Journal of Clinical Monitoring and Computing (2019) 33:871–876
https://doi.org/10.1007/s10877-018-00238-z

ORIGINAL RESEARCH

Anesthesia depth monitoring using alternative placement of entropy sensors: a prospective study

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Received: 3 July 2018 / Accepted: 17 December 2018 / Published online: 19 December 2018

Abstract
Spectral entropy is based on analysis of variations in electroencephalography and frontal electromyography, and is a safe and reliable method for anesthesia depth monitoring. However, standard frontal positioning of entropy electrodes in patients undergoing cardiac surgery is sometimes challenging. The present study aimed to compare standard entropy sensor placement with an alternative (infraorbital) site. This prospective study included 20 patients who underwent cardiovascular surgery at the authors' center. Monitoring was performed with standard and alternative entropy electrode positions from patient admission to surgery to transfer to the intensive care unit. Data were recorded every 15 s; all data were analyzed and compared using Bland–Altman, scatter plot with Pearson correlation coefficient, and sensitivity/specificity analyses. Overall, 20,784 pairs of response entropy (RE) and state entropy (SE) indexes were collected. Bland–Altman analysis revealed a mean difference in RE of 0.37 (95% LOA − 7.09, 7.88) and SE 0.69 (95% LOA − 5.95, 7.31); with 3.46% (720/20,784) RE and 3.40% (706/10,790) SE values lying outside of the limits of agreement. Correlation analysis revealed strong positive correlation in both cases: RE, $r = 0.983$, $p < 0.05$; SE, $r = 0.984$; $p < 0.05$. Sensitivity/specificity analysis revealed 98.1% sensitivity, 93.3% specificity and 97.1% test efficiency for RE, and 99.2%, 95.1% and 98.5% for SE, respectively. Infraorbital entropy sensor placement in patients undergoing cardiovascular surgery is reliable and effective. The strong positive correlation between the two methods of registration enables alternative entropy measurement when frontal placement is not possible.

Keywords Entropy · Spectral entropy · Anesthesia depth · Neuromonitoring

1 Introduction

Determining the optimal depth of anesthesia remains one of the unsolved problems of modern anesthesiology. In cardiac surgery every hemodynamic disturbance can become crucial, for this reason careful titration of anesthetics is often required. Hence anesthesia depth assessment becomes an extremely valuable tool [1]. Entropy is an electroencephalographic-based monitoring method that evaluates the irregularity of a signal. Entropy sensors are positioned on the patient's frontotemporal region of the face. However, in some cases, such an application site is unsuitable, for example, in patients undergoing aortic arch surgery, brachiocephalic vessel interventions and others who require multimodal neuromonitoring using cerebral oximeter monitors and a transcranial Doppler helmet. In such situations, an alternative entropy lead montage can be used instead of the frontotemporal. Recently, several studies have examined alternative positions for bispectral index electrodes [2–4], one of which described successful use of the infraorbital position [5]. We contemplated whether sensor placement inferior to a frontotemporal montage could be useful for certain groups of patients.

Accordingly, the aim of the present study was to determine whether an alternative (infraorbital) entropy sensor position could be used instead of the normal site of placement in patients undergoing cardiovascular surgery.

2 Methods and materials

A prospective study including 20 patients undergoing elective cardiovascular surgery was performed. Local Ethics Committee approval was obtained, as was informed written consent from all individual participants included in the

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study. The study was organized in compliance with the principles of the Declaration of Helsinki. Patients with a history of head injury, brain tumor, stroke, syncope, or maxillofacial trauma were excluded from the study.

