

Received February 15, 2019, accepted April 4, 2019, date of publication April 15, 2019, date of current version April 26, 2019.

Digital Object Identifier 10.1109/ACCESS.2019.2911178

A Dual Parameter Synchronous Monitoring System of Brain Edema Based on the Reflection and Transmission Characteristics of Two-Port Test Network

GEN LI^{1,2}, JINGBO CHEN¹, SHANSHAN GU³, JUN YANG¹, YUJIE CHEN⁴, SHUANGLIN ZHAO¹, JIA XU¹, ZELING BAI¹, (Member, IEEE), JIAN REN⁵, LIN XU¹, MINGSHENG CHEN¹, MINGXIN QIN¹, KWOK WA LEUNG^{1,5}, (Fellow, IEEE), AND JIAN SUN^{1,4,5}

¹College of Biomedical Engineering, Army Medical University, Chongqing 400030, China

²School of Pharmacy and Bioengineering, Chongqing University of Technology, Chongqing 400020, China

³Department of Clinical Psychology, Southwest Hospital, Chongqing 400028, China

⁴Department of Neurosurgery, Southwest Hospital, Chongqing 400028, China

⁵Department of Electronic Engineering, City University of Hong Kong, Hong Kong

Corresponding authors: Mingxin Qin (173117502@qq.com), Kwok Wa Leung (eekleung@cityu.edu.hk), and Jian Sun (30067982@qq.com)

This work was supported in part by the Brain Science Collaborative Innovation Center of Army Medical University, in part by the National Natural Science Foundation of China under Grant 51607181, and in part by the Hong Kong Scholars Program under Grant XJ2017026.

ABSTRACT As a common secondary disease, edema after traumatic brain injury (TBI) can increase brain volume, resulting in elevated intracranial pressure (ICP), brain shift, and cerebral hernia, and can eventually lead to death. The real-time continuous monitoring of edema may significantly reduce mortality and disability. In this paper, a dual-parameter synchronous monitoring system of edema based on the reflection and transmission characteristics of the two-port test network was established; 15 rabbits were chosen to perform 24-h reflection phase shift (RPS) and transmission phase shift (TPS) simultaneously monitoring the experiments of brain edema. With the development of brain edema, the variation law of the RPS and TPS was investigated. Combined with the power amplitude spectrum and the principle of the two-port test network, the influence of frequency on the detection sensitivity of RPS and TPS was analyzed in detail, and the optimal detection frequency point was found. After that, the classification of three different degrees of edema is performed by the BP algorithm. In the animal experiment, the RPS showed a continuous increasing trend within time, and it presented the variation of $(9.35910^\circ \pm 1.65702^\circ)$, $(12.60117^\circ \pm 2.30218^\circ)$, and $(16.33423^\circ \pm 2.11118^\circ)$ after 6, 12, and 24 h, respectively. Meanwhile, the TPS showed a continuous downward trend with the variation of $(-12.62555^\circ \pm 0.99441^\circ)$, $(-19.23976^\circ \pm 1.27488^\circ)$, and $(-27.26285^\circ \pm 2.62291^\circ)$ after 6, 12, and 24 h, respectively. The RPS was negatively correlated with the TPS. The RPS and the TPS together as a recognition feature can achieve 100% accurate classification of three different brain edema severities. Based on these results, it can be concluded that the system established in this paper can monitor gradual increases in brain edema severity. Furthermore, neither the RPS nor the TPS can be set as the recognition feature alone to achieve the completely accurate classification, which shows the necessity of presenting two parameters in the monitoring process.

INDEX TERMS Brain edema, two-port test network, synchronous monitoring, classification.

I. INTRODUCTION

Traumatic brain injury (TBI) is one of the leading causes of death and disability worldwide. TBI serious enough can

The associate editor coordinating the review of this manuscript and approving it for publication was Sabah Mohammed.

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 [1]. Brain edema is a very common secondary disease after TBI. Previous studies demonstrate that the presence of brain edema is a significant independent prognostic factor in TBI [2]–[4].

This suggests that brain edema may lead to secondary damage, which disposes the patient to a less favorable outcome. The additional brain injury stemming from edema may result from local ischemia due to increased intracranial pressure, decreased microcirculatory flow, or neurovascular inflammation [5]–[7]. In addition, the intracellular swelling that characterizes cytotoxic edema after TBI may increase production of reactive oxygen species, known to play an important role in the pathophysiology of TBI [8], [9]. Therefore, the real-time continuous monitoring of brain edema plays a significant role in disease observation, treatment guidance, surgery timing determination and prognosis evaluation for patients after TBI.

Currently, the detection of brain edema mainly depends on imaging equipment, intracranial pressure monitoring, and subjective judgment of clinicians. ICP that is divided into invasive and non-invasive methods can reflect intracranial edema through indirect measurement. With regard to the invasive method, the detection sensors are required to be placed into the cranium, causing pain to patients and easily leading to infection [10]. The non-invasive monitoring of ICP can avoid the risk of infection and cerebral hemorrhage, but it presents several disadvantages in terms of large individual differences, slight inaccuracy and less applications. Non-invasive monitoring of brain edema relies mainly on CT, MRI, DWT, and PET imaging, as well as other detection methods. It is useful to measure computerized tomography (CT) and magnetic resonance image (MRI) within 6 hours of a traumatic brain injury [11]. Serial CT findings in the first 2 days are useful to identify patients at high risk for developing symptomatic swelling [12]. However, imaging detection equipment is very expensive, bulky and difficult to operate. The imaging equipment cannot achieve real-time continuous bedside monitoring for brain edema. The occurrence of brain edema can also be found by the subjective judgments of clinicians [13], but the pathogenesis of brain edema is slow and generally does not cause obvious clinical signs, which obstructs even experienced clinicians to make timely and accurate judgment. Therefore, clinical practice needs a new method for bedside and real-time monitoring of edema urgently.

