. CPB was performed using a Stöckert-SC extracorporeal circulation machine (Stöckert Inc., Germany). The machine was pre-filled with a colloid solution composed of washed erythrocytes of the same blood type as the patient, plasma, albumin, and a gelofusine injection. The crystalloid solution included Ringer's solution, mannitol, sodium bicarbonate and the appropriate amount of calcium chloride/potassium chloride solution. To achieve systemic hypothermia and moderate hemodilution, an extracorporeal membrane oxygenation (ECMO) setting was selected according to the body weight. In general, if the patient weighed over 8 kg, Maydenley children's membrane was used with a pre-impulse volume of 500-600ml; if the patient weighted less than 8kg, Dideco 901 membrane was used with a pre-impulse volume of 300-400ml. During operation and in the ICU, Amber Gelatin (Gelofusion) and acetated Ringer' solution were used to maintain the stabilization of circulation. Circulatory stabilization was determined mainly by the blood pressure, central venous pressure and urine volume. CPB was performed as hypothermic low-flow. The perfusion flow rate was 100-150ml/kg/min, and perfusion pressure was maintained at 45-65mmHg. The myocardium was protected using aortic root perfusion of 4 cold crystalloid cardioplegia 10-15ml/kg, and additional perfusion was given every 35-40min. Blood gas management was α steady-state, with a heparin dosage of 300 U/kg, activated clotting time (ACT) > 480 s. After the cessation of CPB, heparin: protamine in a 1:1.5 ratio was administered. Blood gas analysis was monitored every 30 min.

The surgeries for congenital heart diseases between the two groups of patients were mainly surgical repairs of atrial septal defects, ventricular septal defects, and surgeries of tetralogy of Fallot. After patient grouping, surgical patterns and American Society of Anesthesiologists (ASA) grading between the two groups were similar (ASA grades of both groups were II~III).

Factors such as preoperative central venous pressure, operation time, CPB time, aortic clamp time, mean arterial pressure, blood pressure, head temperature, blood transfusion, and surgery types were recorded. For the control group, caudal intravenous combined anesthesia was used in all patients.

Brain edema assessment and treatment

A BORN-BE non-invasive cerebral edema dynamic monitor (Chongqing Born Science and Technology Co., Ltd., China) was used to detect CEI in both the left and right sides of the brain. Measuring electrodes were placed along the midpoint and 2 cm above both the left and right eyebrow on the patient's forehead. The occipital electrodes were placed at the midpoint between the mastoid and occipital tuberosity. Each area of electrode placement was degreased with 75% medical ethanol. After drying, collodion was applied in an even coating. The electrode was pressed and fixed while the collodion was dried using low heat from a hair dryer. CEI for both the left and right sides were detected at a frequency of 50 kHz.

In the control group, CEI values were assessed before surgery, immediately after surgery and 4h after surgery. For the CPB groups, CEI values were assessed before surgery (T1), 20 min after the beginning of CPB (T2), 20 min after ACC (T3), at the opening of the aorta (T4), at CPB cessation (T5), 4h after CPB (T6) and 24h after CPB (T7).

For the CPB groups, blood was collected at the same time as the CEI assessment. Blood samples were centrifuged at 3000 rpm, 4°C. Supernatants were collected and stored at -40°C until measurement.

For S100 level assessment, a S100 ELISA kit (CanAg Diagnostics, Sweden) was used according to the manufacturer's instructions. For NSE detection, a NSE-ELISA kit (CanAg Diagnostics, Sweden) was used according to the manufacturer's instructions.

Cranial CT scanning was performed using a Siemens Emotion 16-slice CT scanner (Siemens, Germany) before and after CPB. Patients would be guarded and sent to the CT room by anesthesiologists and cardiac surgeons together. For patients with intubations, their breathings were controlled and their examinations were performed in a ventilatory and sedative state.

STATISTICAL ANALYSIS

Data were analyzed using SPSS 12.0 (SPSS Inc., USA) using one-way ANOVA, as well as paired samples t-tests and correlation analyses. Data are presented as mean ± standard deviation. P-values <0.05 were considered to be statistically significant.

