Preoperative Monitoring Using Implantable, Multimodal, Multichannel Probe

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***Abstract*—Epileptic brain activity can be monitored using multiple pathophysiological signals. Thus, a six-channel flexible multimodal multichannel probe that can simultaneously record electrocorticography, hemodynamics, and brain temperature (BrT) was proposed to improve the accuracy of epilepsy diagnosis. The probe has six channels. Elements were arranged such that all modalities measured the same cortical region. In this study, three seizures were detected in epilepsy patients with cortical dysplasia during preoperative monitoring by using the proposed probe. A change in the direct current potential and increase in BrT were observed in all seizures. Regarding hemodynamic changes, although there was a disturbance due to an unknown cause in one seizure, an increase in oxyhemoglobin (HbO_2) and total hemoglobin (HbT), decrease in deoxyhemoglobin (Hbb) followed by a decrease in HbO_2 and HbT, and increase in Hbb were observed in all seizures. These seizure-related changes obtained through each modality were consistent with the results of previous studies.**

I. Introduction

Electrocorticography (ECoG) was measured and near-infrared spectroscopy (NIRS) was simultaneously conducted to examine hemodynamic responses related to epileptic activities. ECoG is an intracranial EEG measured by electrodes directly placed onto the brain surface of patients and is commonly used to diagnose neurosurgical diseases. NIRS monitors hemodynamic changes using the transmission properties of near-infrared rays in living tissues. NIRS is also used to measure changes in the concentrations of oxyhemoglobin (HbO_2), deoxyhemoglobin (HHb), and total hemoglobin (HbT) in tissues with high temporal resolution. Concurrently recording ECoG-NIRS results in rats has confirmed changes in hemodynamics related to epileptic seizures [1-2]. In addition, hemodynamic changes at the onset and end of epileptic seizures in children were observed by measuring ECoG and conducting NIRS simultaneously [3]. Epileptic-activity-related changes in brain temperature (BrT) have also been studied. Simultaneous measurement of ECoG and BrT revealed that epileptiform discharges evoke a temperature increase [4]. In addition, another study showed that BrT is significantly elevated by epilepsy, and this elevation accelerates epileptic discharges [5].

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Measurement of ECoG is a basic procedure in the preoperative monitoring of epilepsy, accompanied by electrode implantation on the brain surface [6,7]. However, the measurement of NIRS is commonly used as a noninvasive measurement and exhibits low accuracy owing to the low signal-to-noise (S/N) ratio and spatial resolution [8]. Therefore, to improve measurement accuracy, the NIRS function was integrated into a developed probe to obtain hemodynamics changes directly from the cortical surface. Furthermore, integrating multiple measurement functions into a single probe and simultaneously measuring the multiple pathophysiological signals at various points reduces the risk of infection and bleeding and enhances the possibility of diagnosing and observing the spread of brain pathology from different aspects. Therefore, flexible multimodal multichannel probes that record ECoG, hemodynamics, and BrT simultaneously were developed. We have used this probe to observe the pathological neural activity in an epileptic patient during surgery and in postoperative monitoring [9]. In this study, preoperative monitoring was performed in epilepsy patients with cortical dysplasia and changes in each modality (ECoG, NIRS, and BrT) related to observed epileptic seizures were discussed. The probe structure, measured pathophysiological signals, experimental procedure, and signal processing after the monitoring are discussed in Section II. The experimental results are detailed and the seizure-affected changes in each modality are discussed in Section III, while the conclusion of this research and opportunities for future work are summarized in Section IV.

II. Materials and Methods

A. Multimodality Probe

The developed probe was designed to measure ECoG, hemodynamics, and cortical temperature in six regions simultaneously. The probe head outer shape was similar to that of the strip electrode, commonly used in neurosurgery. The probe head had a 10-cm length, 8-mm width, and 0.7-mm maximum total thickness. In addition, flexible printed circuit technology was adopted; hence, the probe head had a suitable