Magnetic induction phase shift (MIPS) is a non-contact technology which uses induction to obtain electrical parameters from the sample, eliminating the need for electrodes and their related drawbacks [14]. It is well established that the complex electrical impedance of tissue, when measured over a range of frequencies, can be used for tissue characterization [15]. This suggested to us that our design goals could be accomplished with a device that could measure the complex impedance of tissue thus providing valuable information about tissue structure. The volumetric electromagnetic phase-shift spectroscopy (VEPS) method presented by Gonzalez et al. is self-referencing and can be performed in short time, providing instantaneous information [16]. VEPS can be used for diagnosis to detect brain damage and even distinguish patients with edema from those with hematoma [17]. O'Toole et al. described a multi-frequency magnetic induction spectroscopy (MIS) system suitable for industrial-scale,

non-contact, spectroscopic bioimpedance measurement over a bandwidth of 156 kHz–2.5 MHz [18]. However, these measurements were made at a lower frequency range and the limited number of frequencies were restricted to learn detailed information tissue structure. Therefore, in our previous work, a MIPS detection system which can sweep the measured target within the entire frequency range of 300 kHz~200 MHz was constructed [19]. Although this system is basically capable of monitoring gradual increases in the edema solution volume by observing the real-time MIPS change trend, it can't classify and identify the severity of brain edema. For different individuals, the progression of brain edema after TBI are not the same [20]. Therefore, the classification concerning the severity of brain edema can help clinicians to make accurate judgments more effectively and more directly [21], [22]. In addition, the two-port network test system contains the characteristics of reflection and transmission, as mentioned in the previously reported studies, merely using the reflection phase shift (RPS) or Transmission phase shift (TPS) presents disadvantages in terms of low sensitivity and large individual differences [23]–[25], which has brought difficulties for classifying the severity of brain edema. In addition, how the frequency of excitation signal can impact on test results within a wide frequency band and how the RPS and TPS present their variation law after the pathological changes of brain and the relationship each other are not clearly illustrated. These are of great significance for using the magnetic induction method to detect the cerebrovascular diseases such as cerebral hemorrhage, brain edema, and cerebral ischemia and so on [26]–[30].

In this study, a dual parameter synchronous phase shift spectrum monitoring system of brain edema was established by making use of the reflection and transmission characteristics of the two-port test network. In the 24-hour brain edema monitoring experiment of 15 rabbits, the power amplitude spectrums of reflected and transmitted signals within the frequency band of 300kHz–300MHz were obtained. Then, with the development of brain edema, the variation law of both reflection phase shift spectroscopy (RPSS) and transmission phase shift spectroscopy (TPSS) composed of the phase shifts on 1601 frequency points in the scanning range was studied. Combined with the variation of RPSS and TPSS, the power amplitude spectrum and the two-port network test principle, the influence of frequency on the sensitivity was analyzed in detail, and the optimal detection frequency of RPS and TPS was found. Finally, via BP neural network, the classification of three different degrees of brain edema are performed based on 24-hour data of the RPS and TPS at the optimal frequency. By using RPS and TPS respectively as identification features, and both as identification features together, the accuracy of the classification was compared.

II. MATERIALS AND METHODS

A. EXPERIMENTAL SYSTEM

The dual parameter synchronous phase shift spectrum monitoring system of brain edema, as shown in Figure 1, mainly

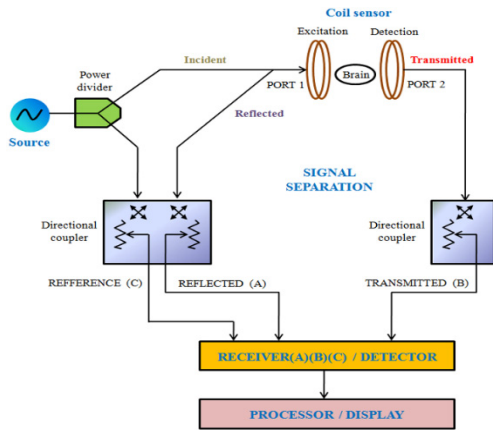


FIGURE 1. Construction of the dual parameter synchronous phase shift spectrum monitoring system.

consists of the coil sensor, the source, the signal separation module, the amplitude and phase receiver and the data processor and display.

The coil sensor consists of the excitation and detection coils with radius $R_1 = R_2 = 5.2$ cm. The two coils were circled by copper lines at the two ends of an organic glass pipe with a diameter of 0.8 mm, and the number of turns $N_1 = N_2 = 10$. The axes of the two coils were symmetrically centered and were arranged in parallel with a distance of 10 cm between them [31]. The excitation signal provided by the source was generally obtained by using the power sweep and frequency sweep approaches. Internally direct digital synthesis (DDS) technique and phase-locked loop (PLL) frequency synthesis technique were adopted, and the frequency resolution was 1 Hz. The signal separation module contained the power divider and the directional coupler. The power divider separates the excitation signal into two identical signals: one is for the incident signal and the other is for the reference signal. The directional coupler separates the incident and reflected waves from the input of the object so as to avoid the crosstalk. The amplitude and phase receiver convert the received radio-frequency signal into the intermediate-frequency signal as required. What's more, the reference signal, the transmission signal and the reflected signal are separately received and processed. The processor and display are for the data processing and display of the test results.

B. DETECTION PRINCIPLE

The excitation signal is divided into the incident signal and the reference signal by the signal separation module. The incident signal is partly transmitted from port 1 to port 2 through the measured target and is partly reflected back to port 1 without passing through the measured target. The reflection coefficient refers to the relationship between the reflected signal and the incident signal:

$$\text{Reflection Coefficient} = \frac{V_{\text{reflection}}}{V_{\text{incident}}} = \rho \angle \theta \quad (1)$$

The transmission coefficient refers to the relationship between the transmission signal and the incident signal:

$$\text{Transmission Coefficient} = \frac{V_{\text{transmitted}}}{V_{\text{incident}}} = \tau \angle \varphi \quad (2)$$

where ρ and τ are the amplitude of reflection coefficient and transmission coefficient respectively. θ and φ are the phase of reflection coefficient and transmission coefficient respectively.

The size of ρ and τ determines the efficiency of reflection and transmission, affecting the sensitivity and stability of the entire monitoring system. This brings the problem of impedance matching. When the impedance matching is better, the loss of the entire monitoring system is lower, the detection sensitivity is higher, the stability is better and the anti-interference ability is stronger [32]. In this study, the power sweep method is adopted to study the impedance matching problem by scanning the amplitude spectrum of the reflection and transmission.

The magnitude of θ and φ are related to the dielectric properties of the measured target [33]. When its dielectric property is changed, the θ and φ will shift, being defined as RPS and TPS respectively. Regardless of the mechanisms of edema, accumulation of fluid and a change in the water composition of the tissue is bound to change the dielectric properties of tissue. Through the RPSS and TPSS variation which contains 1601 RPS and TPS within the frequency range of 300 kHz-300MHz respectively, a dual parameter synchronous dynamic monitoring of brain edema was achieved in this study. Furthermore, the monitoring system is equipped with a software controller to complete the setting of the measurement parameters and realize the real-time continuous data collection of the RPSS and TPSS automatically.