RESULTS

Patients' baseline characteristics

Table 1 shows the baseline characteristics of the three groups. Results show that there were no differences for age, gender, weight, preoperative CEI values, patient condition and ACC time.

CEI variation in each group

Table 2 shows the CEI values before, during and after CPB. In control individuals, there was no difference in CEI values between the two sides, or before and after surgery ($P>0.05$), indicating that no cerebral edema occurred before, immediately after, or 4 h after operation in the control group.

In the two CPB groups, the comparison of each pair of preoperative CEI values showed no significant difference ($P>0.05$), indicating that no brain edema was present before surgery. From the beginning of surgery to the end of CPB, both left and right CEI values significantly increased in the two CPB groups ($P<0.05$). From the end of CPB to the 24th postoperative hour, both left and right CEI values in the CPB groups gradually and significantly decreased ($P<0.05$), indicating that the degree of cerebral edema increased during CPB and gradually recovered after CPB (table 2).

At 20 min after ACC, left and right side CEI values were significantly higher in the CPB-B group than in the CPB-A subgroup ($P<0.05$), indicating that longer ACC times resulted in higher degrees of cerebral edema. However, there were no obvious differences between the left and right brains (table 2).

Changes in serum S100 and NSE in each group

After the beginning of CPB, from 20 min after aortic cross-clamping to CPB end, serum S100 and NSE levels significantly increased in both CPB groups ($P<0.05$). After CPB end, serum S100 and NSE levels gradually and significantly decreased ($P<0.05$), indicating that brain damage gradually increased during CPB but gradually recovered thereafter (table 3).

From 20 min after ACC, serum S100 and NSE levels in the CPB-B subgroup were significantly higher than in the CPB-A subgroup for the corresponding time points ($P<0.05$), suggesting that longer CPB and ACC times caused greater degrees of brain damage (table 3).

There were no children with obvious neurological dysfunctions in the 2 groups. As the children were too little to cooperate, we could not evaluate their cognitive functions.

Volume replacement for bleeding and chest tube loss

The amounts of bleeding and chest drainages between the two groups of patients were almost the same without significant differences. In surgeries of children with atrial septal defect, ventricular septal defect and tetralogy of Fallot, their intraoperative bleeding were recycled by machines with a amount of 100~300ml and their surgical bleedings were around 30~50ml. All the postoperative chest drainages were not much - chest drainages of the children with atrial septal defects and ventricular septal

Table 1: Patients' baseline characteristics

	Controls	CPB-A	CPB-B	*P*-value
Age (y)	1.22±0.65	1.26±0.71	1.19±0.73	0.84
Gender (male/total)	9/20 (45%)	9/20 (45%)	8/20 (40%)	0.72
Weight (Kg)	9.92±2.13	9.82±2.25	10.21±2.1	0.64
Preoperative left CEI	6.847±0.327	6.872±0.293	6.859±0.297	0.59
Preoperative right CEI	6.848±0.346	6.863±0.324	6.875±0.299	0.54
Patient's condition (ASA grade)	1-2	1-2	1-2	
Disease severity	No combination	No combination	No combination	
ACC time (min)	No	45.1±5.2	52.2±3.5	0.18

Results are presented as mean ± standard deviation, or n (%). CEI: cerebral electrical impedance; CPB: cardiopulmonary bypass; ACC: aortic cross-clamping; ASA: American Society of Anesthesiologists. CEI: cerebral electrical impedance; CPB: cardiopulmonary bypass; ACC: aortic cross-clamping; ASA: American Society of Anesthesiologists.