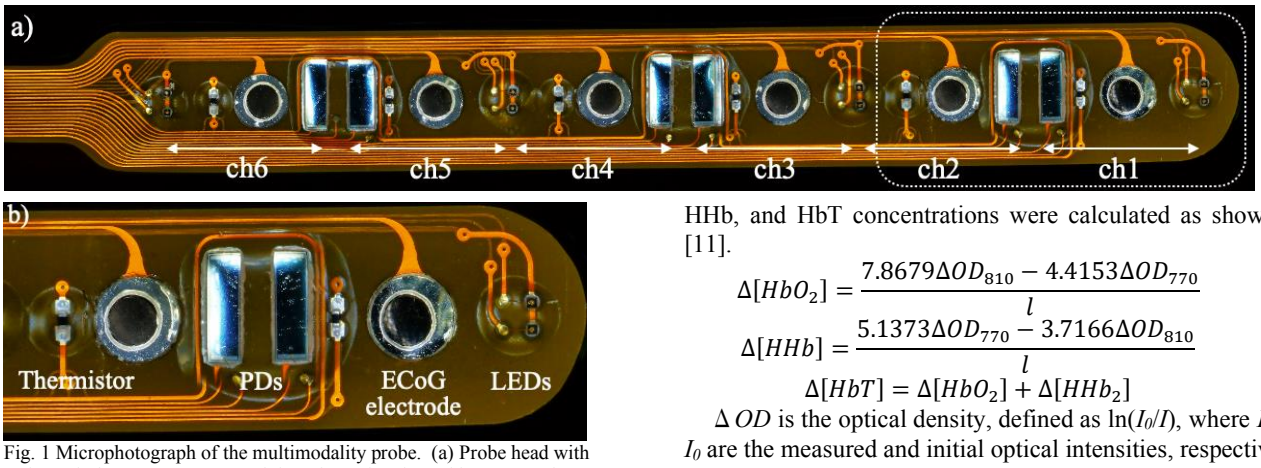

Fig. 1 Microphotograph of the multimodality probe. (a) Probe head with 6 channels for ECoG, NIRS, and thermistor signals. White arrows show the distribution of ch1–ch6. (b) Enlarged view of the white dotted area.

thickness for subdural implantation, and the probe could be mass-produced for disposable usage.

For ECoG measurements, six 3-mm diameter platinum electrodes were arranged at 1-cm intervals. NIRS was used to monitor the hemodynamics. Hence, infrared LED bare chips that emit the two different types of wavelengths (C770-40P for 770 nm and C810-40P for 810 nm, 0.4×0.4×0.25 mm, Epitex, Kyoto, Japan) and a photodiode (PD) bare chip that received emitted near-infrared rays (PD2501, 1.3×3.1×0.3 mm, Epitex) were used to calculate the changes in HbO_2, HHb, and HbT concentrations. These LEDs and PDs were located on both sides of the platinum electrode to measure the same cortical region as the ECoG electrode. Negative-temperature-coefficient thermistors (ERTJZEG103FA, 10 kΩ at 25 °C, 0.6×0.3×0.3 mm, Panasonic, Osaka, Japan) were used to measure the surface temperature of the cerebral cortex. The thermistors were placed next to the ECoG electrodes.

After the assembly of the circuit, all electronic components were sealed with nontoxic, transparent silicone. Afterward, all components and substrates were coated with a 10-μm-thick Parylene-C layer to improve insulation and biocompatibility during chronic implantation. Thus, the acute toxicity of the developed probe was removed from the probe surface. Performing these procedures caused the maximum total thickness of the probe head to be approximately 0.7 mm.

B. Hemoglobin Concentration from NIRS

The hemoglobin concentration was determined using six channels as in Fig. 1. In addition, ch2–ch5 shared the same LEDs (770-nm and 810-nm LEDs). The LEDs were run in the following order: the 770-nm LED of ch1 was turned on for 20 ms and then off for 20 ms. Subsequently, the 810-nm LED of ch1 was turned on for 20 ms. Then, the LEDs for ch2–ch6 were turned on/off in the same manner. After 240 ms from the start of lighting, when all sequences of the six NIRS channels were completed, all LEDs were turned off for 260 ms.