C. ANIMAL EXPERIMENT

All animal experiments were performed in accordance with the guidelines from the Administration of Animal Experiments for Medical Research Purposes issued by the Ministry of Health of China. The protocol used was reviewed and approved by the Animal Experiments and Ethical Committee of Third Military Medical University (TMMU, Chongqing, China). All efforts were made to minimize the suffering of rabbits during experiments. Fifteen rabbits (available from the Laboratory Animal Center of the Third Military Medical University, weighing 2.0-2.6 kg and marked No.1 to No.15) were first injected with urethane (25%, 5 ml) in an ear vein for anesthesia. The hair was removed from the head, and then a hole was drilled beside the "cross stitch" of the brain, forming a 5 mm × 5 mm bone window and exposing the dura-mater. Next, a cryopencil was immersed in liquid nitrogen for a sufficient time and was then put into the bone window for freezing. The freezing temperature was -196°C and the freezing time was 120 seconds; dental cement was used to seal the bone window.

As shown in Figure 2, the rabbits were placed into the coil sensor after above operation. When the life physical signs of

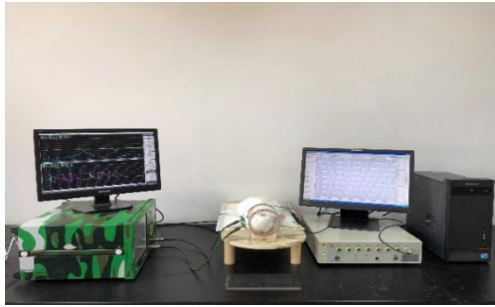


FIGURE 2. Experimental setup to monitor brain edema in rabbits with the dual parameter synchronous phase shift spectrum monitoring system.

the rabbit were stable, a 24-hour continuous collection of the RPSS and TPSS data was conducted with a sampling rate of 2 times / hour.

D. STATISTICAL ANALYSIS

All the data are expressed as the mean \pm standard deviation from 10 independent experiments at least. In the animal experiment, the RPS after 6, 12 and 24 hours and the TPS after 6, 12 and 24 hours at the optimal detection frequency were analyzed with a paired-samples t-test respectively. The significance level was set at $\alpha = 0.05$. In addition, The Pearson correlation analysis of the 24-hour RPS and the 24-hour TPS was performed at the optimal detection frequency. The significance level was set at $\alpha = 0.05$. Statistical analyses were performed using SPSS software version 19.0 (SPSS Inc., Chicago, USA).

E. BP NEURAL NETWORK FOR BRAIN EDEMA SEVERITY

Brain edema after TBI is a complex process. Based on the reported work, rabbits developed a severe brain edema 6 hours after freezing outside the dural mater, and the development of edema presented a progressive feature and peaked at the 24th hour [34]. Brain water content obtained by wet-dry weighing method is an accurate quantitative index for evaluating the severity of pathological changes in brain edema. Previous studies have shown that the brain water content of the brain tissue after 6 hours, 12 hours, and 24 hours were (79.875 \pm 0.28454)%, (81.016 \pm 0.28764)%, (82.126 \pm 0.2785)% and there was significant difference [35]. The model of brain edema and the surgical procedure are exactly the same as before. Therefore, 6 hours, 12 hours and 24 hours after freezing were defined as the three degrees of brain edema in this work. By using BP neural network, the classification of the three degrees of brain edema was performed at the optimal detection frequency points. Twelve groups of experimental data (N = 36) were randomly selected as training samples, and three experimental data (N = 9) were used as test samples. In the process of identification, RPS and TPS respectively and both together were used as recognition features, and the test samples were identified for three times. The MATLAB neural network toolbox was used to set up the model, the hidden layer node was set to 6 and the output layer

node was set to 1. The hidden layer function was set as hyperbolic tangent sigmoid function and the output layer function was set as linear regression function. The training target was set to 0.00001. What's more, normalization was performed before the feature entered the neural network training.

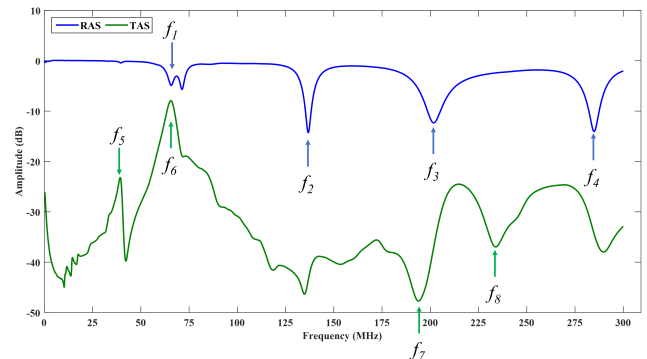


FIGURE 3. The average power amplitude spectrum of the reflected and transmitted signals in 15 rabbits.

III. RESULTS

A. EFFECT OF FREQUENCY ON RPSS AND TPSS DETECTION

The power amplitude spectrums of the reflected and transmitted signals were shown in Figure 3. f_1 (64.14859 \pm 0.77481MHz), f_2 (136.8913 \pm 1.88573MHz), f_3 (202.88471 \pm 2.06434) and f_4 (285.56394 \pm 2.68748) were four frequency points of excitation signal. They presented larger return loss of the reflected signal, and f_1 corresponded to f_6 (64.14396 \pm 0.31592MHz) which featured in the minimum insertion loss of the transmission signal. This indicated that the return loss of f_1 was due to the fact that most of the incident signal was transmitted to port 2 through the brain. Under this condition, the impedance matching was good, the efficiency of the entire monitoring system was higher so that both the RPS and the TPS should present higher sensitivity. In contrast, f_2 , f_3 and f_4 corresponded to the three frequency points which feature in larger insertion loss of the transmission signal. It indicated that most of the energy was lost in the signal transmission and reflection process. Then the impedance matching was very poor. The poor impedance matching will lead to the relatively weak energy of the incident signal itself [36]. These combined factors cause the lower sensitivity and stability of the RPS and the TPS.

According to above analysis of power and amplitude spectrum from reflected and transmission signals based on two-port testing principle, it can be inferred that when detecting brain edema on the system established in this work, f_1 is the ideal detection frequency point for RPS and f_6 is the optimal frequency point for TPS detection. Ideally, the frequency which features in the maximum transmission efficiency should correspond to the frequency of minimum reflection efficiency [37]. In this work, the frequency which features in the maximum amplitude of the transmission signal can be used in both RPS and TPS detection within a certain error range.

