Comparison of spectral entropy and bispectral index electroencephalography in coronary artery bypass graft surgery

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Comparability of Spectral Entropy and Bispectral Index EEG in Coronary Artery Bypass Graft Surgery

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**Objective:** The study’s aim was to compare Response (RE) and State Entropy (SE) with Bispectral Index (BIS) electroencephalography (EEG) as an alternative cerebral monitoring tool in patients scheduled for coronary artery bypass graft surgery.

**Design:** Prospective, observational single-center study

**Setting:** University Hospital

**Participants:** Thirty patients undergoing coronary artery bypass graft surgery receiving remifentanil-propofol anaesthesia.

**Interventions** Surgery was performed with cardiopulmonary bypass (CPB) and cardiac arrest in fifteen patients, with CPB without cardiac arrest in nine patients and without CPB in six patients.

**Measurements and Main results** RE, SE, BIS, burst suppression ratio (BSR) and frontal electromyography (f-EMG) were detected simultaneously. RE and SE compared favorably to BIS and their correlations were strong ($r^2 = 0.6$, $r^2 = 0.55$, respectively). Mean bias of RE and BIS was -1.8, but limits of agreement were high (+20.5/-24.1). RE and SE tended to be lower than the BIS values in the CPB subgroups. Detection of BSR was similar with RE and SE, and the BIS. A strong correlation existed between BIS and f-EMG ($r^2 = 0.62$), in contrast to RE ($r^2 = 0.45$) and SE ($r^2 =0.39$). BIS monitoring was significantly more disturbed than RE and SE with 9.1 ±10.9% and 0.1±0.2% of the total anesthesia time, respectively. Neither implicit nor explicit memory was demonstrated.

**Conclusion** RE and SE are comparable with the BIS but showed significantly less interference from f-EMG and superior resistance against artefacts. Thus, Spectral Entropy is more suitable than the BIS during propfol-remifentanil anesthesia in cardiac surgery patients.

**Words:** 248
Introduction

The most frequently used electroencephalographic (EEG) device for monitoring the level of sedation during anesthesia is the bispectral index (BIS) monitor [1]. This device has been extensively studied and validated over the past 10 years in adult and pediatric cardiac anesthesia [2]. However, BIS is associated with a high degree of inter-patient variability, variable responses to different classes of anaesthetic drugs, and a high degree of mechanical and electrical signal interference during surgery [3, 4]. Cardiac surgery patients also are at high risk of intraoperative awareness and of disturbances in cerebral perfusion and oxygenation [5, 6], mainly during cardiopulmonary bypass (CBP), aortic surgery and particularly during the period of luxation the heart in coronary artery bypass graft surgery without CPB. Hence, reliable and more robust electroencephalographic devices are needed to secure continuous cerebral monitoring. One such method may be the spectral entropy of EEG realized in the M-entropy module (GE Healthcare, Brussels, Belgium) that was introduced in 2004 [7]. With this device, the digitized raw EEG signal is first transformed into the frequency domain by fast Fourier transformation to identify sinusoidal components and calculate its power spectrum. Second, the Shannon function is applied to assign each frequency a specific value. The exact algorithm has been described in detail elsewhere [8]. In contrast to other cerebral monitoring devices, the M-entropy module digitizes the EEG at a much higher sampling rate (400Hz) and, to detect artefacts, the power in the frequency range (200 – 1000 kHz) is continuously measured, The M-entropy module generates two distinct numbers for response entropy (RE) and state entropy (SE) between 100 to 0 and 91 to 0, respectively. RE is reflecting the cortical state of the patient as well as frontal electromyographic (f-EMG) components, whereas SE separately expresses the cortical state. RE approximates SE when the f-EMG power is equal to zero. The difference between RE and SE seems to be [9] an indicator of f-EMG activation.
The aim of this study was to compare the performances of RE and SE, as a reliable alternative method of detecting cerebral activity, against the BIS during coronary artery bypass graft surgery (CABG). We hypothesized that RE and SE would be more accurate than BIS in reflecting the electrical activity of the brain, as well as more resistant to artefacts during cardiac surgery.
Materials and Methods

Upon receiving ethics committee approval and obtaining written informed consent, 30 patients scheduled for coronary artery bypass grafting were enrolled. Exclusion criteria were non-German-speaking patients, unstable hemodynamics, age <18 years, pre-existing neurological disorder, alcohol or drug abuse, hearing problems, severely impaired renal or hepatic function, emergency surgery, and significant stenosis of carotid or vertebral arteries. Premedication included oral flunitrazepam (1 to 2mg) the evening before surgery and oral midazolam (7.5 to 15mg) 45 min before transfer to the operating room.