The photoelectric current obtained by the PD was processed using the method described in [10]. Then, changes in the HbO_2, HHb, and HbT concentrations were calculated as shown in [11].

$$\Delta[HbO_2] = \frac{7.8679\Delta OD_{810} - 4.4153\Delta OD_{770}}{l} \quad (1)$$

$$\Delta[HHb] = \frac{5.1373\Delta OD_{770} - 3.7166\Delta OD_{810}}{l} \quad (2)$$

$$\Delta[HbT] = \Delta[HbO_2] + \Delta[HHb_2] \quad (3)$$

ΔOD is the optical density, defined as $\ln(I_0/I)$, where I and I_0 are the measured and initial optical intensities, respectively. The coefficients of ΔOD were calculated from the molecular extinction coefficients at each wavelength [12]. l is the average optical path length obtained via the Monte Carlo simulation [13]. The simulation was performed assuming that the probe directly measured the cortical surface without reflection and scattering. As a result, a value of l = 37.4 mm was derived for the PDs and LEDs placed at an 8-mm distance [14].

C. Thermistor

The cortical temperature was obtained from the thermistor resistance monitored by a thermal signal conditioner (M3LU, M-System Co., Ltd., Osaka, Japan). The signal conditioner's output was set linearly in the range of 0–10 V for temperatures in the range of 0–45 °C using the thermistor temperature resistance table of the thermistor. The thermal voltage (V_T) signals were collected by a digitizer and fed into a computer simultaneously with the NIRS and ECoG signals, and the values were transformed into Celsius temperature (θ) using $\theta = 4.5\,V_T$ in offline post-processing.

D. Preoperative Monitoring of Epilepsy Surgery

The experimental procedure conformed to the Helsinki Declaration and was approved by the Yamaguchi University Institutional Review Board. The patient and their family agreed to participate in our study after being adequately informed of the aims, methods, anticipated benefits, and the potential risks and discomfort associated with their involvement; the participant also had the right to withdraw from the study at any time.

The measurement was performed using a prototype probe before epilepsy resection surgery. The participant (31-month-old female) was an epilepsy patient with cortical dysplasia in the right frontal lobe. The developed probe was installed under the dura mater in the right temporal area during electrode implantation surgery so as not to interfere with the diagnosis, as shown in Fig. 2. After this surgery, simultaneous measurement of each modality (ECoG, BrT, and NIRS) was performed for 55 h at a sampling frequency of 200 Hz.

E. Signal Processing after the Monitoring

The direct current (DC) potential was extracted from the ECoG signal by applying a 0.01-Hz low-pass filter. Then, a

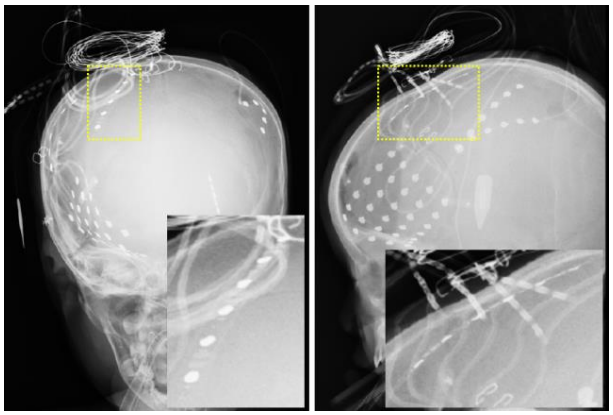

Fig. 2 X-ray images after the electrode implantation surgery. Subdural electrodes were installed around the epileptic focus in right frontal lobe for diagnosis. The proposed probe was placed at the right temporal area to avoid interfere with the diagnosis. The area around the proposed probe is indicated by the yellow dotted square and magnified.

0.0025-Hz Butterworth high-pass filter was used. The thermistor signal and NIRS signal were calculated using the method explained in the previous section and filtered using a Butterworth filter. The cut-off frequencies were 0.001 Hz and 0.0025 Hz, respectively. Each value obtained from the probe was processed offline using MATLAB (version 9.5).

III. Results and Discussion

During the monitoring, three seizures (s1–s3) were confirmed using the proposed probe. The changes in DC, BrT, and hemoglobin concentration within 20 min before and after the onset of the seizure are illustrated in Figs. 3–5. The start time of the seizure was estimated based on the time when symptoms appeared and was reported by the caretaker. This time was set to zero and indicated with the green line labeled "seizure". Hence, the green line does not show the time determined from the pathophysiological signals such as ECoG.