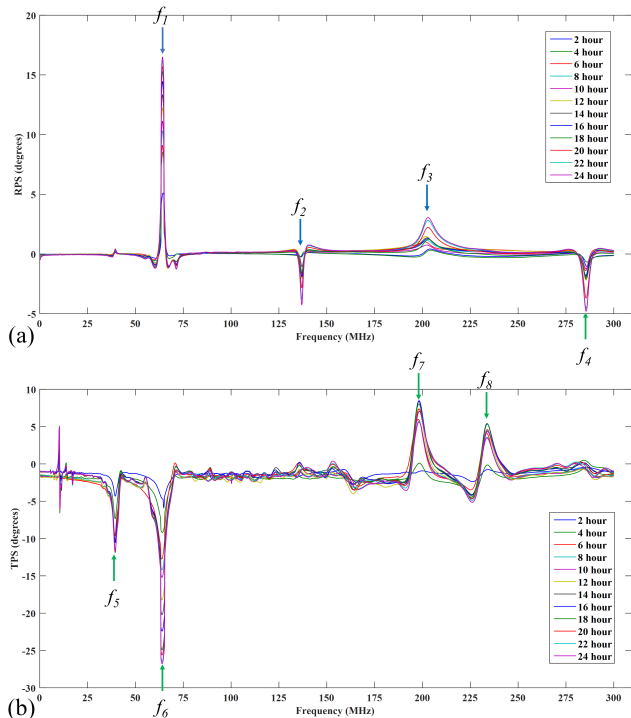


FIGURE 4. (a) The 24-hour average RPSS results of the 15 rabbits after freezing. (b) The 24-hour average TPSS results of the 15 rabbits after freezing.

B. RPSS AND TPSS CHANGES IN 24-HOUR

The 24-hour average RPSS results of the 15 rabbits after freezing were shown in Figure 4(a). With the development of brain edema, the RPS of f_1, f_2, f_3 and f_4 presented obvious variation where f_1 had the largest variation range. And the rest of the frequency points on the band of 300 KHz-300 MHz had no obvious changes. In the 24-hour average TPSS results of the 15 rabbits, as shown in Figure 4(b), the TPS of f_5, f_6, f_7 and f_8 showed obvious changes, and the detection sensitivity of f_6 was the highest. The remaining frequency points also presented variation but with no obvious variation law, featuring in smaller variation range. These results were consistent with the inference that f_1 was the ideal detection frequency point for RPS and f_6 was the optimal frequency point for TPS detection.

Figure 5 showed the 24 hours variation trend of the RPS at f_1 and the TPS at f_6 . The RPS at f_1 showed a continuous increase trend within time, and it presented the variation of $9.35910 \pm 1.65702^\circ$, $12.60117^\circ \pm 2.30218^\circ$ and $16.33423 \pm 2.11118^\circ$ after 6,12 and 24 hours respectively. Meanwhile, the TPS on the frequency of f_6 performed a downward trend in 24-hour, which was consistent with our previous work. It showed the variation of $-12.62555 \pm 0.99441^\circ$, $-19.23976 \pm 1.27488^\circ$ and $-27.26285 \pm 2.62291^\circ$ after 6,12 and 24 hours respectively. Edema can lead to the variation in the total dielectric coefficient of the brain, thus inevitably leading to variation in the reflected signals [16], [17], [19]. Hence the continuous increase trend of the RPS at f_1 can also reflect the development of brain edema.

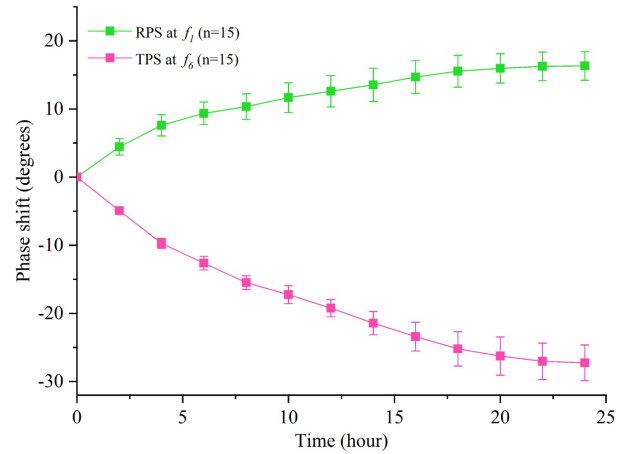


FIGURE 5. The mean \pm standard deviation 24-hour trend of the RPS at f_1 and the TPS at f_6 .

For the RPS after 6, 12 and 24 hours and the TPS after 6, 12 and 24 hours, the paired T-test, featuring in a significant level of 0.05, were conducted. And the results were shown in Table 1. The P values of each group were less than 0.05, indicating that there were significant differences in the RPS and TPS at 6h, 12h and 24h after freezing. Therefore, the RPS and the TPS at the 3 time points (6, 12, 24 hours post freezing) were used for classification of brain edema severity levels in this study.

TABLE 1. Paired t-test of TPS and RPS after 6, 12, and 24 hours.

Parameter	Sample	Confidence Interval		t	df	sig.
		Upper Limits	Lower Limits			
RPS	6h & 12h	-3.845	-2.351	-8.891	14	3.921×10^{-7}
	6h & 24h	-7.776	-5.706	-13.967	14	1.302×10^{-9}
	12h & 24h	-4.544	-2.742	-8.671	14	5.294×10^{-7}
TPS	6h & 12h	5.816	7.247	19.585	14	1.427×10^{-11}
	6h & 24h	12.827	15.902	20.036	14	1.048×10^{-11}
	12h & 24h	6.701	8.965	14.844	14	5.830×10^{-10}

C. CLASSIFICATION OF BRAIN EDEMA SEVERITY

Three different severity levels (1, 2, 3) of the brain edema corresponding to the RPS and TPS were classified. Twelve group were selected as training samples (N = 36). As shown in Figure 6 (a), the number of training sessions reached 1000 times and took 4 seconds under ordinary PC. As the number of training increased, the mean square error gradually decreased, indicating that the training gradually converged. As shown in Figure 6 (b), the R value was 0.97992 in the given fitting equation, indicating that the fitting effect was very good.

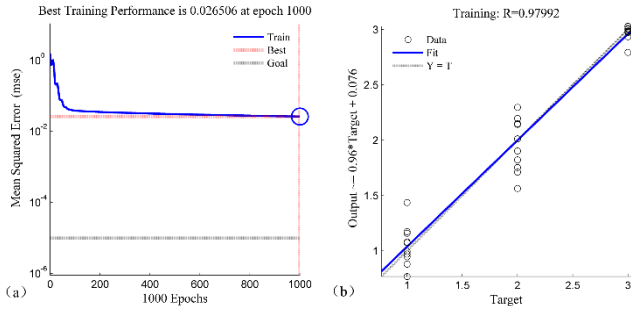


FIGURE 6. (a) Error performance analysis of the BP algorithm. (b) Regression analysis of the BP algorithm.

The rest three groups (A, B, C) were set as test samples (N = 9), which were numbered in the chronological order as A1, A2 and A3; B1, B2 and B3; C1, C2 and C3 respectively. The test results were shown in Figure 7.