Standard instrumentation was used in the operating theatre: a 5-lead ECG (Hellige SMU 612 monitor, Marquette Hellige Medical Systems, Freiburg i.Br, Germany), pulse oximetry using a finger clip (Nellcor Durasensor, Model DS-100A), and continuous arterial blood pressure monitoring via a fluid-filled catheter system (Baxter Healthcare Corp. Cardiovascular Group, Irvine, CA, USA) connected to a cannula in the nondominant radial artery. Then the forehead and, bilaterally, the temporal part of the patient’s head were gently rubbed with EEG abrasive skin prepping gel (Nuprep; D.O. Weaver & Co, Aurora, CO, USA). In accordance with the manufacturer’s instructions, a BIS sensor with four elements (BIS Quatro Sensor; Aspect Medical Systems International, Leiden, The Netherlands) connected to the BIS monitor module (S/5 BIS Module, BIS XP) and a three-element disposable entropy sensor (GE Healthcare, Brussels, Belgium) connected to the M-entropy module were applied to the patient’s forehead. Sampling rate for RE and SE was 400 Hz and for BIS 256 Hz.

If the electrode impedance was above 7.5 kΩ for the entropy or 10 kΩ for the BIS, the devices did not provide initial (baseline) index values. Sigma quality index (SQI) values (for the BIS monitor) and the skin impedance values (for the entropy monitor) were inspected at 10-min intervals during the procedure to ensure adequate EEG signal quality. The moving average
The windows used to calculate the entropy values were 2–15 s and 15–60 s for the RE (32–47 Hz) and SE (<32 Hz) values, respectively, compared with a fixed 15-s interval for the BIS value.

The 95% spectral edge frequency, delta ratio, burst suppression ratio (BSR) were calculated using the raw EEG parameter of the M-entropy module. Additionally, f-EMG power (sum of the spectral power between 32 to 47 Hz) was recorded by the M-entropy module. All monitored parameters were saved on a laptop computer (HP Pentium; Hewlett-Packard, Palo Alto, CA, USA). BIS, SE, RE, 95% spectral edge frequency, delta ratio, BSR and frontal EMG were recorded in epochs of 15 s.

Intravenous anesthesia using propofol (1.5 \( \mu \text{g.ml}^{-1} \) to 2.0 \( \mu \text{g.ml}^{-1} \)), supplemented by bolus injections of fentanyl (3 to 10 \( \mu \text{g.kg}^{-1} \)) and pancuronium (Organon; 0.1 mg.kg\(^{-1}\)), was administered to all patients. Anesthesia was maintained with propofol (1.5 \( \mu \text{g.ml}^{-1} \) to 2.6 \( \mu \text{g.ml}^{-1} \)) and remifentanil (0.1 to 0.3 \( \mu \text{g.kg}^{-1}.\text{min}^{-1} \)) to keep the BIS target value at 40 (between 35 to 45). After endotracheal intubation, the patient was mechanically ventilated (Siemens Servo 900; Erlangen, Germany) using a volume-controlled mode. According to institutional requirements, a triple-lumen central venous catheter (Arrow International, Reading, PA, USA) and a 7.5 FG thermistor-tipped, flow-directed pulmonary artery catheter (IntelliCath; Baxter Healthcare Corp.), introduced through an 8.5 FG introducer (Arrow International), were inserted in the right jugular vein. The pulmonary artery catheter was connected to a cardiac output computer system (9520A; Baxter Healthcare Corp.). Finally, video goggles (Eye-Trek; Olympus Medical Systems, Hamburg, Germany) were attached.

During periods of surgery that were expected to be painful (e.g., sternotomy), bolus injections of fentanyl (3 to 7 \( \mu \text{g.kg}^{-1} \)) were administered according to the standard procedures of the institution. To detect implicit memory immediately after skin incision, sternotomy, pericardectomy, and chest closure, the patient’s eyes were manually opened, and 20 combined words of a word-stem completion test in series were played in the video goggles and simultaneously spoken aloud. During these periods, the RE, SE and the BIS values were
observed after 45 s to detect possible changes relating to the procedure. The word stream included only combined words in the national language, German, thus excluding the possibility of misunderstanding.

