Time-frequency Features for Impedance Cardiography Signals During Anesthesia Using Different Distribution Kernels

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Time-frequency distributions, impedance cardiography, entropy, singular value decomposition

Summary
Objective: This work investigates the time-frequency content of impedance cardiography signals during a propofol-remifentanil anesthesia.

Materials and Methods: In the last years, impedance cardiography (ICG) is a technique which has gained much attention. However, ICG signals need further investigation. Time-Frequency Distributions (TFDs) with 5 different kernels are used in order to analyze impedance cardiography signals (ICG) before the start of the anesthesia and after the loss of consciousness. In total, ICG signals from one hundred and thirty-one consecutive patients undergoing major surgery under general anesthesia were analyzed. Several features were extracted from the calculated TFDs in order to characterize the time-frequency content of the ICG signals. Differences between those features before and after the loss of consciousness were studied.

Results: The Extended Modified Beta Distribution (EMBD) was the kernel for which most features shows statistically significant changes between before and after the loss of consciousness. Among all analyzed features, those based on entropy showed a sensibility, specificity and area under the curve of the receiver operating characteristic above 60%.

Conclusion: The anesthetic state of the patient is reflected on linear and non-linear features extracted from the TFDs of the ICG signals. Especially, the EMBD is a suitable kernel for the analysis of ICG signals and offers a great range of features which change according to the patient’s anesthesia state in a statistically significant way.

1. Introduction

In the last years, impedance cardiography (ICG) has proven to be an advantageous, inexpensive, non-invasive technique for monitoring the cardiovascular hemodynamic state of patients undergoing several medical procedures [1, 2, 3, 4, 5, 6, 7]. This work investigates the frequency content of the ICG signals in different moments of an anesthesia procedure: previous to the induction of anesthesia and after the start of an anesthesia procedure in the surgery room.

The spectral content of the ICG signals changes with time and thus time-frequency distributions (TFDs) are a convenient tool to analyze them. High-resolution time-frequency analysis is useful for signals which are nonstationary and/or multicomponent. TFDs is a technique which is often used in the case of analyzing electroencephalogram (EEG) [8, 9, 10], and heart rate variability (HRV) [11, 12, 13, 14], amongst others. Any TFD application would ideally require high definition in spectral components, no cross-terms (in order to avoid confusing real components from artifacts or noise), a low computational complexity and some mathematical properties [15]. A considerable effort has been put into designing appropriate TFD depending on the characteristics of the signal to analyze [10, 16, 17, 18, 19].

Nevertheless, TFDs contain considerably large amounts of data. Therefore, features are to be extracted from the TFDs in order to improve its characterization. Sev-
eral authors have proposed different features applied to TFD in order to describe non-stationary signals or to locate events based on the signal entropy, energy concentration measures or singular values decomposition [20, 21, 22, 23]. This work compiles some of those features in order to apply them to ICG signals. Several kernels including the Extended Modified Beta Distribution (EMBD) are also compared and discriminant analyses were conducted to differentiate between the TFD features from the ICG signals before and after thepatient’s loss of consciousness (LOC).

2. Materials and Methods

2.1 Analyzed Data and Preprocessing

One hundred and thirty-one consecutive patients undergoing major surgery under general anesthesia at the Hospital CLINIC de Barcelona (Spain) were assessed in this observational study. The details of the patients are reported in Table 1. The patient characteristics included age, height, weight, lean body mass (LBM), body surface area (BSA), body mass index (BMI) and gender.

This observational study was conducted in compliance with the requirements of the Institutional Review Board and Ethics Committee of Hospital CLINIC de Barcelona (2013/8356) and adhered to the principles of the Declaration of Helsinki for medical research involving human subjects. All patients gave their written informed consent. Patients under eighteen years old or morbidly obese were excluded.

Propofol and remifentanil were administered. Anesthesia was induced with a target-controlled infusion system. The infusion rate of propofol was controlled by Schneider’s pharmacokinetic model with 3 μg/ml as effect-site target concentration and remifentanil was controlled by Mintos’ pharmacokinetic-pharmacodynamic model with 4 ng/ml as effect-site target concentration.

The impedance cardiography (ICG) was recorded by the qCO monitor (Quantum Medical, Spain) by using 4 electrodes, with one pair injecting a constant current (at 50 kHz), and a second pair of electrodes measuring the resulting voltage. These signals are dimensionless and are recorded with a sampling rate of 250 Hz.