FIGURE 7. The classification result of three different severity levels (1, 2, and 3) of the brain edema.

When the RPS was identified as an identification feature, the A1 was mistakenly recognized as 2, the C2 was mistakenly recognized as 1 and the C3 was mistakenly recognized as 2, but the remaining test samples presented correct recognition, so the correct rate of recognition was 66.67%; when the TPS was identified as a recognition feature, the B1 was mistakenly recognized as 2 and the C3 was mistakenly recognized as 2, so the correct rate of recognition was 77.78%. However, when both the RPS and TPS were identified as identification features, all the 9 test samples were identified correctly and the correct rate of recognition was 100%. In the 24-hour rabbit's brain edema monitoring experiment, both the RPS and the TPS can reflect the increases in the brain edema solution, but in the classification of different degrees of severity, it was better to use both the TPS and the RPS as the recognition features, which presented a better outcome than the respective way. This indicates that using the parameters

of RPS and TPS can achieve a more effective classification concerned.

IV. DISCUSSION

The establishment of the brain edema monitoring system that is safe for animals or human beings was based on the two-port test network and it shows several advantages, namely, being non-invasive, non-contact, small size and so on. After the edema, the changing of brain volume and the brain water content cause the variation in the total average dielectric coefficient of the brain, so that the RPSS and the TPSS are changed. In the previous work, the target field accounts for a small proportion of the whole disturbing magnetic field. Hence, the signal of interest is extremely weak [23]–[30]. In this work, within the frequency range of 300kHz-300MHz, combined with the power amplitude spectrum which reflects the signal reflection and transmission efficiency of the two-port network and the variation of the RPSS and the TPSS which reflected the increase of the brain edema solution volume, the optimal detection frequency featuring in the better impedance matching and the higher sensitivity and stability of the RPS and the TPS were found.

The mechanism of the frozen traumatic brain injury model was single, simple, and easy for qualitative research [38]. The blood-brain barrier in rabbits after freezing was damaged, and vasogenic brain edema rapidly occurred accompanied by cytotoxic brain edema. And the development of edema was progressive and peaked after 24 hours. The BWC at the 24th hour after freezing was significantly higher than that of the rabbits without freezing [19], [35]. The RPS and the TPS showed a trend of a rapid variation in the early period, but a gradual decline in the late period, which was consistent with the mechanism of this brain edema model induced by freezing. Compared with the RPSS and TPSS results of animal experiments, it is not difficult to find that the RPSS is more consistent, but the TPSS is quite different, which is determined by different properties between the transmitted signals and the reflected signals. When the incident signal is transmitted to the measured target through port 1, a part of the signal penetrates the measured target and reaches port 2, that is, the transmission signal. The other part of the signal does not penetrate the measured target, but directly being reflected back to port 1, that is, the reflected signal. Hence the TPSS contains more information on the changes of the internal dielectric coefficient of the measured target than that of the RPSS [39]. According to the law of energy conservation, the energy sum of the reflected signal and the transmitted signal is equal to the energy of the incident signal, and the change of the transmitted signal strength will inevitably cause the change of the reflected signal [40]. The Pearson correlation analysis of the 24-hour RPS and the 24-hour TPS with a significance level of 0.05 was performed at the optimal detection frequency. The results are shown in Table 2. The correlation coefficient between the 24-hour RPS and the 24-hour TPS of 15 rabbits was between -0.993 and -0.949,

TABLE 2. Correlation analysis of RPS and TPS.

Sample	Correlation Coefficient	P values
No.1 rabbit	-0.986	2.068×10^{-38}
No.2 rabbit	-0.967	1.876×10^{-29}
No.3 rabbit	-0.959	2.236×10^{-26}
No.4 rabbit	-0.971	8.338×10^{-31}
No.5 rabbit	-0.987	4.060×10^{-39}
No.6 rabbit	-0.985	9.528×10^{-38}
No.7 rabbit	-0.971	7.858×10^{-33}
No.8 rabbit	-0.988	1.442×10^{-39}
No.9 rabbit	-0.986	6.269×10^{-38}
No.10 rabbit	-0.984	6.320×10^{-37}
No.11 rabbit	-0.966	3.565×10^{-29}
No.12 rabbit	-0.989	2.093×10^{-40}
No.13 rabbit	-0.949	2.809×10^{-25}
No.14 rabbit	-0.993	2.300×10^{-45}
No.15 rabbit	-0.986	2.068×10^{-38}

and the P values were less than 0.05, indicating a highly negative correlation between the RPS and the TPS. Combined with the experimental results of the animal experiments, it is proved that the variation of both the RPS and the TPS can reflect the development of the brain edema.

The BP algorithm learns through the training samples. By changing the weights and thresholds of the internal connection so as to achieve the smallest error between the output value and the target value, thus achieving the purpose of modeling [41]. It is currently one of the most widely used artificial neural networks featuring in the most intuitive way of achievement, the easiest way to understand the computing mechanism and in-depth studies. In this work, the established training model presented fast convergence speed and good fitting effect, which met the expected requirements. However, the differences of compensatory capacity, depth of anesthesia and physical condition, etc. among the 15 rabbits resulted in a certain difference in the 24-hour phase shift at the optimal frequency. Therefore, neither the RPS nor the TPS can be set as the recognition feature alone to achieve the completely accurate classification of different degrees of brain edema. But RPS and TPS together as a recognition feature can achieve 100% accurate classification, which shows the necessity of presenting two parameters in the monitoring process. However, there are some shortcomings in the BP algorithm, such as the initial weights and thresholds should not be artificially created in neural networks. This will cause bias in the model, and also lose the advantages of neural network models as universal function [42]. In addition, the selection of samples is critical to the quality of the training model and should be comprehensive and typical [43]. In the future, the research group will improve the existing algorithm based on the expansion of the sample size and will compare with other algorithms.

V. CONCLUSION

This study established a dual parameter synchronous phase shift spectrum monitoring system of brain edema based on the reflection and transmission characteristics of the two-port network test system. This method has advantages of noninvasiveness, noncontact, good portability, and real-time continuous bedside monitoring. Combined with the power amplitude spectrum of the reflected and transmitted signals and the two-port network test principle, the optimal detection frequency of RPS and TPS with a better impedance matching is found. Based on the RPS and TPS at the optimal detection frequency, three different degrees of brain edema were classified correctly, and the correct rate of recognition was 100%. But the three different degrees of brain edema were only determined by the BWC which is too simple for clinical application. Therefore, other experimental animal models such as weight-drop-induced TBI will be used to mimic closed-head injury in humans [44]. Combined with the neurological function score (NFS) [45], the RPS, the TPS and the ICP monitoring results and the imaging results, the weighted regression analysis will be performed to complete a more comprehensive classification of brain edema, which contributes to the clinical trials in the future.