2.1 Anesthesia

A diverse range of cardiovascular surgery procedures was performed (coronary artery bypass graft; heart valve surgery; ascending aorta replacement, and lower extremity bypass surgery). All patients underwent multicomponent balanced anesthesia using propofol, sevoflurane and fentanyl. Patients received premedication with trimeperedine and chloropiramine 40 min before surgery. Anesthesia was induced using fentanyl (3.0–5.0 µg/kg) and propofol (1.5–2.5 mg/kg). Muscle relaxation was maintained using pipecuronium bromide (0.1 mg/kg). Sevoflurane at a minimum alveolar concentration of 1–1.5 was the main hypnotic agent, except during cardiopulmonary bypass, when fentanyl at 2.0–3.0 µg/kg*h and propofol at 2–4 mg/kg*h were used. Dissociative anesthetic agents were not applied. Normothermic cardiopulmonary bypass was used in 10 of 20 cases.

2.2 Spectral entropy

The entropy module converts irregular content of the electroencephalographic (EEG) signal into an index that reflects the level of anesthesia. Normally, signal is acquired from the skin of the forehead and the side of the head; therefore, it contains an EEG and frontal electromyogram (EMG) component [6]. The entropy module produces two values: response entropy (RE) and state entropy (SE). When SE contains nothing but EEG signal and is computed over the frequency range 0.8–32 Hz, RE includes additional higher frequencies up to 47 Hz therefore contains EMG and is considered to be an indicator of pain [6]. The index is calculated as follows: high levels of entropy during anesthesia demonstrate that the patient is awake, whereas low levels of entropy are correlated with deep unconsciousness.

Before the induction of anesthesia, both normal and alternative (infraorbital) GE Easy Fit entropy (GE Healthcare Finland Oy, Helsinki, Finland) sensors were placed on each patient (Fig. 1). Sites of placement were prepared according to official entropy guidance. The entropy monitor automatically checks electrode impedance. If the impedance of each electrode is within the limit set by the manufacturer, it is deemed to have "passed". No electrode failed at any time during the study. RE and SE indexes were displayed on GE Datex-Ohmeda AS/5 monitors (GE Medical Systems Information Technologies Inc. Milwaukee, WI, USA). All data were acquired in 15 s intervals until the patient had been transferred to the intensive care unit (ICU).

Fig. 1 Both standard and alternative (infraorbital) entropy sensors positions

2.3 Statistical analysis

A variety of statistical methods were used for data analysis. Normal distribution of continuous variables was tested using the D'Agostino & Pearson omnibus normality test. Limits of agreement were determined using Bland–Altman analysis [7]. This method was used for overall data and for each patient separately. The methods were considered to be equivalent, with less than 5% of values lying outside the 95% limits of agreement. Furthermore, correlation analysis was used with Pearson's coefficient calculation (r). Correlation between the methods was regarded to be statistically significant at $p < 0.05$. In addition, analysis of data near the therapeutic threshold of 60 to identify the occurrence of incorrect therapy change when the actual depth of anesthesia according to normal position registration is acceptable. For this purpose, sensitivity/specificity analysis was used with the normal electrode position as the diagnostic "gold standard".

All analyses were performed using STATISTICA 10 software (StatSoft Inc. 1984–2018) and Microsoft Office Excel 2010 (Microsoft Corp., Redmond, WA); $p < 0.05$ was considered to be statistically significant.

3 Results

Demographic and clinical data of the subjects are presented in Table 1. A total of 20,784 pairs of each index (i.e., RE and SE), collected from normal and alternative positions, were analyzed. Bland–Altman analysis revealed 3.46%

Table 1 Patient characteristics

Age (years), Me (IQR)	67 (58–70)
Gender (M/F), %	60/40
Weight, kg	78 (71–116)
Body surface area, m^2	1.98 ± 0.34
CABG	10 (50%)
Combined valve and CABG surgery	3 (15%)
LEBS	2 (10%)
Ascending aorta replacement	5 (25%)

Continuous data are presented as mean standard deviation or median (interquartile range). Categorical variables are frequencies (percentage)

