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A novel method for locating the epileptic seizure with combination of the planted micro-ultrasound-transducers and electrodes

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***Abstract*—The electrode arrays are used for epilepsy lesion localization in the clinical epilepsy surgery. The limitation of electrode is lack of depth orientation information. The existence of neurovascular coupling effect gives ultrasound the possibility of detecting epilepsy in depth. The probe which functional ultrasound (fUS) uses still not be devoted into applications because of its size and price. Based on these reasons, we proposed a novel method which combined the micro ultrasound transducers and electrodes to locate the site of seizure together. The US signals and electrical signals are recorded simultaneously when the epilepsy occurred in the rats. The ultrasound RF signals were processed with power spectrum to monitor cerebral blood volume (CBV). The experiment result has shown that the CBV has correspondence to electrical signal. The micro-ultrasound transducers can detect the seizure depth range from 0 to 2mm under cortex, which could work with electrodes to realize the planted epilepsy 3D detection.**

Keywords—micro-transducers, epilepsy, CBV, power spectrum, neurovascular coupling effect

I. INTRODUCTION

Epilepsy is a chronic disease caused by brain dysfunction which is a sudden abnormal discharge of neurons in the brain[1]. Usually, the main pathogenesis of this disease is that the epileptogenic lesions may have distributed in the brain[2]. In order to cure the epilepsy thoroughly, it is necessary to precisely target the lesions for resection. In clinical epilepsy surgery, ECoG electrode arrays are often placed on cerebral cortex to distinguish the seizure areas[3]. It's a treatment which could get two-dimensional information except depth of the lesions. For the lesions presented in sulus or thalamus, ECoG could not identify the origin of seizure. In addition, it could only provide limited resolution (10mm) on the surface because of the interference between electrodes. So, in many cases, ECoG brings the result that brain tissue was extensively excised regardless of whether the injury will affect other brain areas. In recent years, the hemodynamic changes in the brain are often regarded as a surrogate of neuronal activity[4]. Many researches have indicated that neurovascular coupling effect was certificated in many brain activities such as epilepsy[5]. The actual response of this mechanism is that when neural activity occurs in a particular area, CBV also increases. It means that the measure of epilepsy could be promoted by the detection of blood. In the field of detecting blood with ultrasound, fUS, presented by Tanter et al., is a suitable mean of cerebral blood flow imaging[6, 7]. It is a technique that is capable of imaging whole-brain microvasculature dynamics with high spatiotemporal resolution[8]. In their study, they advocated that the changes of CBV have response to the procedure of epileptic seizure. Although fUS could image the small vascular with good spatiotemporal resolution which is brought by 128 linear arrays probe, it is hard to be applied in clinical long time record because of the big size and exorbitant price. Besides, the variations detected by fUS alone may not only exists in epilepsy. So, the ultrasound should work with electrical record together. In this paper, we proposed a novel method for locating the epileptic seizure with the planted micro ultrasound transducer combined with electrodes. This method associates the advantages that the high temporal resolution of electricity and the ability of ultrasonic three-dimensional positioning. We measured the precise seizure site by combining the information which the electrodes and transducers provided. It may have the prospect that the planted epilepsy 3D detection is feasible.

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II. METHODS

A. Experimental setup

1) Animal preparation

The adult male Sprague-Dawley rats (250g~300g) were deeply anesthetized with intraperitoneal injection of urethan (0.3g/mL). The head of rat was fixed in a stereotaxic apparatus. We incised the skin and drilled a cranial window on the rat's right hemisphere in Fig.1. The window covers an area for 4mm in width and 5mm in length. The size of cranial window is large enough for us to place electrodes and micro transducers inside. It's necessary to open the cranial window to avoid ultrasound wave attenuating when ultrasound wave propagates into the brain. In order to prevent inflammation, the dura which has little effect on the ultrasound echoes had not been removed. We used

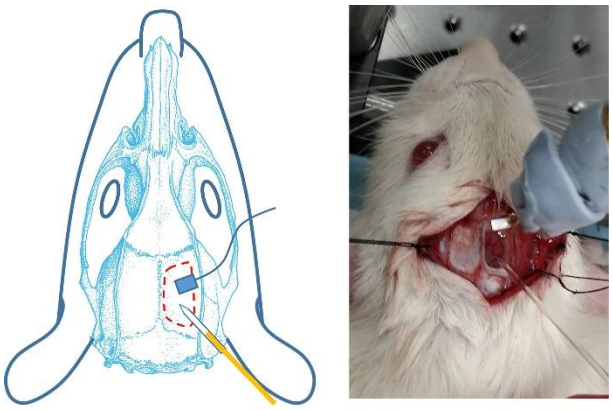

Fig. 1. Surgery procedure, micro transducers and electrodes setup

a glass electrode with 4-aminopyridine (4-AP; Sigma-Aldrich) solution (25mmol/L) to insert into cortex. The epilepsy was induced by injecting 0.5uL 4-AP solution.

