The Estimation of the Depth of Anesthetic Using Higher-Order Spectrum Analysis of EEG Signals

Jong-duk Park[1], Soo-Young Ye[2], Gye-Rok Jeon[3], Young Huh[4]

[1]*Dept. of Biomedical Engr., College of Medicine, Pusan National University*
[2]*BK21 Medical Science Education Center, College of Medicine, Pusan National University*
[3]*Dept. of Biomedical Engr., School of Medicine, Pusan National University,* [4]*Korea Electrotechnology Research Institute*
(Received December 5, 2006. Accepted February 12, 2007)

Abstract

The researchers have studied for a long time about the depth of anesthesia but they don't make criteria for the depth of anesthesia. Anesthetists can't make a prediction about patient's reaction. Therefore, patients have potential risk such as poisonous side effect, late-awake, early-awake and strain reaction.

In this study, the distributed characteristics on the bispectrum and bicoherence, the type of nonlinear signal processing, as a result of the coupling of EEG were presented according to depth of anesthesia. These results were consistent with a trend of delta ratio that the index of evaluation for the depth of anesthesia. The higher-order spectrum (HOS), the bispectrum and bicoherence, gives the useful information about depth of anaesthesia than other indexes.

Key words : bispectrum, bicoherence, the depth of anesthesia, delta ratio, higher-order spectrum

I. INTRODUCTION

The anesthesia can be defined as a state of drug-induced unconsciousness in which the patients neither perceive nor recall the noxious stimulation[1]. Some patients have considered it as their worst experiencein the hospital. The post-traumatic stress disorder could occur in those who were severely affected. In spite of the use of clinical signs for assessing 'depth of anesthesia' universally, the method is notoriously unreliable.

The purpose of the estimation of depth of anesthesia is to protect the awareness and to maintain the suitable condition of anesthesia by injecting an anesthetic to the patients adequately, moreover to protect the waste of the anesthetic and make side effect minimized for awareness as soon as possible[2-4].

There are many methods to estimate the depth of anesthesia. The heart rate variability(HRV) was used [5]. The HRV has become known that it reflected interaction of autonomic nervous system to regulate the cardiovascular function. Because HRV analysis can calculate quantity of effects on autonomous nervous system, the HRV analysis is available to estimate the depth of anesthesia[6]. The Anemon is the instrument to estimate the depth of anesthesia using HRV. It has been developed and applied to clinical operation. But the analysis method using the HRV can't regularly reflected the anaesthesia depth because of effects of other factors such as endotracheal tube placed during anaesthetic procedure, external stimulation like skin incision.

Recently in the analysis of a brain wave, the bispectrum used as one of HOS analysis and nonlinear analysis that express the depth of anesthesia. The bispectral index(BIS, Aspect Co. USA) was developed to estimate the depth of anesthesia by bispectrum analysis[7-10]. The BIS has been introduced that it can be used to estimate of the depth of anesthesia objectively by Sigl in 1994[11]. And the use of BIS index reduced the incidence of awareness during surgery. And in order to use an estimated bispectrum of a stochastic EEG signal to detect nonlinearity or for phase-estimation, it is necessary to normalize the bispectrum by a product of the signal's spectrum[12].

This study was designed to investigate the ability of bispectrum parameter and bicoherence parameter to identify awareness by detecting recovery of consciousness.

This study was supported by a grant from the Korea Health 21 R&D Project, Ministry of Health & Welfare, Republic of Korea (Grant No A040032).
Corresponding Author : Ye Soo Young
3rd floor, nam-kyong building, 33-5,
Bu-min dong 3-ga, seo-gu, Busan
Tel : +82-51-257-2866 / Fax : +82-51-257-2867
E-mail : syye@pusan.ac.kr

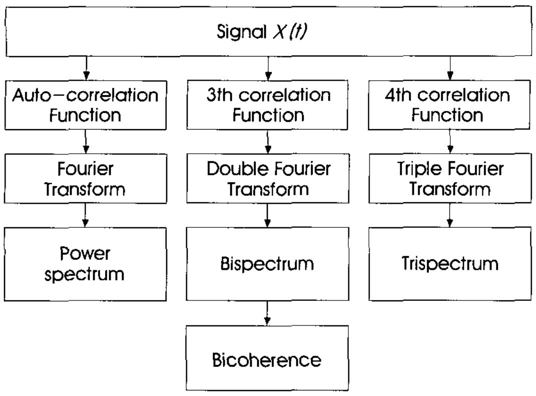

Fig.1. The higher-order spectrum analysis.