BIS, SE, RE, 95% spectral edge frequency, delta ratio, BSR, f-EMG, heart rate, mean arterial pressure (MAP), $P_{a}CO_{2}$, $P_{a}O_{2}$, $P_{ET}CO_{2}$, and body temperature were documented at the following time points: (101) before induction of anesthesia, (102) after induction of anesthesia, (103) before and (104) after endotracheal intubation, (105) after skin incision, (106) after sternotomy, (107) after pericardectomy, (108) after cannulation of the vessels, (109 through 119) every 15 min during cardiopulmonary bypass or (in off-pump cases) every 15 min during bypass grafting, (120) at the end of bypass, (121) after chest closure and (122) at the end of surgery. The EEG parameters were documented in duplicate using online and offline data acquisition. Eighteen hours after extubation and on the third day after surgery, a structured Brice questionnaire [10] was administered to the patient, and 18 h after tracheal extubation the word-stem completion test was repeated with only one investigator.

**Statistics**

For comparison, the median value over a collection period of 15s was calculated for RE, SE, BIS, 95% spectral edge frequency, delta ratio, BSR and f-EMG. Results are expressed as the mean ± standard deviation and median (range) where appropriate unless otherwise stated. Continuous and ordinal data were compared using a Kruskal-Wallis test. Nominal data were compared using the chi-square test and Fisher’s exact test when appropriate. The Mann-Whitney test and Fisher exact test with Bonferroni correction were used for post-hoc comparisons. Time-dependent data were analyzed with ANOVA for repeated measurements with Greenhouse-Geisser correction. Bonferroni correction was used for comparisons
between specific time points, between groups and coherence, and between temperature and various processed EEG parameters. Agreement between BIS and RE values was assessed by Bland-Altman analysis [11] on all data and on data of the three subgroups. Bland Altman was performed only for analysis agreement between BIS and RE because both indexes are numbered between 0 – 100. Simple regression analysis was used to compare (i) BIS with SE and (ii) BIS, RE and SE with BSR, 95% spectral edge frequency and delta ratio. P values of <0.05 were considered significant. SPSS 16 (SPSS Schweiz Ag, Zurich, Switzerland) were used for statistical analyses.
**Results**

Twenty-nine men and one woman were enrolled in the study. Coronary artery bypass grafting (CABG) was performed with cardiopulmonary bypass (CPB) and cardiac arrest (CPB arrest) in 15 patients, with CPB without cardiac arrest (CPB beating) in nine, and without CPB (OPCAB) in six patients. The patients’ characteristics are listed in Table 1. The median age was highest in the OPCAB group, but this was only significant in comparison with the CPB arrest group (p = 0.007). No difference was found in the duration of anesthesia and surgery, but the number of coronary artery bypass grafts performed was significantly higher in both CPB groups compared to the OPCAP group (p < 0.05). Body temperature (p = 0.0001) and cumulative doses of propofol (p = 0.0001) were significantly lower in the CPB arrest group compared to the OPCAP group.

Changes in the mean values of RE and SE recorded during the 22 data collection periods were similar to those of BIS. RE ($r^2 = 0.6$) and SE ($r^2 = 0.55$) showed a strong correlation with the BIS (table 2). Overall, Bland-Altman analysis of RE and BIS values resulted in a mean bias -1.8 but high limits of agreement (table 2). Post-hoc analysis of the subgroups demonstrated primarily lower mean values for RE compared to BIS in the CPB arrest and CPB beating subgroups, whereas mean values of RE were higher than those of the BIS in the OPCAB subgroup (Fig 1a-d). This observation was only significant between the CPB arrest and OPCAP subgroups (p = 0.03) (table 1).

RE and SE were moderately correlated with the 95 % spectral edge frequency ($r^2 = 0.14$ and 0.15, respectively). In contrast to RE and SE, a high correlation of BIS with f-EMG patterns (table 2) was found. Linear correlation between BIS, RE and SE with BSR were $r^2 = 0.41$, 0.25 and 0.26, respectively (Fig 2a–c). Multiple regression analysis yielded that BIS, RE and SE were not influenced by heart rate, mean arterial pressure, arterial carbon dioxide tension...
(P<sub>e</sub>CO<sub>2</sub>), endtidal carbon dioxide (P<sub>e</sub>CO<sub>2</sub>) or arterial oxygen tension (P<sub>a</sub>O<sub>2</sub>). RE and SE were significantly influenced by temperature in the CPB arrest subgroup (p = 0.01).