2) Electrical recording

The local field potential (LFP) which the glass electrode recorded last about 15~30 minutes for a group. However, the voltage of original electrical signal is about 1mV which is easy to be affected by noise. So, it is necessary to amplify the original signal to record. The magnification factor of the microelectrode AC amplifier Model 1800 (A-M Systems, Sequim, WA) was set to 1000 times. The amplifier can amplify the electrical signal from about 1mV to 1V. Data acquisition (DAQ) devices USB-6008 (National Instruments, Austin, TX), whose sample rate is 1 kHz, was used to record the amplified signal. Once LFP showed that the seizure arose, it is the time to place micro-ultrasound-transducer over the cranial window about 2mm.

3) Ultrasonic recording

We used a micro transducer whose central frequency is 12MHz. The sizes of the transducer are 2mm*0.7mm*0.8mm. Vantage (Verasonics, Kirkland, WA) was used to emit US signals. The PRF we applied is 200Hz. When each ultrasonic recording starts, the vantage can provide a trigger signal to mark the recording on the LFP. Because of this, the electrical signals and ultrasonic echoes are recorded simultaneously. During each ultrasonic recording, we emitted ultrasound signals for 20 seconds, and stop for 40 seconds to save echoes data. In every electrical recording, we tried to record as many as possible ultrasonic sequences to cover seizure and non-seizure.

B. Processing of data

After reception of US echoes, we obtained many sequences of RF s(z,t). For each ultrasound sequence, we smoothed s(z,t) with the rectangular window in the direction of depth. Then we filtered slow-time signals with a 70Hz cut-off frequency high pass filter in order to reduce the noise which is brought by tissue movement caused by breathing. Within the measured 8mm depth from transducer, $s_B(z,t)$ at each depth, is divided into many periods which are processed with power spectrum and the spectrum are integrated to describe the intensity of blood. The energy of each period represents the intensity of this period and this depth. I(z,t), which we got by this method, can describe the changes of blood intensity at different depth and time to locate the seizure and show the path of blood flow.

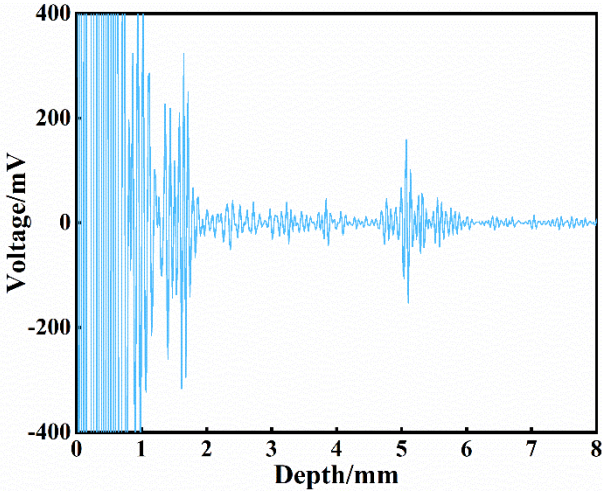

Fig. 2. The RF signals locate the depth of cortex at 1.2mm.

III. Results and Discussions

A. Results

As shown in Fig.2, the interface of the cortex is determined by RF signals. We connected and smoothed the processed result for all 20 seconds sequences in the depth of 1.5~2.5mm away from transducer, which is recognized as 1mm depth under cortex surface. In Fig.3, the continuous intensity which the dark blue line represents, reveals the variation of CBV that the volume obviously increased for 3 times. Accordingly, we joined the electrical signals together at the corresponding time. The seizures, which are distinctly higher than baseline, also appeared at the same time when the intensity arose. The result showed that the seizures which occurred occasionally in electrical signal have good correspondence to the blood intensity that US signal