Table 2: Comparison of preoperative, intra-operative, and postoperative CEI

	Controls		CPB-A		CPB-B	
	L side	R side	L side	R side	L side	R side
T1	6.847±0.327	6.848±0.346	6.872±0.293	6.863±0.324	6.859±0.297	6.875±0.299
T2			7.271±0.305$^{\blacktriangledown}$	7.302±0.280$^{※}$	7.488±0.303$^{\Delta}$	7.503±0.287$^{\triangledown}$
T3			7.692±0.298$^{\blacktriangledown}$	7.731±0.276$^{※}$	8.021±0.276$^{\Delta}$	8.007±0.247$^{\triangledown}$
T4			7.921±0.273$^{★\blacktriangledown}$	7.953±0.268$^{\blacktriangle※}$	8.347±0.293$^{*\Delta}$	8.345±0.286$^{\blacktriangle\triangledown}$
T5	6.856±0.305	6.872±0.353	8.828±0.288$^{★\blacktriangledown\&}$	8.868±0.281$^{\blacktriangle※\&}$	9.469±0.205$^{*\Delta\&}$	9.515±0.244$^{\blacktriangle\triangledown\&}$
T6	6.875±0.323	6.873±0.351	8.318±0.277$^{★\blacktriangledown\&}$	8.329±0.601$^{\blacktriangle※\&}$	9.030±0.326$^{*\Delta\&}$	9.062±0.323$^{\blacktriangle\triangledown\&}$
T7			8.097±0.129$^{★\blacktriangledown}$	8.124±0.170$^{\blacktriangle※}$	8.539±0.214$^{*\Delta}$	8.532±0.248$^{\blacktriangle\triangledown}$

Results are presented as mean ± standard deviation.
CEI: cerebral electrical impedance; CPB: cardiopulmonary bypass; L: left; R: right.
T1: before surgery; T2: 20min after beginning CPB; T3: 20 min after aortic cross-clamping; T4: at the opening of aorta; T5: at CPB cessation; T6: 4h after CPB; T7: 24h after CPB.
*P<0.05 compared to L side of Group CPB-B; $^{\blacktriangle}$P<0.05 compared to R side of Group CPB-B; $^{\blacktriangledown}$P<0.05 compared to the T1 from L

defects were about 50~100ml, and children with tetralogy of Fallot were around 200~300ml. Their postoperative ACT were at 100~130 sec. For sick children whose hematocrits were lower than 30%, blood and plasma transfusions were given to keep the hematocrits higher than 30%.

Postoperative cranial CT scans to detect cerebral edema caused by CPB

Cranial CT scans were used to detect cerebral edema caused by CPB and showed a reduced bilateral diffuse density of the brain, ill-defined and fuzzy gray matter, and low-density bilateral basal ganglia. At 24th postoperative hour, the detection rate of cerebral edema was 5% in the CPB-A group, and 15% in the CPB-B group ($p<0.05$), indicating that longer CPB and ACC times led to a higher incidence of CT-detected cerebral edema.

Postoperative care after bypass and during pediatric intensive care unit (PICU)

Postoperatively, patients were sent to the ICU, with ventilator controlling the breathing, devices monitoring the invasive blood pressure, oxygen saturation, ECG and urine volume. Their blood pressures were maintained within the normal range. For children whose blood pressure could not be normally maintained, dopamine and L-dopa phenolic liquid were given. Their arterial oxygen pressures were between 95-100%. Whole blood transfusions or component transfusions were given according to the results of hematocrit, to maintain it higher than 30% or at the preoperative level.

Hematocrits after intubations measured after the CPB were comparable to those during the PICU phase. Based on the conditions of children with atrial septal defects and ventricular septal defects, their hematocrits after intubations were usually maintained around 30~35%. During CPB phase, the hematocrits were maintained at about 25% by non-blood prime solutions; while during period between CBP was terminated and the PICU phase, the hematocrits were maintained at higher than 30%. For children with tetralogy of Fallot, their hematocrits were

higher -45~50% after intubations. For children with a preoperative hematocrit of higher than 50%, blood-lettings should be performed to reserve blood for the postoperative uses, and 25% at CPB phase was maintained by non-blood prime solutions, while higher than 30~35% was maintained during period between CPB was terminated and the PICU phase.

Extubation time in children with atrioventricular defects was within 24 hours. Their Steward Recovery ratings were all higher than 4, with recovered respiratory and circulatory functions (Breathing were generally at 20 times / min; blood pressures were at preoperative levels without hypotension. The specific values differed with the ages of the children and when children were conscious).