CABG coronary artery bypass graft, *LEBS* lower extremities bypass surgery

(720/20,784) of RE and 3.40% (706/10,790) of SE values lying outside the limits of agreement (Fig. 2). Overall differences between two methods of registration was 0.37 (95% CI − 1.99, 2.74) with an upper limit of agreement of 7.88 and a lower limit of agreement of − 7.09 for RE and 0.69 (95% CI − 1.40, 2.79) with an upper limit of agreement of 7.31 and a lower limit of agreement of − 5.95 for SE. Additionally, Bland–Altman scores were evaluated for each patient separately. The number of values lying outside the limits of agreement was from 1.14 to 4.34%, and from 1.06 to 3.98% for RE and SE, respectively.

Correlation analysis using Pearson's coefficient count revealed a strong linear association between normal and alternative RE and SE measurements: RE, $r = 0.983$, $p < 0.05$; and $r = 0.984$; $p < 0.05$ for SE (Fig. 3).

Using sensitivity/specificity analysis to compare with the normal (i.e., standard) position, the infraorbital site of placement demonstrated 98.1% sensitivity, 93.3% specificity and 97.1% test efficiency for RE, and 99.2% sensitivity, 95.1% specificity and 98.5% test efficiency for SE.

4 Discussion

The main finding of the present study was that use of an alternative placement location for the entropy sensors was equally effective as the standard position. It has major practical significance for all anesthesiologists in cases when classical frontal positioning of the entropy leads is cumbersome or not possible.

Unfortunately, EEG-based monitoring of the depth of anesthesia still has not become a routinely assessed method during all surgical procedures. The economic and clinical benefits of anesthetic depth monitoring have been widely noted in many trials and reviews [8, 9]. Excessively deep anesthesia levels lead to related morbidities such as postoperative nausea, neurocognitive dysfunction, and prolonged ICU stay [9]. Underdosage of anesthetic drugs causes intraoperative awareness, especially in cardiac surgery, in which the incidence of this condition is relatively high (from 0.2 to 2.0%) [10]. Awareness during anesthesia results in the development of sleep disturbances, nightmares, anxiety attacks, distressing flashbacks, inability to concentrate and, probably, post-traumatic stress disorder [11, 12]. In addition, physical signs of intraoperative awareness, such as tachycardia, arterial hypertension, lacrimation and sweating, are not specific [13, 14]. A Cochrane database review reported a decrease in time of awakening after surgery and in ICU stay in the entropy group [2]. Another Cochrane review additionally reported a lower incidence of intraoperative awareness when EEG-based monitoring was performed [15]. Economic benefits have been explained by the use of less anesthetic agent [8, 9].

It has been established that cardiothoracic and vascular surgery often requires advanced anesthesiological monitoring, with many sensors and electrodes requiring placement, which sometimes leads to ergonomic and technical problems. For example, in our practice, we encounter such difficulties in cases of simultaneous positioning of sensors for the cerebral oximeter monitor, transcranial Doppler helmet, and entropy. This problem prompted a reconsideration of how we could place the entropy electrodes in an alternative position. To date, many authors have examined various positions of EEG-based monitor leads, especially in neuroanesthesiology, where electrodes can interfere with surgery [3, 4, 13, 16]. In only one of the studies, the authors used an alternative position for bispectral index sensors that was inferior to the standard position [5]. We did not find any comparable studies with the entropy monitor. Interestingly, even an alternative mandibular position of the sensors was tested, with a predictable negative result [17]. After analyzing previous research, we selected the infraorbital position for the entropy leads.

We analyzed our data using different statistical methods. Bland–Altman analysis revealed that only 3.5% of the values were outside the 95% confidence interval. Limits of agreement were obtained in the ideal interval of 10 units, which shows normal variability for both RE and SE indexes. The majority of values lying outside the limits of agreement refer to the periods of active head and body position change, for example during operative field preparation or placing an internal jugular venous line. During this procedure, physicians always touch the sensors, which results in interference of the entropy registration. We also examined individual Bland–Altman scores, which varied < 5%. Correlation data analysis revealed strong linear relationships between normally and alternatively registered values for both RE and SE.