A change in the DC potential with an amplitude of approximately 20 mV was confirmed within 5 min from the beginning of the seizure. These results are consistent with those of other studies, suggesting that DC potentials were affected by seizures [15-16].

An increase in BrT was also confirmed. This result is concordant with that of previous studies showing that epileptic seizures increase BrT [4-5].

Regarding the NIRS signal, an increase in HbO_2 and HbT with a decrease in Hbb followed by a decrease in HbO_2 and HbT with an increase in Hbb were observed in s2–s3. This indicated that oxygenation followed by deoxygenation were generated related to epileptic seizure. This result is similar to the waveform of the NIRS signal recorded in children at the onset of the seizure [3]. Although there was a disturbance due to an unknown cause, similar trend was observed in s3.

These seizure-related changes were observed simultaneously within 5 min from the beginning of the seizure. However, the changes in DC and NIRS signals were observed within a few seconds before and after the onset of the seizure [3, 15-16]. This difference is probably because of determining

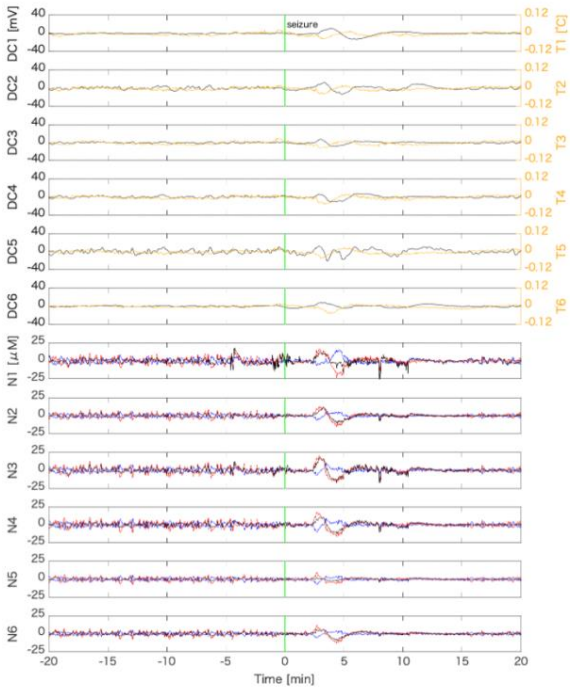

Fig. 3 Simultaneously recorded ECoG, BrT, and hemodynamics in s1. In the NIRS traces, $\Delta[HbO_2]$ (red), Δ[HHb] (blue), and Δ[HbT] (black) are displayed. As a seizure related changes, DC fluctuation, BrT elevation, and increase in $\Delta[HbO_2]$ and Δ[HbT] with decrease in Δ[HHb] followed by decrease in $\Delta[HbO_2]$ and Δ[HbT] with increase in Δ[HHb] were observed.

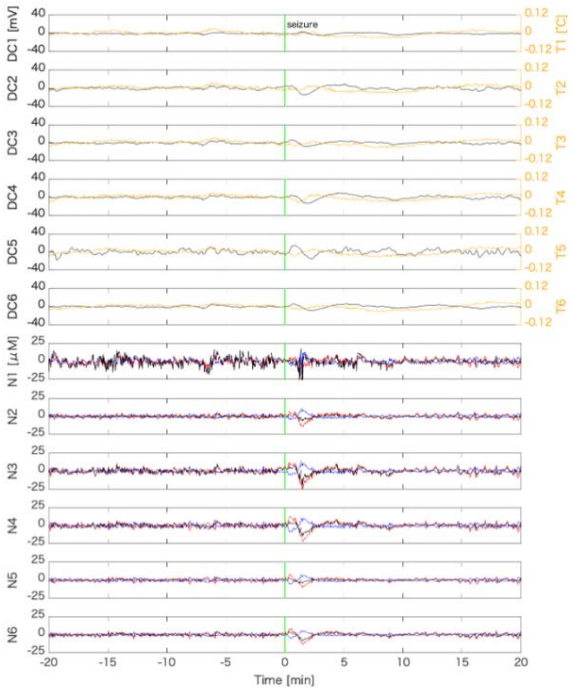

Fig.4 Simultaneously recorded ECoG, BrT, and hemodynamics in s2. In the NIRS traces, $\Delta[HbO_2]$ (red), Δ[HHb] (blue), and Δ[HbT] (black) are displayed. As a seizure related changes, DC fluctuation, BrT elevation, and increase in $\Delta[HbO_2]$ and Δ[HbT] with decrease in Δ[HHb] followed by decrease in $\Delta[HbO_2]$ and Δ[HbT] with increase in Δ[HHb] were observed.