Ⅱ. HIGHER-ORDER STATISTICS

A. The Principle Of Higher-Order Spectrum

The HOS measurements are extensions of second-order measurements such as the autocorrelation function and power spectrum to higher orders. The HOS indicates the expectation of more than two values of a stochastic process. The third-order HOS measurement of the time domain and frequency domain was defined, assuming a zero mean and discrete signal $s(n)$.

The third-order statistic, called the third-order cumulant, has the following mathematical form in the time domain[13]:

$$c_3 = (t_1, t_2) = \sum\{s(n)s(n+t_1)s(n+t_2)\} \tag{1}$$

where, { } is the expectation operator. The third-order moment, c_3, depends on two lags t_1 and t_2. The higher-order moments can be formed in a similar way by adding lag terms to the above equation.

The signal cumulants can be easily derived from the moments. The cumulant was defined as following. The nth-order cumulant is a function of the moments of orders up to n. For the reasons of mathematical convenience, the HOS equations more often deal with a signal's cumulants rather than the signal's moments.

In the frequency domain, the second-order measurement is called the power spectrum.

The bispectrum is defined as the two-dimensional fourier transform of the third-order cumulant.

$$C_3(\omega_1, \omega_2) = \sum_{t_1=-\infty}^{+\infty} \sum_{t_2=-\infty}^{+\infty} c_3(t_1, t_2) \exp\{-j(\omega_1 * t_1 + \omega_2 * t_2) \tag{2}$$

$$|\omega_1|, |\omega_1| \le \pi$$

Thus, the bispectrum is a three-dimensional function with the magnitude of bispectrum plotted against the two frequencies ω_1 and ω_2. It measures the correlation among the three spectral peaks at the frequencies ω_1, ω_2 and $(\omega_1+\omega_2)$ and thereby estimates the phase coupling between them. As it has twelve regions of symmetry, the knowledge of any one region, for example $\omega_2 > 0$, $\omega_1 > \omega_2$, and $\omega_1+\omega_2 < \pi$, is sufficient for its complete description. Strongly coupled frequencies can be effectively traced using the bispectrum. Nevertheless, weakly coupled oscillations would result in the same bispectral value as strongly coupled power oscillations. In order to overcome this problem, the bicoherence function is used. The bicoherence function is the normalized form of bispectrum with respect to its power spectrum :

$$B(\omega_1, \omega_2) = \frac{C_3(\omega_1, \omega_2)}{|S(\omega_1)S(\omega_2)S(\omega_1, S(\omega_2)|^{1/2}} \tag{3}$$

where $S(\omega)$ is the estimated power spectrum of the signal. For weak correlation between the three spectral peaks, the bicoherence value is low. And for strong correlation, it is high [3].

B. Application Of Higher-Order Spectrum

The EEG bispectrum has been shown to predict the response on surgery and to detect the consciousness when a variety of anesthetic drugs were used. In order to apply the triple correlation equation, the bispectral EEG analysis acquired the bispectrum array(1Hz - 35Hz) of the one dimension. After the triple correlation was applied, the result appeared by

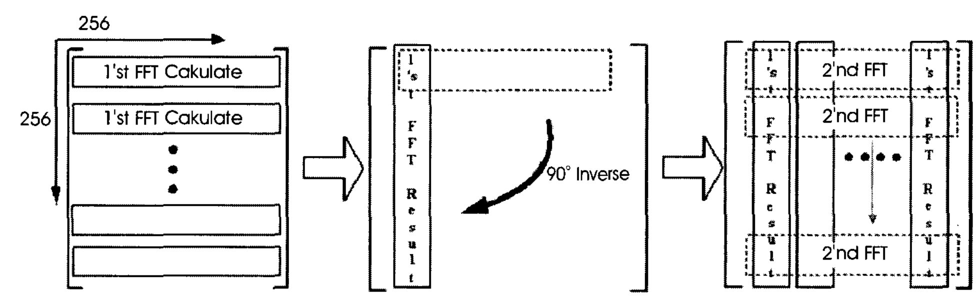

Fig. 2. The execution method for the second order FFT using the first order EEG signals.