This study aims to compare two anesthesia-related patient states: conscious and unconscious. During the induction of anesthesia, the moment of LOC was assumed to occur when patients lost response to verbal stimulation. To characterize each state, the ICG signal corresponding to a ten-second length taken four minutes after LOC (i.e., unconscious state or post-LOC state) was isolated and so was that corresponding to the ten seconds taken four minutes before LOC (i.e., conscious state or pre-LOC state). In the surgery room, ten seconds is a signal duration which generally ensures a quality recording without movement artifacts or other electrical noises.

2.2 Analyzed Time-frequency Distributions

Quadratic TFDs (QTFD) are based on estimating the instantaneous power spectrum of the signal, using a bilinear operator [24] and are the result of a trade-off between the cancelation of cross-terms and the frequency resolution. The Wigner-Ville distribution (WVD) is the basic QTFD and is defined by taking the Fourier transform (FT) of an instantaneous auto-correlation function $K_\tau(t,\tau)$ described in Eq. (1).

$$W_{p}(t,f) = \int_{-\infty}^{+\infty} K_{\tau}(t,\tau) e^{-2\pi \tau f} d\tau$$

where $K_{\tau}(t,\tau)$ is defined as

$$K_{\tau}(t,\tau) = z \left(t + \frac{\tau}{2}\right) z’ \left(t - \frac{\tau}{2}\right)$$

and where $z(t)$ is the analytic associate of a real signal $x(t)$ obtained with the Hilbert transform $z(t) = x(t) + jH[x(t)]$.

Eq.(3) describes a general TFD as the convolution between the WVD and the 2D kernel $g(t,f)$ formulated in the ambiguity domain such as $g(\nu,\tau)$ (where $\nu$ is Doppler and $\tau$ is lag). The WVD provides a high-resolution representation of a signal in time and frequency but includes cross-terms in multicomponent signals. Therefore, the kernel used in the general formulation of the TFD reduces cross-terms although it also blurs auto-terms.

$$\rho_{g}(t,f) = g(t,f) * * W_{p}(t,f) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} g(\nu,\tau) A_{\nu}(\nu,\tau)e^{2\pi \nu (t-\tau)} d\nu d\tau$$

where $A_{\nu}(\nu,\tau)$ is the ambiguity function of the analytic associate of the real signal under analysis.

In this work, several TFD kernels have been used: the Choi-Williams Distribution (CWD), the Modified B-Distribution (MBD) and the Extended Modified B-Distribution (EMBD), the spectrogram with Hanning window, and the Zhao-Atlas-Marks distribution (ZAM). Their parameters have been selected by optimizing the geometrical characteristics of the resulting TFDs of a synthetic ICG signal with known time-frequency (TF) parameters. The optimization was accomplished based on a former work by Sucic and Boashash [19]. The details of the kernels are included in Table 2.
2.3 TFD-derived Parameters

The time variation in the spectrum of a signal can be characterized with several features extracted from its TFDs. This paper analyses a collection of TFD-derived features based on singular value decomposition (SVD), entropy, extended time-domain, energy concentration and sub-bands energy.

2.3.1 SVD-based TFD-derived Features

TFDs can be decomposed using its singular values in the form $\rho = USV^H$, where $U$ is an $N \times N$ matrix, $S$ is an $N \times M$ diagonal matrix with positive real singular values $\sigma_i$, and $V^H$ is an $M \times M$ real unitary matrix. Following previous works [20, 21, 22], in this investigation several features are extracted from the singular values $\sigma_i$ of the TFD, such as: $F_{SVD1}$, the maximum $\sigma_i$; $F_{SVD2}$, standard deviation of $\sigma_i$; and $F_{SVD3}$, the number of non-zero $\sigma_i$.

2.3.2 Entropy-based TFD-derived Features

The concept of Shannon Entropy [26] has been applied to both the design of new TFDs with minimum entropy [23] and the quantification of TFD complexity in TFDs. If the TFD is interpreted as a quasi-probability distribution, a highly-concentrated TFD with a small number of components has a lower entropy than a signal with a large number of signal components. The TFD complexity (TFCM) in Eq.(4) uses both SVD and Shannon entropy concepts and it represents the magnitude and the number of the non-zero singular values of the TFD [20, 21]. It is a useful feature as their magnitudes have a strong relationship with the information content in the TFD.

$$TFCM = -\sum_{i=1}^{N} \bar{\sigma}_i \log \bar{\sigma}_i$$  (4)

where $\bar{\sigma}_i$ are the $N$ normalized singular values, i.e.: $\bar{\sigma}_i = \sigma_i / \sum_{i=1}^{N} \sigma_i$.