ACKNOWLEDGMENT

(Gen Li and Jingbo Chen contributed equally to this work.)

REFERENCES

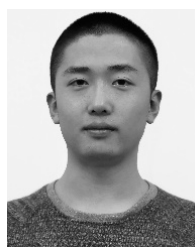
- [1] B. Tucker *et al.*, "Early brain edema is a predictor of in-hospital mortality in traumatic brain injury," *J. Emergency Med.*, vol. 53, no. 1, pp. 18–29, 2017.
- [2] F. Corrigan, A. Arulsamy, J. Teng, and L. E. Collins-Praino, "Pumping the brakes: Neurotrophic factors for the prevention of cognitive impairment and dementia after traumatic brain injury," *J. Neurotrauma*, vol. 34, no. 5, pp. 971–986, 2016.
- [3] M. S. Sekhon, N. Mclean, W. R. Henderson, D. R. Chittock, and D. E. Griesdale, "Association of hemoglobin concentration and mortality in critically ill patients with severe traumatic brain injury," *Crit. Care*, vol. 16, no. 4, p. R128, 2012.
- [4] F. Lauzier *et al.*, "Clinical outcomes, predictors, and prevalence of anterior pituitary disorders following traumatic brain injury: A systematic review," *Crit. Care Med.*, vol. 42, no. 3, pp. 712–721, 2014.
- [5] C. J. C. Trepte *et al.*, "Electrical impedance tomography (EIT) for quantification of pulmonary edema in acute lung injury," *Crit. Care*, vol. 20, no. 1, pp. 1–18, 2015.
- [6] R. M. Jha *et al.*, "Sulfonylurea receptor-1: A novel biomarker for cerebral edema in severe traumatic brain injury," *Crit. Care Med.*, vol. 45, no. 3, pp. e255–e264, 2017.
- [7] X. Dai *et al.*, "High intracranial pressure induced injury in the healthy rat brain," *Crit. Care Med.*, vol. 44, no. 8, pp. e633–e638, 2016.
- [8] F. Clausen, N. Marklund, A. Lewén, and L. Hillered, "The nitron free radical scavenger NXY-059 is neuroprotective when administered after traumatic brain injury in the rat," *J. Neurotrauma*, vol. 25, no. 12, pp. 1449–1457, 2008.
- [9] Y. Xing, Y. Hua, R. F. Keep, and G. Xi, "Effects of deferoxamine on brain injury after transient focal cerebral ischemia in rats with hyperglycemia," *Brain Res.*, vol. 1291, no. 4, pp. 113–121, 2009.
- [10] V. Rajajee, R. J. Fontana, A. J. Courey, and P. G. Patil, "Protocol based invasive intracranial pressure monitoring in acute liver failure: Feasibility, safety and impact on management," *Crit. Care*, vol. 21, no. 1, p. 178, 2017.
- [11] E. L. Yuh *et al.*, "Magnetic resonance imaging improves 3-month outcome prediction in mild traumatic brain injury," *Ann. Neurol.*, vol. 73, no. 2, pp. 224–235, 2013.