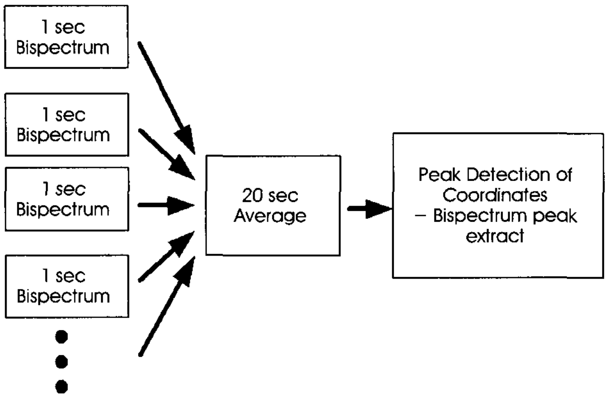

Fig.3. The peak extract by the averaged bispectrum of the period of 20 sec.

two-dimensional matrix. We made the two-dimensional FFT at the two-dimensional matrix. Fig. 2. shows executing method for the second-order FFT.

The second-order FFT was executed during 1 sec of EEG data. We averaged the data of 20 sec and calculated maximum peaks about each coordinate. Fig. 3. shows peak extract method in bispectrum.

The result matrix appeared in three dimensions. After mapping into two dimensions, if there were many peaks, the red color appears in the two-dimensional map. Otherwise, blue color appear.

C. Parameter Of Higher-Order Spectrum

The number of peaks of bispectrum which are objective value is the parameters to estimate the depth of anesthesia. The number of peaks of bispectrum appeared at the color map of two dimensions. The color was red when the number of peaks of bispectrum was plenty of value and blue when the number of peaks of bispectrum was short.

Thus, the reconstructed map into two dimensions by the number of peak appearance was showed at Fig. 4. The two-dimensional map was divided into four area like Fig. 4(b) to observe the amount of peak appearance at each area.

The vertical and horizontal axises also were divided into four ranges. The ranges are the frequency band of the brain wave that is δ, Θ, α, and β wave.

At each frequency band, the four parameters were calculated by the equation (4),(5),(6),(7).

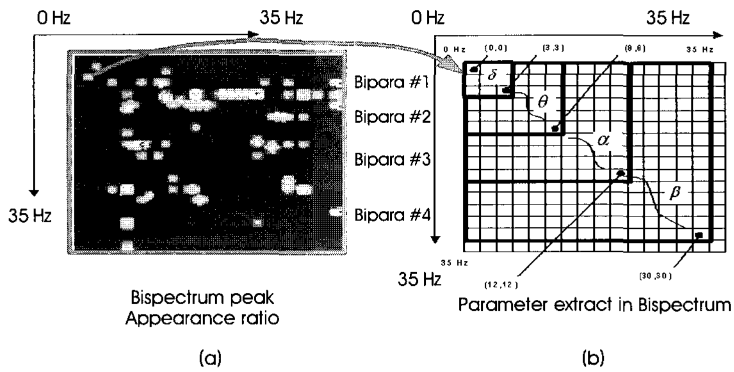

Fig.4. The peak extract in two-dimensional map of the bispectrum by divided into four area.
(a) The two-dimensional map, (b) The parameters according to the frequency band.

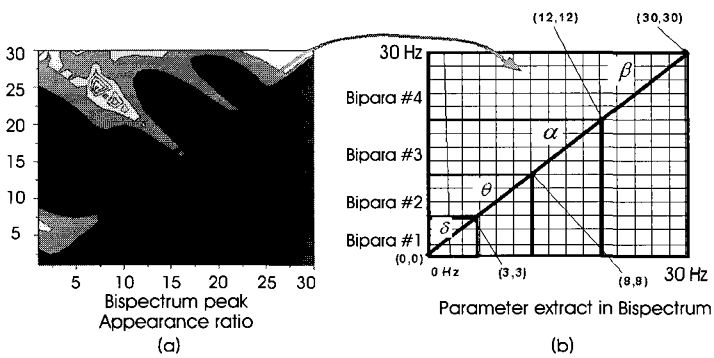

Fig. 5. The peak extract in two-dimensional map of the bicoherence by divided into four area.
(a) The two-dimensional color map, (b) The parameters according to the frequency band.