the onset of the seizure based on the time when symptoms appeared and reported by the caretaker; however, change in pathophysiological signal was used in previous studies. In addition, each of the changes took approximately 5 min, whereas it took only a few seconds in the other studies [1, 2, 3, 15-16], which could be due to the different device locations, that is, between the epileptic foci in previous studies and away from the foci in this study.

IV. Conclusion

In this study, a flexible, multimodal, multichannel probe that simultaneously measures ECoG, hemodynamics, and the cortical surface temperature was proposed. All modalities had six channels and measured the same cortical region. The probe had an outer shape similar to that of the strip electrode, which is commonly used in neurosurgery. The probe surface was coated with Parylene-C for biocompatibility. Preoperative monitoring in an epilepsy patient who also had cortical dysplasia was conducted by using the proposed probe. We observed changes in DC, an increase in BrT, and changes in the concentrations of HbO_2, HHb, and HbT, which were related to epileptic seizures. These seizure-related changes were consistent with the results of previous studies and simultaneously observed in all modalities. However, the waveforms of HbO_2, Hbb, and HbT were disturbed during the seizure-related changes in one seizure, and the cause of the disturbance was unclear. The limitation of this study are as follows: the beginning of the seizure, probe location, and number of participants defined in this study may result in different observations in practice. In this study, the time when symptoms appeared and reported by the caretaker was used to estimate the onset of the seizure. To study the time series of seizure-related changes, estimating the seizure start time by using pathophysiological signals is critical. In addition, the probe was placed away from the cortical dysplasia so as not to interfere with the diagnosis. However, in the future, measuring the seizure-related changes in the pathophysiological signal from the vicinity of the focal point would be necessary. Furthermore, further studies are needed on a larger number of participants to conduct a more in-depth analysis on the characteristics of changes in the pathophysiological signals.

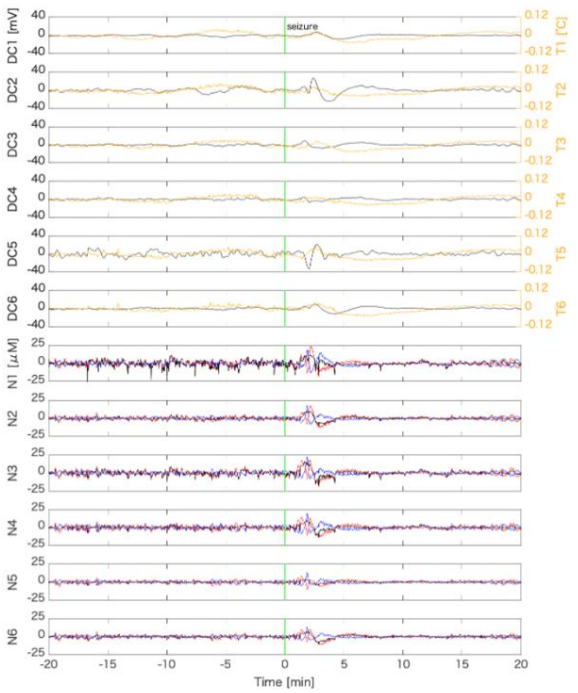

Fig. 5 Simultaneously recorded ECoG, BrT, and hemodynamics in s3. In the NIRS traces, Δ[HbO_2] (red), Δ[HHb] (blue), and Δ[HbT] (black) are displayed. The DC fluctuation and BrT elevation were observed. The NIRS waveform was consistent with the increase in Δ[HbO_2] and Δ[HbT] with the decrease in Δ[HHb] followed by the decrease in Δ[HbO_2] and Δ[HbT] with the increase in Δ[HHb]. However, the waveforms of Δ[HbO_2], Δ[HHb], and Δ[HbT] were disturbed during the increase of Δ[HbO_2] and Δ[HbT] with the decrease in Δ[HHb].

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