If the entropy of a TFD is to be calculated without using its singular values, the Time-Frequency Rényi entropy (TFRE) in (5) is used in substitution of the Shannon entropy [27]. The latter cannot be used for the majority of TFDs as these are non-negative. TFRE is a statistical tool sensitive to the number of signal components, their time duration and bandwidth, and their amplitude ratios.

$$TFRE_q = \frac{1}{1 - q} \log_2 \sum_{n=1}^{N} \sum_{m=1}^{M} \rho^q[n,m], q > 2$$

The TFRE for odd values of $q$ causes zero-mean cross-terms to diminish due to the summation operation. Thus, the TFRE cannot discriminate a high-resolution TFD with significantly reduced cross-terms from a high-resolution TFD without any suppression of cross-terms. The TFD normalized Rényi entropy (TNFRE) in Eq.(6) solves this issue so that cross-terms have an overall effect of reducing the TFRE.

$$TFRE_q = -\frac{1}{2} \log_2 \sum_{n=1}^{N} \sum_{m=1}^{M} \left( \frac{\rho[n,m]}{\sum_{n=1}^{N} \sum_{m=1}^{M} \rho[n,m]} \right)^q + \log_2 \delta_t \delta_f$$

where $\delta_t$ and $\delta_f$ are the time and frequency sampling steps, respectively. Baraniuk et al. [28, 29] analyzed the influence of the parameter $q$ when calculating both TFRE and TNFRE and concluded that non-integer orders are yield complex values and so appeared of limited utility (6). In this study, a large range of $q$ values ($q = 3, 4, \ldots, 14, 15, 18, 21, 24, 27, 30, 35, 40, 45, 50$) have been selected for TFRE and TNFRE in order to analyze its influence.

2.3.3 Extended Time-Domain TFD-derived Features

In order to use statistical time-domain features, such as mean and variance, the one-dimensional time-domain moments have

<table>
<thead>
<tr>
<th>TFD</th>
<th>Kernel $g(v,\tau)$</th>
<th>Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>CWD</td>
<td>$e^{-v^2 \tau^2 / \sigma}$</td>
<td>$\sigma = 4.12$</td>
</tr>
<tr>
<td>MBD</td>
<td>$</td>
<td>\Gamma(\beta + j \tau \nu)</td>
</tr>
<tr>
<td>EMBD</td>
<td>$</td>
<td>\Gamma(\beta + j \tau \nu)</td>
</tr>
</tbody>
</table>

Spectrogram $w(\nu + \tau / 2)$ $w(\nu - \tau / 2)$ Hanning, $W=919$

ZAM $w(\tau) = \frac{a}{2|\tau|} \text{sinc} \left(\frac{2\pi \tau}{a}\right)$ $a=2.3$

Tab. 2 Kernels for the QTFDs [25] and their parameter values used for the ICG characterization. The parameters $a$, $\alpha$, $\beta$ and $\sigma$ and the window length $W$ define the kernel shape.

Tab. 3 Time-frequency extension of time-domain features.

<table>
<thead>
<tr>
<th>Feature</th>
<th>TF Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>TFD Mean</td>
<td>$m_{TF} = \frac{1}{NM} \sum_{n=1}^{N} \sum_{m=1}^{M} \rho[n,m]$</td>
</tr>
<tr>
<td>TFD Variance</td>
<td>$\sigma_{TF}^2 = \frac{1}{NM} \sum_{n=1}^{N} \sum_{m=1}^{M} (\rho[n,m] - m_{TF})^2$</td>
</tr>
<tr>
<td>TFD Skewness</td>
<td>$\gamma_{TF} = \frac{1}{(NM - 1)\sigma_{TF}^3} \sum_{n=1}^{N} \sum_{m=1}^{M} (\rho[n,m] - m_{TF})^3$</td>
</tr>
<tr>
<td>TFD Kurtosis</td>
<td>$k_{TF} = \frac{1}{(NM - 1)\sigma_{TF}^4} \sum_{n=1}^{N} \sum_{m=1}^{M} (\rho[n,m] - m_{TF})^4$</td>
</tr>
<tr>
<td>TFD Coefficient of variation</td>
<td>$c_{TF} = \frac{\sigma_{TF}}{m_{TF}}$</td>
</tr>
</tbody>
</table>
been replaced with the corresponding two-dimensional TF characteristics according to [30]. Table 3 includes all extended time-domain features.