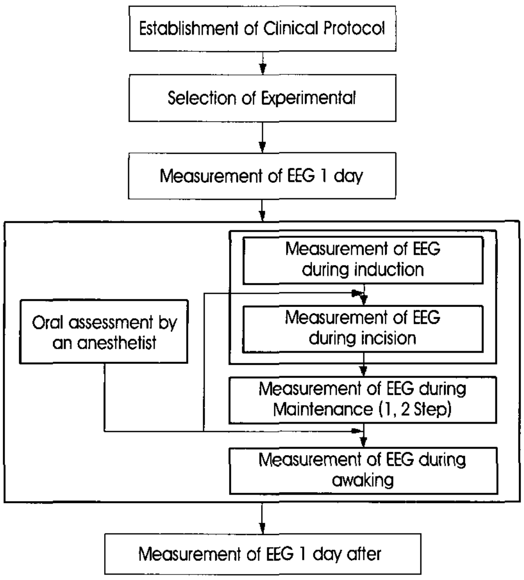

Fig. 6. The flowchart of the EEG signal measurement according to the anesthetic process.

$$Bipara\#1 = \frac{\delta\, power}{\alpha\, power + \beta\, power + \theta\, power + \delta\, power} \times 100 \quad (4)$$

$$Bipara\#2 = \frac{\theta\, power}{\alpha\, power + \beta\, power + \theta\, power + \delta\, power} \times 100 \quad (5)$$

$$Bipara\#3 = \frac{\alpha\, power}{\alpha\, power + \beta\, power + \theta\, power + \delta\, power} \times 100 \quad (6)$$

$$Bipara\#4 = \frac{\beta\, power}{\alpha\, power + \beta\, power + \theta\, power + \delta\, power} \times 100 \quad (7)$$

The parameters are Bipara #1, Bipara #2, Bipara #3 and Bipara #4.

The bicoherence parameters were divided into four areas as the same method. Accordingly, the segmented bicoherence parameters put Bicpara #1, Bicpara #2, Bicpara #3 and Bicpara #4. Each parameter was showed at Fig. 5.

III. METHODS

The 50 ASA I and II woman subjects were participated for about 2 hours under the general anesthesia. The study was approved by the hospital's ethics committee and the informed consent was obtained from all participants.

The subjects with the history of cardiovascular, pulmonary or neurological disease were not involved. The depth of anesthesia was investigated as following 6 stages; 1 day before operation(Pre.), Anesthesia Induction(Induc.), During first 1 hour on operation 1(Oper.1), During second 1 hour on operation(Oper. 2), Awaking(Awa.), 1 day after operation 1(Post.). Thus, the series process about EEG signal acquisition flowchart was shown at Fig. 6.

The EEG signal was acquired by using the bio-signal measurement instrument, Physiolab 400(Sertoec Instrument Co., KOREA). The electrodes were attached to Fp1 which one of the 10-20 electrode system for measurements of EEG. During preparing for anesthesia, the three electric electrode were attached to reference electrode of the patient's forehead and to negative electrode of the left of the reference electrode and to positive electrode of the bottom of the left ear. The sampling rate was 256 Hz and the low-frequency and high-frequency filters were set at 35 Hz and 0.1Hz. The A/D transformation of 12 bits was used. The EEG was transferred continuously to IBM computer for the off-line analysis. We applied the two preprocess to exclude DC component and floating phenomenon, and the one was base line correction and the other was linear trend.