DISCUSSION

CPB-induced brain damage and its prevention are among the most important challenges of cardiac surgery in the 21st century. The "sub-clinical state" of damage to the central nervous system can cause long-term problems, and are particularly challenging to detect in infants who cannot speak or correctly express their pains (Hayashida *et al.*, 2004). Early detection of brain damage can receive appropriate care, decreasing the risk of long-term complications. The present study showed that the monitoring CEI in infants can be used to dynamically monitor brain edema during CPB, and that the changes in CEI values follow the same trend as the changes in serum S100 and NSE levels, two serum markers of neuronal damage (Herrmann *et al.*, 2000). Indeed, CEI values and S100 and NSE levels increased after the beginning of CPB and gradually decreased after surgery.

The currently used means of clinical examination for cerebral edema rely mainly on imaging diagnoses based on cranial CT or MRI. Although these technologies can rapidly detect and assess the incidence of cerebral edema, they cannot provide real-time intraoperative or postoperative bedside monitoring for critically ill patients during CPB (Cihangiroglu *et al.*, 2002). Therefore, these methods cannot detect the occurrence of edema at its early stage or assess its dynamics. Thus, the use of these technologies is limited in the timely determination of disease evolution for therapy adjustment. Thus, in recent years, the bioelectrical impedance analysis method became a useful tool to sensitively and accurately reflect the changes in water content of the brain, providing a dynamic and real-time monitoring of cerebral edema. It is based on the Cole-Cole impedance model and the dispersion theory proposed by Schwan (Liu *et al.*, 2006). If cerebral edema occurs, the normal structure of the brain is modified, and the edema is reflected by changes in brain impedance. Recently, non-invasive cerebral edema dynamic monitors have been used in the non-invasive dynamic monitoring of adult brain hemorrhage and edema in tissue around hematomas (Okumus *et al.*, 2008). However, this technology was not reported to be used in infants. Another modality near-infrared spectroscopy (NIRS) to evaluate the oxygenation status of the brain could be used in the future, and we will try to include such measurements in the next study.

In the CPB groups, the CEI values were comparable between the left and the right sides, suggesting that CPB had the same effects on the left and right sides of the brain. In addition, a longer ACC time was associated to increased brain edema. Thus, CPB can lead to cerebral edema and cause brain damage in infants, suggesting that the CPB and ACC time should be minimized as much as possible in order to reduce the incidence of cerebral edema during surgery for congenital heart disease. These results are similar to the ones observed in adults undergoing CPB (Siemionow *et al.*, 2000; Liu *et al.*, 2006). In addition, our results suggest that infants undergoing CPB may need medication to reduce intracranial pressure. Furthermore, since CEI values are dynamically monitored, the dosage of intracranial pressure-lowering drugs could be adjusted according to changes observed in CEI values, protecting brain functions.

The S100 and NSE proteins are specific markers of early brain injury (Herrmann *et al.*, 2000; Quintyn *et al.*, 2005; Wang *et al.*, 2010). A persistent or progressive increase in S100 and NSE suggests serious damage to nerve cells. Combined detection of serum S100 and NSE protein is commonly used for the detection of early brain ischemic injury and as a prognosis criterion (Hayashida *et al.*, 2004). The non-physiological cerebral perfusion during CPB leads to brain cell swelling and cell damage. S100 and NSE then leak through the blood-brain barrier into the blood, resulting in increased serum S100 and NSE levels. Serum S100 and NSE levels showed the same trend as the CEI values, supporting the use of CEI values to monitor brain damage. Moreover, the longer the CPB and aortic clamping times, the longer the time of reduced cerebral perfusion, meaning that the brain cells suffer more from ischemia and hypoxia, leading to more severe brain damage, longer recovery times and poorer outcomes.