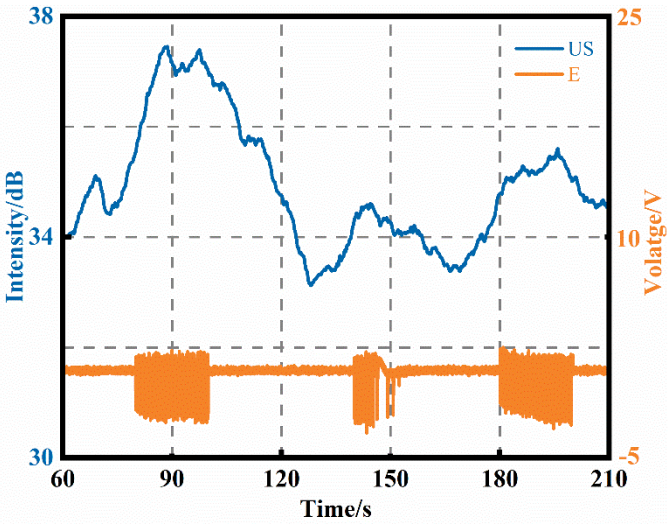

Fig. 3. The processed ultrasound blood intensity and electrical signal. The orange line is the connective electrical signal when the ultrasonic recording happened. The distinct part is the time of seizure. The dark blue line is the smoothed signal of all the 20s sequences which is spliced together.

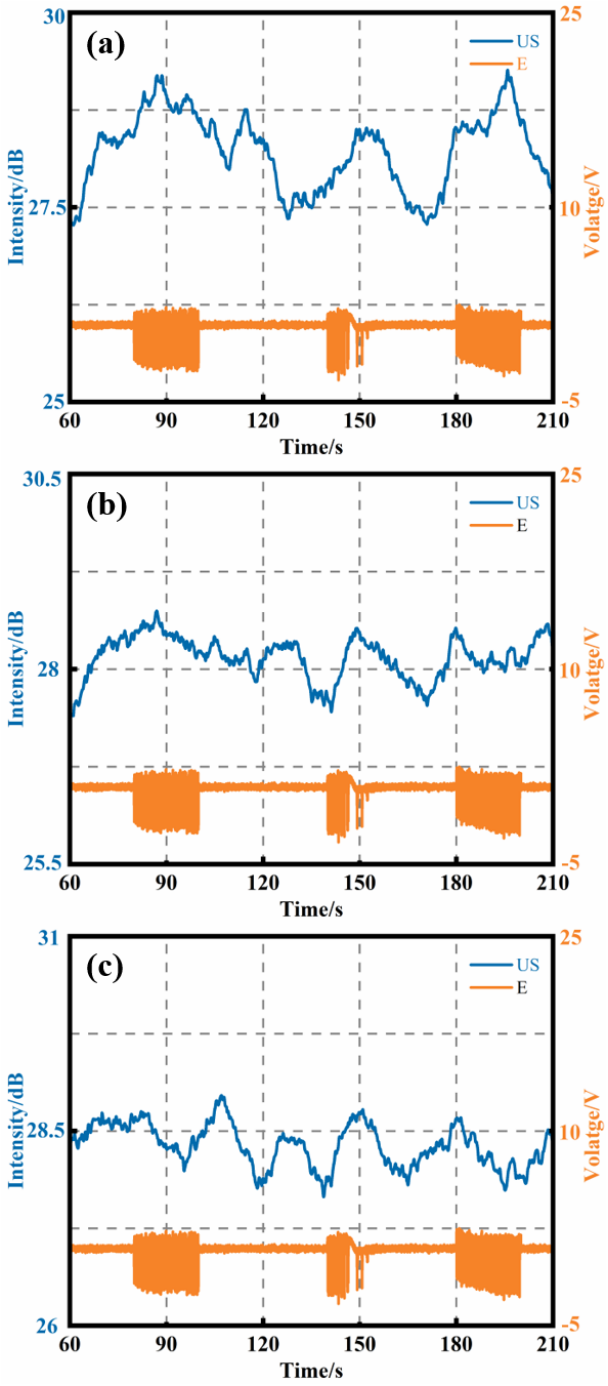

Fig. 4. The blood intensity and electrical signal at different depth (a) 2~3mm from transducer (b) 2.5~3.5mm from transducer (c) 3~4mm from transducer

represent. Also, in Fig.4, the similar correspondence between intensity and electrical signal appeared in the deeper tissue. When the investigation depth reaches 3.5mm, the intensity can still correspond to electrical signal very well. The depth where US signal matched electrical signal can be considered as the seizure area. Moreover, when we move the investigation window to 3~4mm in the thalamus of rat. The circumstance revealed that the change of blood intensity in thalamus cannot correspond to LFP. This depth was not involved in seizure area.

B. Discussion

Compared with traditional method, our method could provide seizure depth and improve resolution by setting many transducers as a grid array. Furthermore, it associates electrodes to distinguish the actual non-seizure and seizure area. This would offer more precise information in the clinical epilepsy surgery. Although, in this paper, the recording of the blood intensity in the thalamus did not show the seizure, it may be caused by the short recording which lead to the miss of rare change. It is necessary to get the long recording in the following study for judging the precise site of epilepsy.

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