Regarding cases of inappropriate additional anesthetic drug administration or failure to change therapy when it was indicated, we performed sensitivity/specificity

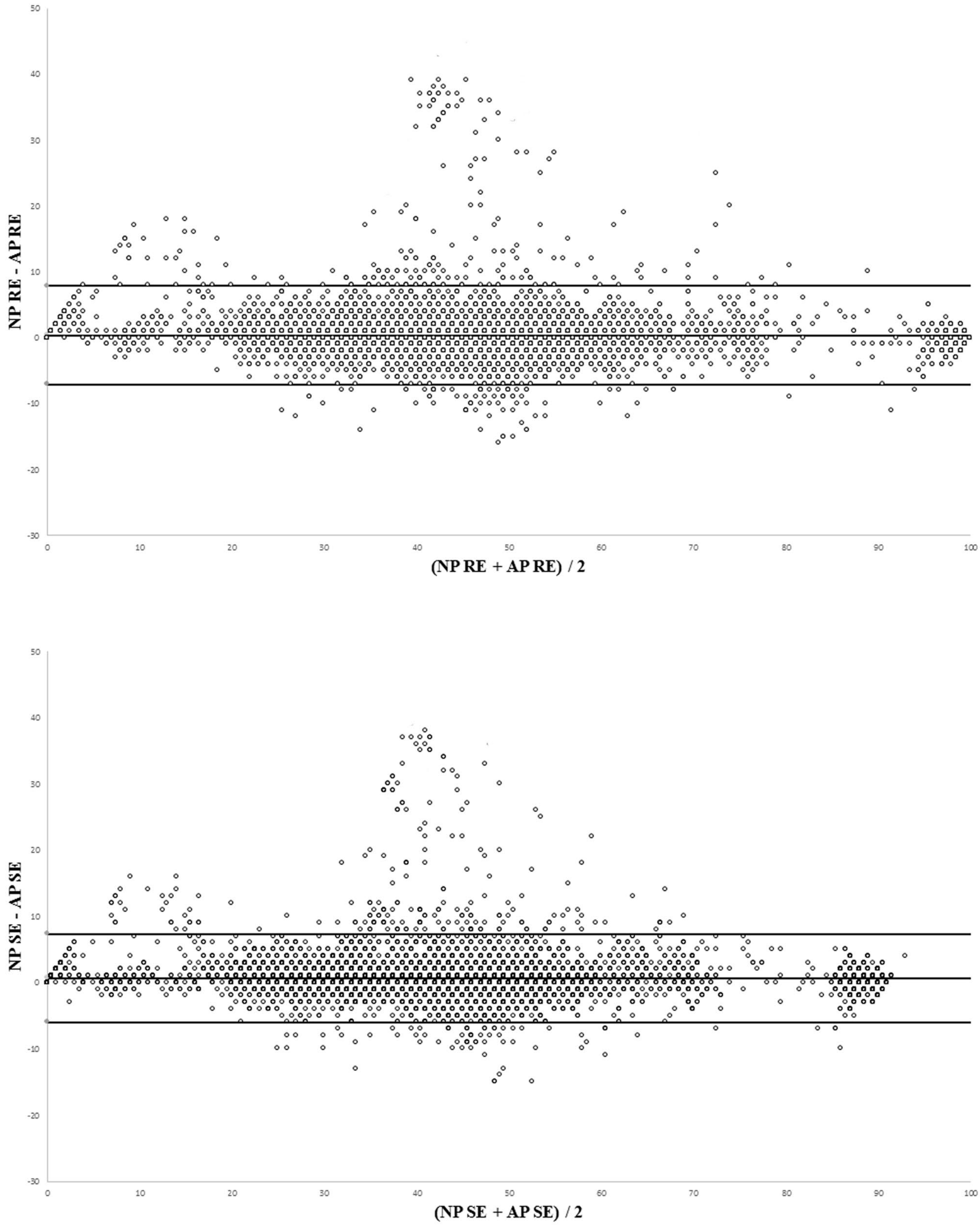

Fig. 2 The overall Bland–Altman plots, comparing standard and alternative entropy positions for both SE and RE indexes. The mean difference (continuous middle line) and upper and lower limits of agreement (upper and lower continuous lines respectively) are shown