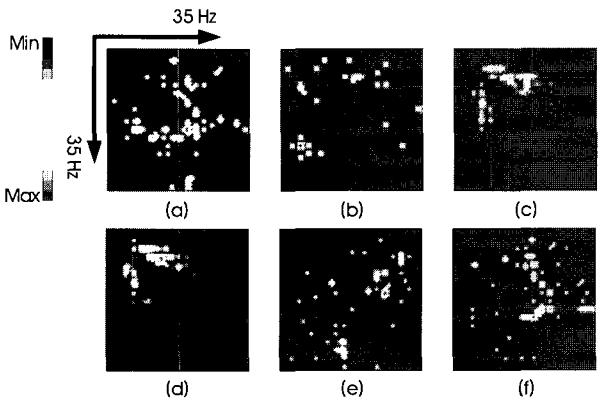

Fig. 7. The two-dimensional color map at stages of the anesthesia. (a) Pre., (b) Induc., (c) Oper. 1, (d) Oper. 2, (e) Awa., (f) Post..

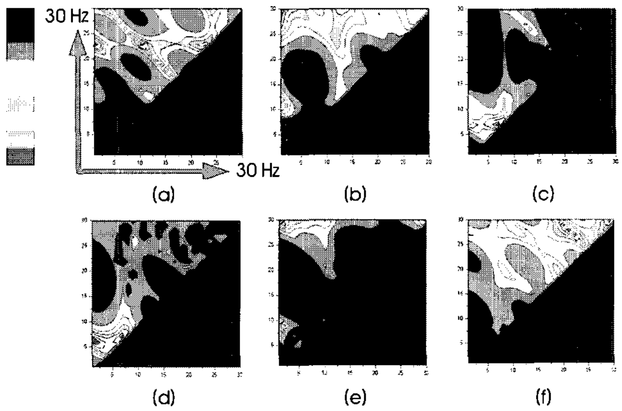

Fig. 8. Color map of bicoherence at the anesthesia stages; (a) Pre., (b) Induc., (c) Oper. 1, (d) Oper. 2, (e) Awa., (f) Post..

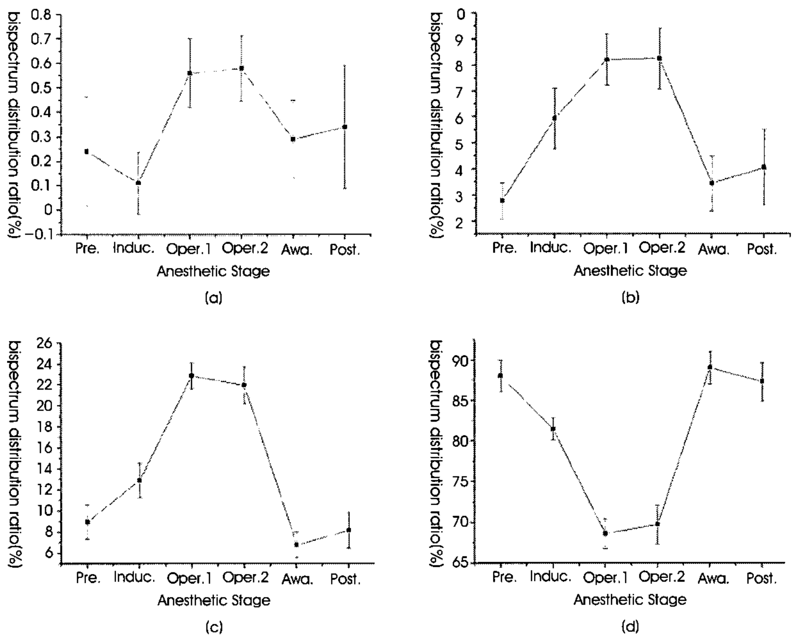

Fig. 9. The trend of bispectrum parameter variability at each stage of anesthesia; (a) Bipara#1, (b) Bipara#2, (c) Bipara#3, (4) Bipara#4.

The signal process analysis software used visual C++ 6.0 (Microsoft Corporation, USA). The parameter analysis used the paired sample t-test as the statistical process and the statistical level of significance (p) is 0.01. The statistical process software analyzed the data using SPSS 12.0 (SPSS Inc. USA).

Ⅳ. RESULTS

The appearance rate of bispectrum peaks was calculated by bispectrum operation according to the depth of anesthesia. The two-dimensional color map represented the appearance rate of bispectrum peak. The distribution on appearance of the bispectrum peak at each anesthesia stage was shown at Fig. 7.