- [12] E. F. Wijdicks *et al.*, "Recommendations for the management of cerebral and cerebellar infarction with swelling: A statement for healthcare professionals from the American Heart Association/American Stroke Association," *Stroke*, vol. 45, no. 4, pp. 1222–1238, 2014.
- [13] X. Meng and B. Shi, "Traumatic brain injury patients with a glasgow coma scale score of ≤ 8 , cerebral edema, and/or a basal skull fracture are more susceptible to developing hyponatremia," *J. Neurosurg. Anesthesiol.*, vol. 28, no. 1, pp. 21–26, 2016.
- [14] H. Griffiths, "Magnetic induction tomography," *J. Commun. Technol. Electron.*, vol. 12, no. 8, pp. 1126–1131, 2001.
- [15] H. Scharfetter, R. Casanas, and J. Rosell, "Biological tissue characterization by magnetic induction spectroscopy (MIS): Requirements and limitations," *IEEE Trans. Biomed. Eng.*, vol. 50, no. 7, pp. 870–880, Jul. 2003.
- [16] C. A. González, C. Villanueva, C. Vera, O. Flores, R. D. Reyes, and B. Rubinsky, "The detection of brain ischaemia in rats by inductive phase shift spectroscopy," *Physiol. Meas.*, vol. 30, pp. 809–819, Jun. 2009.
- [17] C. A. González, J. A. Valencia, and M. Alfredo, "Volumetric electromagnetic phase-shift spectroscopy of brain edema and hematoma," *PLoS ONE*, vol. 8, no. 5, 2013, Art. no. e63223.
- [18] M. D. O'Toole, L. A. Marsh, J. L. Davidson, Y. M. Tan, D. W. Armitage, and A. J. Peyton, "Non-contact multi-frequency magnetic induction spectroscopy system for industrial-scale bio-impedance measurement," *Meas. Sci. Technol.*, vol. 26, no. 3, 2015, Art. no. 035102.
- [19] G. Li, K. Ma, J. Sun, G. Jin, M. Qin, and H. Feng, "Twenty-four-hour real-time continuous monitoring of cerebral edema in rabbits based on a noninvasive and noncontact system of magnetic induction," *Sensors*, vol. 17, no. 3, p. 537, 2017.
- [20] D. W. McBride, J. I. Szu, C. Hale, M. S. Hsu, V. G. J. Rodgers, and D. K. Binder, "Reduction of cerebral edema after traumatic brain injury using an osmotic transport device," *J. Neurotrauma*, vol. 31, no. 23, pp. 1948–1954, 2014.
- [21] X. Wang, X. Gao, S. Michalski, S. Zhao, and J. Chen, "Traumatic brain injury severity affects neurogenesis in adult mouse hippocampus," *J. Neurotrauma*, vol. 33, no. 8, pp. 721–733, 2016.
- [22] L. A. S. Chapple, M. J. Chapman, K. Lange, A. M. Deane, and D. K. Heyland, "Nutrition support practices in critically ill head-injured patients: A global perspective," *Crit. Care*, vol. 20, no. 1, p. 6, 2016.
- [23] G. Jin *et al.*, "A new method for detecting cerebral hemorrhage in rabbits by magnetic inductive phase shift," *Biosensors Bioelectron.*, vol. 52, no. 4, pp. 374–378, 2014.
- [24] W. Pan *et al.*, "Detection of cerebral hemorrhage in rabbits by time-difference magnetic inductive phase shift spectroscopy," *PLoS ONE*, vol. 10, no. 5, 2015, Art. no. e0128127.
- [25] A. Barai, S. Watson, H. Griffiths, and R. Patz, "Magnetic induction spectroscopy: Non-contact measurement of the electrical conductivity spectra of biological samples," *Meas. Sci. Technol.*, vol. 23, no. 8, pp. 755–766, 2012.
- [26] M. Zolgharni, P. D. Ledger, D. W. Armitage, D. S. Holder, and H. Griffiths, "Imaging cerebral haemorrhage with magnetic induction tomography: Numerical modelling," *Physiol. Meas.*, vol. 30, pp. S187–S200, Jun. 2009.
- [27] G. Jin *et al.*, "A special phase detector for magnetic inductive measurement of cerebral hemorrhage," *PLoS ONE*, vol. 9, no. 5, 2014, Art. no. e97179.
- [28] G. Li *et al.*, "Construction of a cerebral hemorrhage test system operated in real-time," *Sci. Rep.*, vol. 7, Feb. 2017, Art. no. 42842.
- [29] J. Sun, G. Jin, and M. X. Qin, "Detection of acute cerebral hemorrhage in rabbits by magnetic induction," *Brazilian J. Med. Biol. Res.*, vol. 47, no. 2, pp. 144–150, 2014.
- [30] J. Ljungqvist *et al.*, "Clinical evaluation of a microwave-based device for detection of traumatic intracranial hemorrhage," *J. Neurotrauma*, vol. 34, no. 13, pp. 2176–2182, 2017.
- [31] Q. G. Yan, G. Jin, M. Qin, J. Zhao, J. Wang, and J. Sun, "Experimental study on the detection of rabbit intracranial hemorrhage using four coil structures based on magnetic induction phase shift," *Biomed. Eng./Biomed. Tech.*, vol. 62, no. 1, pp. 23–36, 2016.
- [32] C. Qian and W. W. Brey, "Impedance matching with an adjustable segmented transmission line," *J. Magn. Reson.*, vol. 199, no. 1, pp. 104–110, 2009.
- [33] S. Laufer, S. B. Solomon, and B. Rubinsky, "Tissue characterization using electrical impedance spectroscopy data: A linear algebra approach," *Physiol. Meas.*, vol. 33, no. 6, pp. 997–1013, 2012.
- [34] N. Kawai, M. Kawanishi, M. Okada, Y. Matsumoto, and S. Nagao, "Treatment of cold injury-induced brain edema with a nonspecific matrix metalloproteinase inhibitor MMI270 in rats," *J. Neurotrauma*, vol. 20, no. 7, pp. 649–657, 2003.
- [35] G. Li *et al.*, "A non-invasive non-contact continuous monitoring system of brain edema based on magnetic induction phase shift and computer programming," *Nanosci. Nanotechnol. Lett.*, vol. 9, no. 10, pp. 1470–1477, 2017.
- [36] S. Z. Li, H. Li, J. Zhang, S. Wang, Y.-X. Wang, and Z.-J. Jin, "Effect of transmission line on impedance matching of atmospheric-pressure radio-frequency capacitive microplasma discharge," *IEEE Trans. Plasma Sci.*, vol. 42, no. 6, pp. 1654–1660, Jun. 2014.
- [37] T. Günel, "A genetic approach to the synthesis of composite right/left-handed transmission line impedance matching sections," *AEU-Int. J. Electron. Commun.*, vol. 61, no. 7, pp. 459–462, 2007.
- [38] D. Nassehi *et al.*, "Vascular endothelial growth factor A protein level and gene expression in intracranial meningiomas with brain edema," *Apmis*, vol. 119, no. 12, pp. 831–843, 2011.
- [39] J. B. Nitsch, R. Rambousky, and S. Tkachenko, "Introduction of reflection and transmission coefficients for nonuniform radiating transmission lines," *IEEE Trans. Electromagn. Compat.*, vol. 57, no. 6, pp. 1705–1713, Dec. 2015.
- [40] A. M. Niknejad, M. Bohsali, E. Adabi, and B. Heydari, "Integrated circuit transmission-line transformer power combiner for millimetre-wave applications," *Electron. Lett.*, vol. 43, no. 5, pp. 47–48, Mar. 2007.
- [41] L. Zhang, K. Wu, Y. Zhong, and P. Li, "A new sub-pixel mapping algorithm based on a BP neural network with an observation model," *Neurocomputing*, vol. 71, nos. 10–12, pp. 2046–2054, 2008.
- [42] T. P. Lillicrap, D. Cownden, D. B. Tweed, and C. J. Akerman, "Random synaptic feedback weights support error backpropagation for deep learning," *Nature Commun.*, vol. 7, Nov. 2016, Art. no. 13276.
- [43] L. Li, Y. Chen, T. Xu, R. Liu, K. Shi, and C. Huang, "Super-resolution mapping of wetland inundation from remote sensing imagery based on integration of back-propagation neural network and genetic algorithm," *Remote Sens. Environ.*, vol. 164, pp. 142–154, Jul. 2015.
- [44] F. Büchele *et al.*, "Novel rat model of weight drop-induced closed diffuse traumatic brain injury compatible with electrophysiological recordings of vigilance states," *J. Neurotrauma*, vol. 33, no. 13, pp. 1171–1180, 2016.
- [45] K. Ding, H. Wang, J. Xu, X. Lu, L. Zhang, and L. Zhu, "Melatonin reduced microglial activation and alleviated neuroinflammation induced neuron degeneration in experimental traumatic brain injury: Possible involvement of mTOR pathway," *Neurochem. Int.*, vol. 76, no. 10, pp. 23–31, 2014.

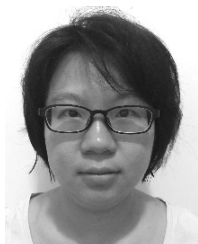


GEN LI was born in Wanzhou, China, in 1990. He received the Ph.D. degree from Chongqing University, Chongqing, in 2018.

Since 2018, he has been an Assistant Professor with the School of Pharmacy and Bioengineering, Chongqing University of Technology. His research interests include biomedical signal processing and design of advanced medical devices. He has a strong interest in the exploration of interdisciplinary fields between engineering and medicine.



JINGBO CHEN received the master's degree from Army Logistics University, Chongqing, in 2017. He is currently pursuing the Ph.D. degree with the Department of Biomedical Engineering, Army Medical University, Chongqing. His research interests include biomedical engineering and electromagnetic field and electromagnetic wave. He has a strong interest in the design and application of bioelectromagnetic sensor.



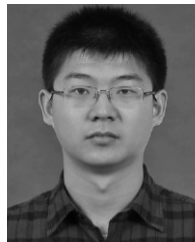
SHANSHAN GU received the master's degree from the Zhou Enlai School of Government, Nankai University, Tianjin, in 2010. From 2010 to 2018, she was a doctor with the Department of Clinical Psychology, Southwest Hospital, Chongqing. Her research interests include biomedical signal processing and statistical analysis.