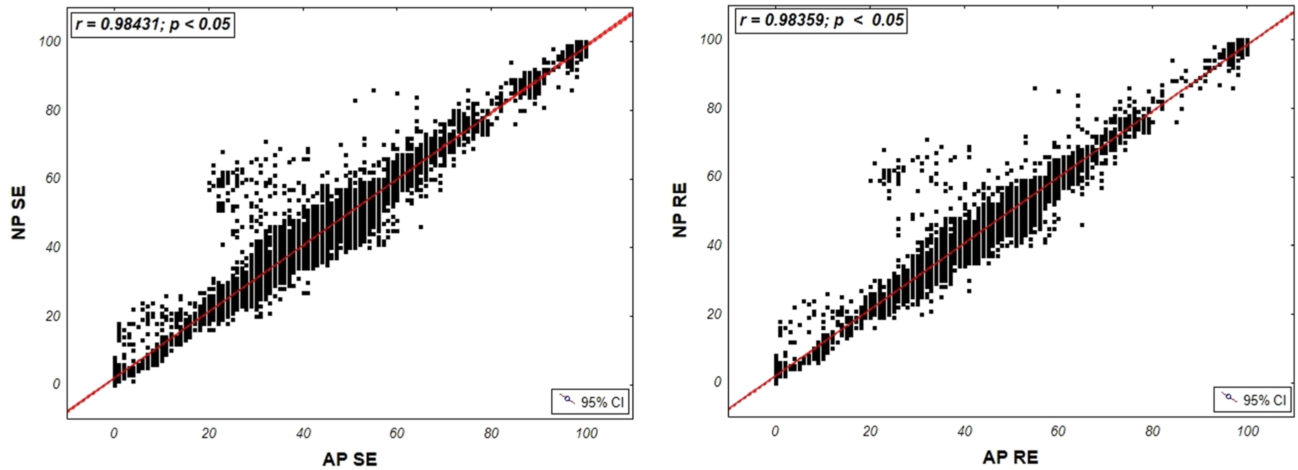

Fig. 3 The overall scatter plots, comparing normal and alternative entropy positions for both SE and RE indexes

analysis and found relatively high values for both alternative RE and SE. We found that only 172 values (1.31%) for RE and 61 (0.51%) for SE were above the threshold of 60, when normally registered indexes were in 40–60 interval. In contrast, the alternative position RE was in 40–60 gap, when normal position demonstrated values > 60 in 182 (1.47%) and SE in 112 (0.97%) cases. In our opinion, such frequencies of false-positive results are concerning because appropriate therapy would not have been administered in cases when it was needed. Despite the fact that the number of false-positive and false-negative ratios is relatively low, this issue requires additional research because of its clinical relevance.

5 Limitations

There were several limitations to our study. We did not draw any conclusions about the general use of entropy in cardiothoracic and vascular surgery. Moreover, we did not examine differences in various stages of anesthesia. The biopotential obtained from entropy electrodes is a complex composition of EEG, EMG (from multiple muscles), and environmental mechanical and radiofrequency electrical signals. Infraorbital electrode placement can potentially alter the relative contribution of these generators to the entropy composite. Consequently, the contribution of the cerebral cortical generator may be diminished. The potential risk of such placement is diminished sensitivity to noteworthy change(s) in cortical entropy. Determining the probability of a false-negative response would require a study with a very large sample size. Further trials, therefore, are warranted.