Mechanical or electrical stimulation resulted in significantly more disturbances in the BIS (p < 0.0001) than in the spectral entropy EEG with total disturbance periods of 9.1 ±10.9% and 0.1±0.2% of the anesthesia time, respectively (table 3).

During the periods where the word-stem completion tests were performed, RE, SE and BIS values remained constant and neither explicit nor implicit memory was revealed postoperatively by the patients’ performances on the questionnaires.
Discussion

The main findings of this study are that RE and SE compare favourably to BIS during propofol-remifentanil anaesthesia, although the agreement between RE and BIS was only moderate. Contrary to the BIS, RE and SE were significantly less influenced by frontal EMG and were considerably more resistant to mechanical or electrical artefacts.

Several investigators have compared spectral entropy parameters with BIS using different anesthetic drugs during the period of induction of anesthesia [12-14], but their results were inconsistent. In the present study, the comparability of RE and SE, and BIS was investigated during the period of maintenance of the propofol-remifentanil anaesthesia, where the remifentanil concentration was kept constant, and fentanyl was added at expected painful periods. Altogether, a strong correlation between BIS and spectral entropy parameters was found in the present investigation. Recently, White and colleagues [12] reported a good correlation between SE and BIS during induction and maintenance anesthesia with propofol and desflurane in patients undergoing major laparascopic surgery. Similar to the results of the current study, changes in RE and SE favored comparably with those in the BIS during the perioperative period. They concluded that the entropy module is a cost-equivalent alternative to the BIS monitor.

To our knowledge, only two studies were performed comparing RE and SE with BIS during cardiac surgery. Tiren and colleagues [15] reported an acceptable agreement only in approximately 60% of the 109 simultaneously detected data pairs of RE and SE and BIS during CPB and anesthesia with midazolam/fentanyl and propofol. This may be due to the predominant midazolam-fentanyl based anesthesia with added propofol used in their study. After using total intravenous midazolam-fentanyl anesthesia, Driessen and colleagues [16] discovered that the BIS is a not very reliable monitor of global anesthetic adequacy in cardiac
surgery patients. Most recently, Haenggi and colleagues [17] reported large intra-individual and inter-individual variability in BIS and entropy values in midazolam-remifentanil sedated volunteers and concluded that it was impossible to determine sedation levels by processed EEG. In 66 midazolam-sufentanil anesthetized patients undergoing coronary artery bypass graft surgery, Lehmann and colleagues [18] found no relationship between BIS levels and RE and SE at two different BIS-guided stages of a midazolam-sufentani anesthesia. In contrast to sedative drugs, intravenous or volatile hypnotic drugs, with the exception of ketamine, nitrous oxide and xenon, show dose-dependent comparable responses of RE, SE and the BIS. The only moderate agreement of BIS and RE may be explained by the different sample times for actualisation of the BIS value (time window of 15 to 60s) and the RE value (2 to 15s). The significant time delays reported for indices from the BIS by Pilge and colleagues [19] potentially explain the disparity between BIS and RE demonstrated in the current investigation. However, the findings in the current study suggest that the M-entropy module is a reliable alternative to the BIS during propofol-remifentanil anesthesia in coronary artery bypass graft surgery patients.

The observation of significantly lower RE and SE values compared to the BIS in the CPB arrest subgroup is in agreement with the findings of Lehmann and colleagues [18] and probably explained by the smooth hypothermic condition (32 to 35 degree) of the patients during CPB. As expected, the propofol concentration required to achieve the desired BIS level was significantly lower in this subgroup. That temperature has an effect on the BIS has been previously reported by Schmidlin and co-workers [3] and Mathew et al [20]. Because anesthetic drug concentrations during the current study where guided by BIS levels that were kept between 35 and 45, the impact of temperature on the BIS has been excluded. As neither explicit nor implicit memory was detected in the patients, sufficient depth of anesthesia has to be assumed. Hypothermia may be the principal reason for the lower values of RE and SE, but
it is well known that low temperatures reduce consciousness and EEG activity, which may be expressed in the observed lower RE and SE values. The BSR is stated to be a reliable parameter to estimate the intensity of suppression of electrical brain activity [21] and it is one electroencephalographic component of the algorithm of the BIS [22]. Although no significant differences were found between BIS, RE and SE in detecting burst suppression states, similar to Bruhn and co-workers [23], BIS showed a nearly linear correlation only with BSR ≥ 30% in the current study (fig 2 a – c) whereas BSR values ≤ 30% were not detected by the BIS. Recently, Takizawa and colleagues [24] compared propofol plasma concentrations with contemporaneously detected BIS values using the Aspect A-2000 device during cardiac surgery. They reported unaltered BIS values at propofol plasma concentrations generating BSR ≤ 40%, however, a significant propofol plasma concentration dependent reduction for BSR ≥ 40%. The authors concluded that increasing unbound propofol concentrations, causing BSR ≤ 40%, were not adequately reflected by BIS. These findings may support the hypothesis that BIS values between 35 and 45 cannot definitely detect the intensity of suppressed brain electrical activity. To what extent the RE and SE may better detect the level of the anesthetized brain cannot be determined in the current study and needs further investigation.