ZELING BAI (M'95) was a Research Assistant with the Department of Electronic Engineering, Army Medical University, Chongqing. From 2016 to 2018, he devoted to study detection of intracranial hemorrhage. His research interests include antenna design and magnetic induction tomography applied to medicine.



JUN YANG received the master's degree in military medical equipment from Army Medical University, Chongqing. From 2016 to 2018, he devoted to study TBI detection by bioelectromagnetic signal. His current research interests include antenna design and magnetic induction tomography applied to medicine.



JIAN REN was born in Dezhou, China, in 1989. He received the B.Sc. degree in electronic engineering and the M.Eng. degree in electromagnetics and microwave technology from Xidian University, Xi'an, China, in 2012 and 2014, respectively. He is currently pursuing the Ph.D. degree with the City University of Hong Kong, Hong Kong. In 2015, he was a Research Assistant at the City University of Hong Kong. His research interests include microwave circuits, metamaterials, RFID, and dielectric resonator antennas.



YUJIE CHEN was born in Chongqing, China, in 1982. He received the M.D. and Ph.D. degrees in neurosurgery from the Department of Neurosurgery, Southwest Hospital, Army Medical University, in 2015.

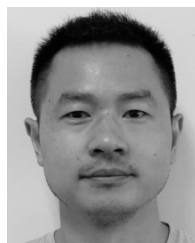
He is a Neurosurgeon of Southwest Hospital, Army Medical University, who completed research training at the Center of Neuroscience Research, Loma Linda University, Loma Linda, CA, USA. From 2012 to 2014, he studied as a Visiting Graduate Student with the Center for Neuroscience Research, Department of Physiology and Pharmacology, Loma Linda University. His research has focused on the cerebrovascular disease, especially on blood-brain barrier disruption and other pathophysiology of hemorrhagic stroke.



LIN XU was born in Yichang, China, in 1983. He received the master's degree from the College of Biomedical Engineering, Chongqing University, in 2010. Since 2010, he has been a Teacher with the Department of Electronic Engineering, Army Medical University. His research interests include bioelectrical impedance technique and electromagnetics. He has a strong interest in the exploration of bioelectrical impedance fields and electromagnetics in biomedical engineering.



SHUANGLIN ZHAO received the bachelor's degree from the College of Biomedical Engineering, Army Medical University, Chongqing, in 2018, where she is currently pursuing the master's degree. Her research interest includes magnetic induction technology for non-invasive brain monitoring. She keeps a rigorous attitude in the research processing.



MINGSHENG CHEN was born in Yingshan, China, in 1983. He received the master's and Ph.D. degrees from the College of Electronic Science and Engineering, National University of Defense Technology, Changsha, in 2006 and 2012, respectively. From 2014 to 2018, he studied as a Postdoctoral Fellow with the Department of Biomedical Engineering, Army Medical University, Chongqing. His research interests include biomedical engineering and medical signal processing.



JIA XU received the B.S. degree in engineering from the School of Optics and Photonics, Beijing Institute of Technology, Beijing, in 2004, and the M.S. degree in engineering from the College of Biomedical Engineering, Chongqing University, Chongqing, in 2008. She has been a Lecturer with Army Medical University, since 2008. Her research interests include brain electromagnetic monitoring technology, biomedical signal processing, and cerebral autoregulation.



MINGXIN QIN was born in Guilin, China, in 1960. He received the Ph.D. degree from Xidian University, Xi'an, in 2007. In 2010, he joined the College of Biomedical Engineering, Army Medical University, where he is currently a Professor and the Head of the Electronics Engineering Department. Since 2008, he has been a Committee Member of the International Bioelectrical Resistance Research Promotion Council (ICPRBI). His research interests include biomedical engineering and bioelectromagnetics.



KWOK WA LEUNG (S'90–M'93–SM'02–F'11) was born in Hong Kong. He received the B.Sc. degree in electronics and the Ph.D. degree in electronics engineering from The Chinese University of Hong Kong, Hong Kong, in 1990 and 1993, respectively. In 1994, he joined the Department of Electronic Engineering (EE), City University of Hong Kong (CityU), where he is currently a Chair Professor and the Associate Head of the EE Department. In 2006, he was a Visiting Professor

with the Department of Electrical Engineering, The Pennsylvania State University, State College, PA, USA. His research interests include antenna designs, guided wave theory, computational electromagnetics, and mobile communications.

Prof. Leung received the International Union of Radio Science (USRI) Young Scientists Awards in Japan and Russia, in 1993 and 1995, respectively. He also received the CityU Research Excellence Award, in 2013, and the Departmental Outstanding Teacher Awards, in 2005, 2010, and 2011, respectively. He also received the highly prestigious First-Class Award (Natural Science) in the 2016 Higher Education Outstanding Scientific Research Output Awards (Science and Technology) of the Ministry of Education, China. His students received the 2015 iWEM Student Best Paper Award, the 2015 IEEE AP-S Eugene F. Knott Memorial Pre-Doctoral Research Award, and the 2014 IEEE MTT-S Undergraduate/Pre-Graduate Scholarship. He was the Chair of the IEEE AP/MTT Hong Kong Joint Chapter for 2006 and 2007. He was the Technical Program Chair of the 2008 Asia-Pacific Microwave Conference, Hong Kong, and the Technical Program Co-Chair of the 2006 IEEE TENCON, Hong Kong. He was a Guest Editor of the *IET Microwaves, Antennas and Propagation*. He served as an Associate Editor for the IEEE ANTENNAS AND WIRELESS PROPAGATION LETTERS. He was also an Associate Editor of the IEEE TRANSACTIONS ON ANTENNAS AND PROPAGATION and received the Transactions Commendation Certificates twice, in 2009 and 2010, for his exceptional performance. He was the Editor-in-Chief of the Transactions, from 2013 to 2016. He was a Distinguished Lecturer of the IEEE Antennas and Propagation Society.



JIAN SUN was born in Yancheng, China, in 1984. He received the master's degree from the College of Physical Sciences, Nankai University, in 2010, and the Ph.D. degree from Army Medical University, Chongqing, in 2014.

From 2016 to 2017, he studied as a Post-doctoral Fellow with the Department of Neurosurgery, Southwest Hospital, Chongqing. Since 2018, he has been a Senior Researcher with the Department of Electronic Engineering, City University of Hong Kong. His research interests include biomedical engineering and bioelectromagnetic signal processing. He has a strong interest in the exploration of interdisciplinary fields of engineering and medicine.

...