6 Conclusions

Our preliminary study demonstrated that infraorbital entropy sensor placement in patients undergoing cardiovascular surgery is reliable and effective. The strong positive correlation between the two methods of registration enables the use of alternative entropy measurement when frontal placement is not possible.

Acknowledgements This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Arutyunyan OM, Yavorovsky AG, Seleznev MN, Guleshov VA, Bunyatyan AA. Entropy monitoring of anesthetic depth at cardiac surgery. Vestnik Anestesiologii I Reanimatologii. 2011;6:17–23.
2. Chhabra A, Subramaniam R, Srivastava A, Prabhakar H, Kalaivani M, Paranjape S. Spectral entropy monitoring for adults and children undergoing general anaesthesia. Cochrane Database Syst Rev. 2016;3:CD010135.
3. Dahaba AA, Xue JX, Zhao GG, et al. BIS-vista occipital montage in patients undergoing neurosurgical procedures during propofol remifentanil anesthesia. Anesthesiology. 2010;112:645–51.
4. Hall JD, Lockwood GG. Bispectral index: comparison of two montages. Br J Anaesth. 1998;80:342–4.
5. Nelson P, Nelson JA, Chen AJ, Kofke WA. An alternative position for the BIS-Vista montage in frontal approach neurosurgical cases. J Neurosurg Anesthesiol. 2013;25:135–42.

6. Viertiö-Oja H, Maja V, Särkelä M, Talja P, Tenkanen N, Tolvanen-Laakso H, et al. Description of the entropy algorithm as applied in the Datex-Ohmeda S/5 entropy module. Acta Anaesthesiol Scand. 2004;48:154–61.
7. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet. 1986;1:307–10.
8. Jiahai M. Spectral entropy monitoring reduces anesthetic dosage for patients undergoing off-pump coronary artery bypass graft surgery. J Cardiothorac Vasc Anesth. 2012;26:818–21.
9. Shepherd J, Jones J, Frampton G, Bryant J, Baxter L, Cooper K. Clinical effectiveness and cost-effectiveness of depth of anaesthesia monitoring (E-Entropy, Bispectral Index and Narcotrend): a systematic review and economic evaluation. Health Technol Assess. 2013;17(34):1–264.
10. Leon S. Awareness in cardiac anesthesia. Curr Opin Anesthesiol. 2010;23:103–8.
11. Yu H, Wu D. Effects of different methods of general anesthesia on intraoperative awareness in surgical patients. Medicine (Baltimore). 2017;96(42):e6428.
12. Messina AG, Wang M, Ward MJ, Wilker CC, Eggers M, Miller DB, et al. The effectiveness of anaesthetic interventions for prevention of wakefulness and awareness during and after surgery. Cochrane Database Syst Rev. 2008;3:803–8.
13. Shiraishi T, Uchino H, Sagara T, et al. A comparison of frontal and occipital bispectral index values obtained during neurosurgical procedures. Anesth Analg. 2004;98:1773–5.
14. Singh S, Bansal S, Kumar G, Gupta I, Thakur JR. Entropy as an indicator to measure depth of anaesthesia for laryngeal mask airway (LMA) insertion during sevoflurane and propofol anaesthesia. J Clin Diagn Res. 2017;11(7):1–3.
15. Messina AG, Wang M, Ward MJ, Wilker CC, Smith BB, Vezina DP, Pace NL. Anaesthetic interventions for prevention of awareness during surgery. Cochrane Database Syst Rev. 2016;10.
16. Akavipat P, Hungsawanich N, Jansin R. Alternative placement of bispectral index electrode for monitoring depth of anesthesia during neurosurgery. Acta Med Okayama. 2014;68:151–5.
17. Lee SY, Kim YS, Lim BG, Kim H, Kong MH, Lee IO. Comparison of bispectral index scores from the standard frontal sensor position with those from an alternative mandibular position. Korean J Anesthesiol. 2014;66:267–73.