At the Pre. and Awa. stages, a strong appearance rate was represented in all area (0 ~ 35Hz) like Fig. 7 (a), (e). The result implied that patient's stress and disquietude for stamen were reflected. During the anesthesia, Fig. 7 (c) and (d) showed a strong appearance rate at the low frequency area (3 ~ 15Hz) and a weak appearance rate viewed in the other frequency range. These aspects are judged that patient's state reflected disappearance of reflection function and consciousness and beginning of regular breath.

As a result, the analysis method of bispectrum provides the

Table 1. Mean and standard deviation and values of bispectrum parameter at anesthesia steps

parameter	Pre.	Induc.	Oper.1	Oper.2	Awa.	Post.
Bipara#4	88.02 ± 1.94	81.49 ± 1.40	68.64 ± 1.83	69.74 ± 2.42	89.03 ± 1.98	87.27 ± 2.41
Bipara#3	8.97 ± 1.63	12.91 ± 1.65	22.85 ± 1.26	21.96 ± 1.72	6.78 ± 1.24	8.16 ± 1.68
Bipara#2	2.78 ± 0.69	5.94 ± 1.18	8.20 ± 0.98	8.24 ± 1.69	3.44 ± 1.07	4.05 ± 0.46
Bipara#1	0.24 ± 0.22	0.11 ± 0.13	0.56 ± 0.14	0.58 ± 0.13	0.29 ± 0.16	0.34 ± 0.25

* : p<0.01

Table 2. Mean and standard deviation and values of bicoherence parameter at anesthesia steps

parameter	Pre.	Induc.	Oper.1	Oper.2	Awa.	Post.
Bicpara#1	0.82 ± 03	0.54 ± 0.24	3.78 ± 1.59	4.24 ± 1.51	0.95 ± 0.38	0.59 ± 0.25
Bicpara#2	2.94 ± 1.17	2.06 ± 0.5	15.89 ± 2.71	15.29 ± 1.90	2.74 ± 0.62	2.02 ± 0.52
Bicpara#3	4.98 ± 1.99	3.70 ± 1.24	11.74 ± 2.63	13.25 ± 2.57	3.39 ± 1.13	2.04 ± 0.68
Bicpara#4	91.28 ± 3.56	93.76 ± 1.43	69.77 ± 4.81	70.31 ± 4.70	92.92 ± 1.87	95.39± 1.04

* : p<0.01

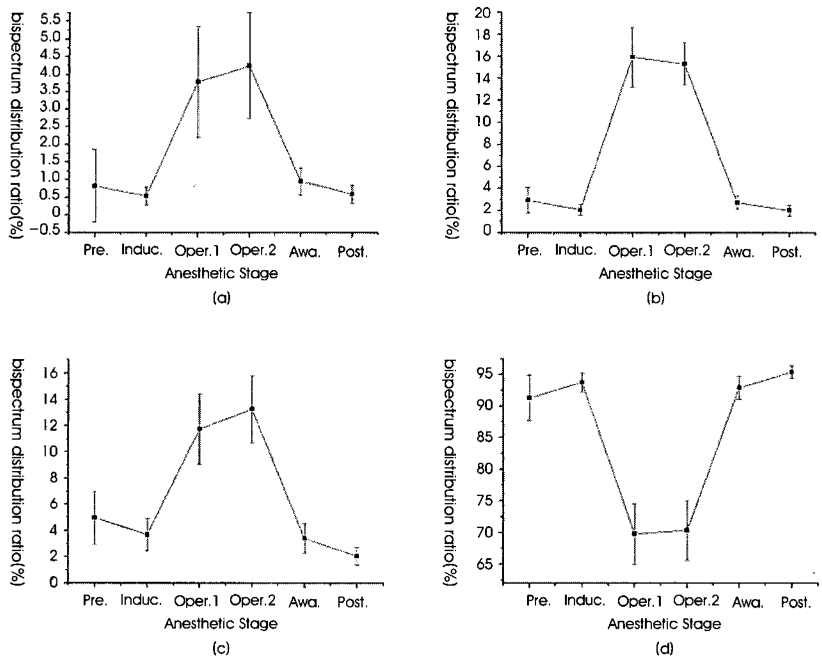

Fig. 10. The trend of bicoherence parameter variability at each stage of anesthesia (a) Bipara#1, (b) Bipara#2, (c) Bipara#3, (4) Bipara#4.

useful information about the level of unconsciousness and suppression.