### 2.3.4 Energy Concentration

The energy concentration measure (ECOME) determines the concentration of the dominant component at each location in the TF domain. Signals with TFD distributed in the TF plane will have a larger ECOME, while concentrated TFDs will have a smaller ECOME.

\[
ECOME = \left( \sum_{n=1}^{N} \sum_{m=1}^{M} |n[m]|^r \right)^{1/r}, r > 1
\]  

(12)

### 2.3.5 Sub-Bands Energy-based Features

Sub-band energy-based features represent the energy of the ICG signal in different frequency sub-bands. To the best of the authors’ knowledge, no previous studies have been published regarding the spectral content of the ICG signals. Therefore, the frequency plane of the TFDs has been divided by visual inspection and by using pairs of logarithmically spaced values. In total, 138 frequency bands have been analyzed and their corresponding features have been calculated using Eq.(13).

\[
F_{Band_i} = \sum_{n=1}^{N} \sum_{m=M_{10}}^{M_{1i}} \rho[n, m], i = 1 \ldots 138
\]  

(13)

where \( M_{10} \) and \( M_{1i} \) are the starting and end frequencies of the \( i \)-th band. Most of the content of the ICG signals is in the band between 0.5 Hz and 4 Hz. Therefore, the spectrum has initially been divided in 55 logarithmically-distributed partitions (i.e. a partition is a single value). Bands have then been defined: A. for each partition; B. for each group of two successive partitions; and C. for the frequencies from 0 Hz until each partition.

### 2.4 Selected Features and Statistical Analysis

In order to characterize signals corresponding to the segment previous to the LOC and that after the LOC, a range of features were selected in our study. These features are listed in Table 4.

Statistical analyses were performed using SPSS (Version 24, IBM, USA) and MATLAB® (MathWorks, USA). Quantitative data are presented as mean ± standard deviation and qualitative data as frequency (percentage). A non-parametric test, the Wilcoxon signed-rank test, was
used to investigate whether the analyzed features changed after induction of anesthesia. Features that satisfy this condition were considered for building a linear discriminant function. The leave-one-out method was used for validation. Sensitivity (Sen), specificity (Spe) and the area under (AUC) the Receiver operating characteristic (ROC) curve were calculated to assess the ability of the studied features to predict the occurrence of LOC. Sen represents the proportion of pre-LOC ICG segments correctly classified and Spe represents the proportion of post-LOC ICG segments correctly classified. Grouped sensitivities and specificities are presented as mean [95% confidence interval (CI)]. In the classification, the cut-off values are always the main of the centroids of the groups. Predicted membership is calculated by first producing a discriminant score for each case using a linear discriminant function. Then cases are classified in a concrete group depending on whether their discriminant score is smaller or larger than the cut-off value. Relationship between time-frequency derived indices and patient characteristics was assessed using Pearson’s coefficient of correlation ($\rho$). Significance level is always set at $p<0.05$.

3. Results

After isolating ten-second segments from before and after the LOC, TFDs were calculated with different kernels and, then, the features were extracted and analyzed. Figure 1 displays an example of a case analyzed using an EMBD. Figure 1A shows the pre-LOC TFD and Figure 1B shows the post-LOC TFD. The main differences between the two states are the content below 1Hz and the instantaneous frequencies, which seem to be lower in Figure 1B. The subsequent results aim to show tables and figures how the several TFD-derived Features reported in Table 4 are related to the patient’s state.

### 3.1 SVD-based TFD-derived Features

SVD-based TFD features change from before to after the LOC in a statistically significant manner in the case of $F_{SVD1}$, $F_{SVD2}$ and $F_{SVD3}$ values. Table 5 shows the average values for these features for all the TFD kernels. It can be seen that the defined SVD features are higher before LOC than after LOC. These results have been obtained with values of Sen, Spe and AUC very similar for all kernels and all SVD-based TFD features. In this way, over the different kernels used, Sen($\%$) is 76.4 [75.3,77.5] for $F_{SVD1}$, 78.0 [77.4,78.6] for $F_{SVD2}$ and 65.0 [61.8,68.2] for $F_{SVD3}$. Spe($\%$) is 49.2 [48.8,49.6] for $F_{SVD1}$, 51.0 [50.6,51.4] for $F_{SVD2}$ and 57.0 [54.5,59.5] for $F_{SVD3}$.