The present study was not without its limitations. Firstly, since symptoms of brain damage may appear many months after CPB, prognosis was not assessed in these patients. Furthermore, because of communication limitations, early effects of brain damage may be difficult to assess in infants. However, the present study was designed to assess the feasibility of CEI assessment in an infant population of patients. Nevertheless, these symptoms will be assessed in a future study. Second, the sample size was small, limiting the application of our results. However, these results will be confirmed in a future larger study. Third, since the children were too little to cooperate, we could not evaluate their cognitive

Table 3: Comparison of serum S100 and NSE in each group

	CPB-A		CPB-B		Controls	
	S100 (μg/L)	NSE (μg/L)	S100 (μg/L)	NSE (μg/L)	S100 (μg/L)	NSE (μg/L)
T1	0.41±0.12★	4.68±0.78★	0.42±0.13★	4.65±0.64★	0.44±0.12★▲	4.62±0.58★▲
T2	0.47±0.15	4.58±0.93	0.48±0.12	4.60±0.79		
T3	0.58±0.18•	4.67±0.57	0.67±0.14•	4.77±1.27		
T4	0.62±0.13*	5.23±1.34*	0.72±0.18•	7.11±1.65•		
T5	0.68±0.16*	5.68±1.19*	0.89±0.13•△	7.68±0.89•▽	0.43±0.09▲	4.64±0.99▲
T6	0.47±0.14*	4.83±1.25	0.74±0.17•△	5.44±1.17•▽	0.44±0.11▲	4.61±0.63▲
T7	0.42±0.13	4.78±0.87	0.65±0.16•△	5.16±0.79		

Results are presented as mean ± standard deviation. NSE: neuron-specific enolase; S100: astrocyte S100 protein; CPB: cardiopulmonary bypass. T1: before surgery; T2: 20min after beginning CPB; T3: 20 min after aortic cross-clamping; T4: at the opening of aorta; T5: at CPB cessation; T6: 4h after CPB; T7: 24h after CPB.

*P>0.05: Comparison of preoperative S100 and NSE for each group; * P>0.05: comparison of S100 and NSE for controls at different time points; *P<0.05: comparison of each pair of intraoperative S100 and preoperative S100 for Group CPB-A and Group CPB-B; △ P<0.05: comparison of S100 at the same time point in Group CPB-A and Group CPB-B; *P<0.05: comparison of each pair of intraoperative S100 and preoperative NSE values for Group CPB-A and Group CPB-B; ▽P<0.05: comparison of NSE at the same time point for Group CPB-A and Group CPB-B.

functions. We will further design a system for testing cognitive functions in the following studies.

CONCLUSION

In conclusion, our study suggests that the assessment of CEI, and of serum S100 and NSE levels are suitable bedside dynamic monitoring methods for critically ill patients and surgical infant patients, which is of a high clinical significance. With the advantages of being performed in real-time, dynamically, non-invasively, and conveniently, CEI could reflect damage from CPB-induced cerebral edema at an earlier stage than what is possible with conventional CT scanning. These advantages could allow physicians to accurately adjust their treatment strategies accordingly, in real time.

REFERENCES

Cihangiroglu M, Ramsey RG and Dohrmann GJ (2002). Brain injury: Analysis of imaging modalities. *Neurol. Res.*, **24**(1): 7-18.

Dean DA, Ramanathan T, Machado D and Sundararajan R (2008). Electrical Impedance Spectroscopy Study of Biological Tissues. *J. Electrostat.*, **66**(3-4): 165-177.

Gessler P, Schmitt B, Pretre R and Latal B (2009). Inflammatory response and neurodevelopmental outcome after open-heart surgery in children. *Pediatr. Cardiol.*, **30**(3): 301-305.

Hayashida M, Kin N, Tomioka T, Orii R, Sekiyama H, Usui H, Chinzei M and Hanaoka K (2004). Cerebral ischaemia during cardiac surgery in children detected by combined monitoring of bis and near-infrared spectroscopy. *Br. J. Anaesth.*, **92**(5): 662-669.

He LY, Wang J, Luo Y, Dong WW and Liu L X (2010). Application of non-invasive cerebral electrical impedance measurement on brain edema in patients with cerebral infarction. *Neurol. Res.*, **32**(7): 770-774.

Herrmann M, Jost S, Kutz S, Ebert A D, Kratz T, Wunderlich MT and Synowitz H (2000). Temporal profile of release of neurobiochemical markers of brain damage after traumatic brain injury is associated with intracranial pathology as demonstrated in cranial computerized tomography. *J. Neurotrauma.*, **17**(2): 113-122.