The bicoherence detects the second-order phase coupling of EEG using the second-order spectrum analysis. So, bicoherence is used on phase coupling analysis of EEG. The normalized bispectrum and bicoherence are calculated by using the bispectrum and power spectrum of AR models according to the depth of anesthesia. The two-dimensional color map is represented for objectivity of the bicoherence value. Fig. 8 showed distribution of bicoherence peak according to the stage of anesthesia.

As a result, appearance rate of bicoherence value was observed that a strong appearance rate was represented in high frequency range(15 ~ 30Hz) at the stage of Awa., Pre. and Post. During the anesthesia, a strong appearance rate appeared at the low frequency area(0 ~ 10Hz) and a weak appearance rate appeared at the high frequency range(15 ~ 30Hz). The bicoherence analysis method provides the useful information about quadratic phase coupling according to the level of unconsciousness and are more reliable than other estimation factors at the stages of anesthesia.

The two-dimensional map of the appearance rate is divided into four sections for analysis of more objective value at the stages of anesthesia.

The results of bispectrum and bicoherence showed at the Table 1, Fig. 9, Table 2 and Fig. 10.

The four bispectrum parameters are calculated by using the percentage of a appearance rate. As the result, Bipara #1, Bipara #2, Bipara #3 and Bipara #4 parameters are extracted. We shown the average and standard deviation of anesthesia stages each parameter in Table 1. And Bipara #1, Bipara #2, Bipara #3 and Bipara #4 change the trend of parameters appeared at Fig 9.

As a result, the Bipara #1 and Bipara #2 changed the bispectrum distribution rate extremely at the stage of anest- hesia. it is difficult to distinguish each anesthesia stage. The Bipara #3 and Bipara #4 has the less change rate at each stage of anesthesia.

At the stage of anesthesia, the level of significance appeared below 0.01. Then, the parameters were reliable to estimate the depth of anesthesia. In the result of bispectrum analysis, all parameters were changed according to the depth of anesthesia, but Bipara #3 and Bipara #4 are considered the best parameter which showed the stage of anesthesia. And Bipara #3 and Bipara #4 show the consciousness and sedation level. As the results, a change of Bipara #1, Bipara #2, and Bipara #3 increased gradually according to the stage of anesthesia, but Bipara#4 decreased at the stage of Oper. Therefore, that showed a conscious state of the patient.

The bicoherence parameters as same with bispectrum were divided into four sections for analysis of more objective value on stages of anesthesia. The four bicoherence parameters set Bicpara #1, Bicpara #2, Bicpara #3 and Bicpara #4. We expressed the average and standard deviation of each parameter at the stage of anesthesia in Table 2. The trend of parameter appeared at Fig. 10.

Also the two-dimensional map of the appearance rate is divided into four sections for more objectivity. The four bicoherences were calculated by using the percentage of a appearance rate. As the result, Bicpara #1, Bicpara #2, Bicpara #3 and Bicpara #4 parameters were extracted. As a result of bicoherence analysis, all parameters were changed according to the stage of anesthesia, The Bicpara #2 and Bicpara #4 are considered the best parameters which showed the stage of anesthesia effectively.

V. CONCLUSION

In this paper, to develop the parameter for estimation of the depth of anesthesia, the data of EEG at each stage of anesthesia were received from the twenty-five patients who agreed to investigate themselves during operation with enflurane-anesthesis. The anesthetic depth was investigated at six stages as following. The EEG is applied to filtering of signal, base line correct and linear detrend to get more reliable analysis.

An appearance rate of bispectrum peak at each stage was observed in all area(0 ~ 35Hz). During the anesthesia, a strong appearance rate revealed at the low frequency area(3 ~ 15Hz). In case of bicoherence, appearance rate was strongly observed in high frequency range(15 ~ 30Hz) at the Awa., Pre., and Post.. During the anesthesia, a strong appearance rate appeared in the low frequency area(0 ~ 10Hz). The analysis method of bispectrum and bicoherence provides the useful information about quadratic phase coupling according to the level of unconsciousness and are more reliable than other estimation factors at the stages of anesthesia.