Several investigators evaluating BIS devices [25, 26], reported a significant impact of the f-EMG on BIS, whereas only a few studies demonstrated less impact of f-EMG on SE [9, 27]. In the present investigation the strong effect of f-EMG on BIS was confirmed, but RE and in particular SE were significantly less impaired by muscle activity. These findings are important in cardiac surgery patients at our institution because application of the neuromuscular blocking agent is performed only during induction of anesthesia. During the process frontal muscle activity is continuously increased when neuromuscular blockade
disappears and that may influence the BIS significantly whereas RE and SE seems to be less affected.

Another important finding of the current investigation was the presence of significant disturbances in the BIS from mechanical and electrical artefacts. Electrical, electromagnetic and mechanical stimulations are frequently used during cardiac surgery. Hemmerling and colleagues [28] found a significant interference of electromagnetic operating systems with BIS in otorhinolaryngology surgery. The same results have been reported during propofol and sevoflurane anesthesia in laparascopic surgery [12] and most recently in anesthetized brain death patients [29]. Like otorhinolaryngology surgery, in cardiac surgery stimulation by the surgeon is performed close to the head and thus near to the cerebral monitoring sensors. Therefore, the probability of interference is much higher than during surgery in areas far from the head. To our knowledge, only Schmidlin and colleagues [3] have reported detection failures of BIS in cardiac surgery patients. In the present study, considerable detection failures of BIS have been observed during electrical, electromagnetic and mechanical interferences, whereas RE and SE were nearly resistant to these artefacts. While time periods of undetected BIS ranged between 2 to 135 min during anesthesia, RE and SE were only disturbed in a range of 0 to 3 min.

Cerebral monitoring during cardiac anesthesia is not only monitoring the depth of anesthesia in this high-risk patient population, but also serves as a tool for real time detection of cerebral perfusion and oxygen supply to the brain. The decreased impact of f-EMG on RE and most notably on SE and the considerably superior resistance against mechanical and electrical artefacts are important advantages of the spectral entropy EEG over the BIS.

We conclude that RE and SE seem to be the more suitable cerebral monitoring tool during propofol-remifentanil anesthesia in patients undergoing coronary artery bypass graft surgery,
because of superior resistance against electrical and mechanical artefacts and significantly less interference by f-EMG patterns.
References


23. Bruhn J, Bouillon TW and Shafer SL: *Bispectral index (BIS) and burst suppression: revealing a part of the BIS algorithm*. J Clin Monit Comput 16:593-6, 2000


Figure legends

Figure 1a-d Changes RE - BIS in all patients [1a], patients receiving on pump [1b], beating heart [1c] or off pump [1d] coronary artery bypass surgery at the following time points: before (101) and after (102) induction, before (103) and after (104) intubation, skin incision (105), sternotomy (106), pericardectomy (107), aortic cannulation (108), during cardiopulmonary bypass (109 to 119), after cardiopulmonary bypass (120), after chest closure (121) and at end of surgery (122). Error bars represent 95 % CI of Mean.

Abbreviations: BIS, bispectral index; RE, response entropy; SE, state entropy; RE – BIS, Difference between mean values of RE and BIS; CI, confidence interval