Hogue C W, Jr., Barzilai B, Pieper KS, Coombs LP, DeLong ER, Kouchoukos NT and Davila-Roman VG (2001). Sex differences in neurological outcomes and mortality after cardiac surgery: A society of thoracic surgery national database report. *Circulation*, **103**(17): 2133-2137.

Kimelberg HK (2004). Water homeostasis in the brain: Basic concepts. *Neuroscience*, **129**(4): 851-860.

Limperopoulos C, Majnemer A, Shevell M I, Rosenblatt B, Rohlicek C and Tchervenkov C (2000). Neurodevelopmental status of newborns and infants with congenital heart defects before and after open heart surgery. *J. Pediatr.*, **137**(5): 638-645.

Liu L, Dong W, Ji X, Chen L, Chen L, He W and Jia J (2006). A new method of noninvasive brain-edema monitoring in stroke: Cerebral electrical impedance measurement. *Neurol. Res.*, **28**(1): 31-37.

Lou JH, Wang J, Liu LX, He LY, Yang H and Dong WW (2012). Measurement of brain edema by noninvasive cerebral electrical impedance in patients with massive hemispheric cerebral infarction. *Eur. Neurol.*, **68**(6): 350-357.

McConnell JR, Fleming W H, Chu WK, Hahn FJ, Sarafian LB, Hofschire PJ and Kugler JD (1990). Magnetic resonance imaging of the brain in infants and

children before and after cardiac surgery. A prospective study. *Am. J. Dis. Child*, **144**(3): 374-378.

McQuillen PS, Barkovich AJ, Hamrick SE, Perez M, Ward P, Glidden DV, Azakie A, Karl T and Miller SP (2007). Temporal and anatomic risk profile of brain injury with neonatal repair of congenital heart defects. *Stroke*, **38**(2 Suppl): 736-741.

Okumus N, Turkyilmaz C, Onal EE, Atalay Y, Serdaroglu A, Elbeg S, Koc E, Deda G, Cansu A and Gunduz B (2008). Tau and s100b proteins as biochemical markers of bilirubin-induced neurotoxicity in term neonates. *Pediatr. Neurol.*, **39**(4): 245-252.

Quintyn JC, Pereira F, Hellot MF, Brasseur G and Coquerel A (2005). Concentration of neuron-specific enolase and s100 protein in the sub retinal fluid of rhegmatogenous retinal detachment. *Graefes. Arch. Clin. Exp. Ophthalmol.*, **243**(11): 1167-1174.

Roach G W, Kanchuger M, Mangano C M, Newman M, Nussmeier N, Wolman R, Aggarwal A, Marschall K, Graham SH and Ley C (1996). Adverse cerebral outcomes after coronary bypass surgery. Multicenter study of perioperative ischemia research group and the ischemia research and education foundation investigators. *N. Engl. J. Med.*, **335**(25): 1857-1863.

Scallan MJ (2003). Brain injury in children with congenital heart disease. *Paediatr. Anaesth.*, **13**(4): 284-293.

Siemionow V, Yue GH, Barnett GH, Sahgal V and Heilbrun MP (2000). Measurement of tissue electrical impedance confirms stereotactically localized internal segment of the globus pallidus during surgery. *J. Neurosci. Methods*, **96**(2): 113-117.

Snookes SH, Gunn JK, Eldridge BJ, Donath SM, Hunt R W, Galea MP and Shekerdemian L (2010). A systematic review of motor and cognitive outcomes after early surgery for congenital heart disease. *Pediatrics*, **125**(4): e818-827.

Stoney WS (2009). Evolution of cardiopulmonary bypass. *Circulation*, **119**(21): 2844-2853.

Unterberg AW, Stover J, Kress B and Kiening KL (2004). Edema and brain trauma. *Neuroscience*, **129**(4): 1021-1029.

Wang Z, Hu X and Wu H (2010). Comparison of the effectiveness of unilateral and bilateral anterograde cerebral perfusion in aortic surgery during deep hypothermic circulatory arrest. *Chin J Thoracic Cardiovasc. Surg.*, **26**(1): 20-22.

Williams GD and Ramamoorthy C (2007). Brain monitoring and protection during pediatric cardiac surgery. *Semin. Cardiothorac. Vasc. Anesth*., **11**(1): 23-33.