As a result of the bispectrum parameter analysis, Bipara#3 and Bipara#4 is considered the best parameter which showed the stage of anesthesia. In bicoherence analysis, Bicpara#2 and Bicpara#4 are considered the best parameter which showed the stage of anesthesia effectively.

Bispectrum analysis method has an advantage of getting information about the phase coupling failing to power spectrum. But bispectrum has only a part of the characteristics with the power spectrum. So, the method is under disadvantage because it can't acquire pure phase coupling of the EEG.

Bicoherence method excepts components of the power spectrum from bispectrum, so we can obtain the information about the phase coupling of the EEG.

Therefore, we can estimate the depth of anaesthesia by considering both bispectrum and bicoherence method.

The analysis method of HOS provides the useful information about the index of estimation according to the level of unconsciousness and suppression among other estimation factors on depth of anesthesia. In conclusion, the HOS analysis is a reasonable method to detect a patient's conscious stage. In the future, it is going to use for doctor's diagnosis and was applied to protect a medical accident owing to anesthesia.

REFERENCES

[1] Prys-Robert C, "Anaesthesia: A practical or impractical construct?," *Br. J. Anaesth*, vol.59, pp.1341-5, 1987.

[2] Brockway MS, Bannister J, McClure JH, McKeown DH, Wildsmith JAW, "Comparison of extradural ropivacaine and bupivacaine," *Br. J. Anaesth*, vol.66, no.31-7, 1991.

[3] Capouet V, De Pauw C, Vernet B, Ivens D, Derijcke V, Versichelen L, et al, "Single dose i.v. tropisetron in the prevention of postoperative nausea and vomiting after gynaecological surgery," *Br. J. Anaesth*, vol. 76, pp.54-60, 1996.

[4] Zwass MS, Fisher DM, Wellborn LG, Cot CJ, Davis PJ, Dinner M, et al, "Induction and maintenance characteristics of anaesthesia with desflurane and nitrous oxide in infants and children," *Anesthesiology*, vol.76, pp.373-378, 1992.

[5] Huang HH, Chan HL, Lin PL, Wu CP, Huang CH "Time-frequency spectral analysis of heart rate variability during induction of general anaesthesia," *Br. J. Anaesth*, vol.79, pp. 754-8. 1997.

[6] Sleigh JW, Donovan J, "Comparison of bispectral index, 95% spectral edge frequency and approximate entropy of the EEG, with changes in heart rate variability during induction of general anaesthesia," *Br. J. Anaesth*, vol.82, pp.666-71, 1999.

[7] Bruhn J, "EEG indices and heart rate variability as measures of depth of anaesthesia," *Br. J. Anaesth* , vol.83, pp.687, 1999.

[8] Liu J, Singh H, White PF, "Electroencephalogram bispectral analysis predicts the depth of midazolam-induced sedation," *Anesthesiology*, vol.84, pp. 64-9, 1996.

[9] Doi M, Gajraj RJ, Mantzaridis H, Kenny GNC, "Relationship between calculated blood concentration of propofol and electrophysiological variables during emergence from anaesthesia: comparison of bispectral index, spectral edge frequency, median frequency and auditory evoked potential index," *Br. J. Anaesth*, vol.78, pp.180-4, 1997.

[10] Liu J, Singh H, White PF, "Electroencephalographic bispectral index correlates with intraoperative recall and depth of propofol-induced sedation," *Anesth Analg*, vol.84, pp.185-9, 1997.

[11] Sigl JC, Chamoun NG, "An introduction to bispectral analysis for the electroencephalogram," *J. Clin. Monit.*, vol.10, pp.392-404, 1994.

[12] Helmut Schwilden, "Concepts of EEG processing: from power spectrum to bispectrum, fractals, entropies and all that," *Best Practice & Research Clinical Anaesthesiology*, vol. 20, no. 1, pp. 31 - 48, 2006.

[13] Sebel PS, "Evaluation of anaesthetic depth," *Br. J. Hosp. Med.*, vol.38, pp.116-7, 1987.