Figure 2a - c Simple regression analysis of BSR with BIS, RE and SE

Abbreviations: BSR, burst suppression ratio; BIS, bispectral index; RE, response entropy; SE, state entropy
<table>
<thead>
<tr>
<th></th>
<th>All (n = 30)</th>
<th>CPB Arrest (n = 15)</th>
<th>CPB Beating (n = 9)</th>
<th>OPCAB (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>64 (38-83)</td>
<td>60 (43-83)</td>
<td>67 (50-76)</td>
<td>74 (61-80)</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>29:1</td>
<td>14:1</td>
<td>9:0</td>
<td>6:0</td>
</tr>
<tr>
<td>Body mass index (kg/min²)</td>
<td>27.6 (20-44)</td>
<td>27.7 (20-41)</td>
<td>28 (19.9-31)</td>
<td>26.6 (25-44)</td>
</tr>
<tr>
<td>Preoperative LVEF (%)</td>
<td>60.5 (20-78)</td>
<td>60 (25-73)</td>
<td>70 (20-78)</td>
<td>67 (45-44)</td>
</tr>
<tr>
<td>Surgery time (min)</td>
<td>262.5 (140-380)</td>
<td>295 (185-360)</td>
<td>260 (215-340)</td>
<td>245 (140-380)</td>
</tr>
<tr>
<td>Bypass time (min)</td>
<td>120 (64-180)</td>
<td>120 (64-180)</td>
<td>122.5 (91-180)</td>
<td></td>
</tr>
<tr>
<td>Aortic clamping time (min)</td>
<td>70 (37-118)</td>
<td>70 (37-118)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grafts (n)</td>
<td>4 (1-7)</td>
<td>4 (2-6)</td>
<td>4 (3-7)</td>
<td>3 (1-4)*</td>
</tr>
<tr>
<td>Temperature cumulative (°C)</td>
<td>36.0 (30.0-37.3)</td>
<td>35.8 (30.0-37.3)</td>
<td>36.1 (34.2-37.1)</td>
<td>36.0 (34.8-37.3)</td>
</tr>
<tr>
<td>CPB temperature (°C)</td>
<td>31.8 (30.0-36.4)†</td>
<td>34.6 (34.2-36)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPB duration (min)</td>
<td>120 (64-180)</td>
<td>117 (85-151)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NOTE. Values are number or median (range).

Abbreviations: CABG, coronary artery bypass graft; CPB arrest, CABG performed with CPB and cardiac arrest; CPB beating, CABG performed with CPB without cardiac arrest; OPCAB, CABG without CPB; LVEF, left ventricular ejection fraction.

* p < 0.05.
† p = 0.0001.
<table>
<thead>
<tr>
<th></th>
<th>All  (n = 479)</th>
<th>On Pump  (n = 249)</th>
<th>Beating Heart  (n = 141)</th>
<th>Off Pump  (n = 89)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean bias (L/min)</td>
<td>-1.8</td>
<td>-1.2</td>
<td>-5</td>
<td>+1.6</td>
</tr>
<tr>
<td>LOA (L/min)</td>
<td>+20.6/−24.2</td>
<td>+17/−19.4</td>
<td>+21.2/−31.2</td>
<td>+25.5/−22.3</td>
</tr>
<tr>
<td>BIS v SE (r²)</td>
<td>0.55</td>
<td>0.64</td>
<td>0.48</td>
<td>0.5</td>
</tr>
<tr>
<td>BIS v f-EMG (r²)</td>
<td>0.62</td>
<td>0.63</td>
<td>0.63</td>
<td>0.58</td>
</tr>
<tr>
<td>SE v f-EMG (r²)</td>
<td>0.39</td>
<td>0.42</td>
<td>0.46</td>
<td>0.24</td>
</tr>
<tr>
<td>RE v f-EMG (r²)</td>
<td>0.45</td>
<td>0.48</td>
<td>0.49</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Abbreviations: bias (BIS − RE); LOA, limits of agreement = 2 standard deviations; on pump, coronary artery bypass graft (CABG) with CPB and cardiac arrest; beating heart, CABG with CPB without cardiac arrest; off pump, CABG without CPB; n, numbers of data pairs.
Table 3. Detection Failures of the BIS and RE/SE in Frequencies, Duration in Minutes, and Percent of Total Anesthesia Time

<table>
<thead>
<tr>
<th>Detection Failure</th>
<th>BIS</th>
<th>RE/SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number, n</td>
<td>24.1 ± 10.5, 27 (5-49)</td>
<td>0.7 ± 1.4, 0 (0-6)</td>
</tr>
<tr>
<td>Absolute space of time (min)</td>
<td>33.2 ± 35.3, 24 (2-135)</td>
<td>0.2 ± 0.7, 0 (0-3)</td>
</tr>
<tr>
<td>Relative space of time (%)</td>
<td>9.1 ± 10.9, 6.7 (0-40.4)</td>
<td>0.1 ± 0.2, 0 (0-7)</td>
</tr>
</tbody>
</table>

NOTE. Values are expressed in mean ± SD, median (range).