<table>
<thead>
<tr>
<th></th>
<th>$F_{SVD1}$ pre-LOC</th>
<th>post-LOC</th>
<th>$F_{SVD2}$ pre-LOC</th>
<th>post-LOC</th>
<th>$F_{SVD3}$ pre-LOC</th>
<th>post-LOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>CWD</td>
<td>(4.0 ± 3.0)·10^4</td>
<td>(2.4 ± 1.6)·10^4</td>
<td>(9.8 ± 7.1)·10^2</td>
<td>(5.6 ± 3.7)·10^2</td>
<td>(8.1 ± 1.4)·10^4</td>
<td>(7.4 ± 1.3)·10^4</td>
</tr>
<tr>
<td>MBD</td>
<td>(1.5 ± 1.1)·10^5</td>
<td>(9.2 ± 6.4)·10^4</td>
<td>(3.6 ± 2.6)·10^3</td>
<td>(2.0 ± 1.4)·10^3</td>
<td>(1.3 ± 0.1)·10^2</td>
<td>(1.2 ± 0.2)·10^2</td>
</tr>
<tr>
<td>EMBD</td>
<td>(1.4 ± 1.1)·10^7</td>
<td>(8.4 ± 5.8)·10^6</td>
<td>(3.2 ± 2.3)·10^5</td>
<td>(1.8 ± 1.2)·10^5</td>
<td>(2.4 ± 0.6)·10^6</td>
<td>(2.1 ± 0.5)·10^2</td>
</tr>
<tr>
<td>Spec. (Hann.)</td>
<td>(1.5 ± 1.1)·10^7</td>
<td>(8.3 ± 5.6)·10^6</td>
<td>(3.1 ± 2.3)·10^5</td>
<td>(1.7 ± 1.1)·10^5</td>
<td>(1.0 ± 0.1)·10^2</td>
<td>(9.7 ± 1.2)·10^1</td>
</tr>
<tr>
<td>ZAM</td>
<td>(6.3 ± 4.7)·10^6</td>
<td>(3.8 ± 2.7)·10^6</td>
<td>(1.6 ± 1.2)·10^5</td>
<td>(9.1 ± 6.0)·10^4</td>
<td>(5.4 ± 1.9)·10^2</td>
<td>(4.6 ± 1.4)·10^2</td>
</tr>
</tbody>
</table>

Table 5 Mean and standard deviation of the SVD-based TFD parameters. All changes between pre-LOC and post-LOC are statistically significant. * indicates that Sen > 60 %, Spe > 60 % and AUC > 60 %.
AUC is 0.69 [0.68,0.70] for \( F_{SVD} \), 0.70 [0.70,0.70] for \( F_{PLL} \), and 0.65 [0.64,0.66] for \( F_{SVD} \). The best SVD-based TFD feature is \( F_{SVD} \), calculated with an EMBD kernel, which presents an AUC of 0.63, \( Sen = 67.7\% \) and \( Spe = 60.3\% \).

### 3.2 Entropy-based TFD-derived Features

Regarding the entropy-based TFD features, several results have been obtained. The TFCM presents statistically significant differences between pre-LOC and post-LOC for all kernels (see 2). In average for all kernels, \( Sen(\%) \) is 65.4 [60.9,69.9], \( Spe(\%) \) is 51.6 [50.5,53.2] and AUC is 0.62 [0.59,0.65]. The complexity of the TFD responses is greater during pre-LOC than during post-LOC.

\( TFRE \) always shows statistically significant differences between pre-LOC and post-LOC for all kernels and for all q values. Furthermore, \( Sen, Spe \) and AUC are similar for all q values as seen in Figure 3 and also for all kernels as Table 6 shows. Figure 3A shows the \( TFRE_q \) for an exemplary kernel such as the EMBD for all the different q values. \( TFRE_q \) emphasizes high probabilities when \( q > 1 \). This figures shows how the values converge as the q increases and the values are always higher for the pre-LOC signals than for the post-LOC signals.

\( TFNRE \) also shows statistically significant differences between pre and post-LOC for all q values in the case of the spectrogram and in the case of the EMBD for \( q \geq 6 \). Compared to the \( TFRE \) values, the normalization has decreased the AUC below 0.6 in all cases and \( Sen \) and \( Spe \) are below 60%. Figure 3B also shows the \( TFNRE \) for an exemplary kernel such as the EMBD for all the different q values.

### 3.3 Extended Time-Domain TFD-derived Features

The time-extended TF features show statistically significant differences between the pre-LOC and post-LOC values of \( m_{TF} \) and \( \sigma^2_{TF} \), for all TFD kernels. In addition, there are also statistically significant differences in the case of \( k_{TF} \) for all TFD kernels except for CWD and in the case of the \( \gamma_{TF} \) for all TFD kernels except for CWD and ZAM. The difference between the pre-LOC and post-LOC values of \( c_{TF} \) is only statistically significant for the spectrogram. For all TFD kernels, the AUC for these features is 0.70 for \( m_{TF} \) and \( \sigma^2_{TF} \), and between 0.51 and 0.63 for \( k_{TF} \), \( \gamma_{TF} \) and \( c_{TF} \). \( Spe \) is always lower than 60% (between 38.2 and 54.2) for all time-extended TF features and for all kernels \( Sen(\%) \) is in average 75.5 [75.2,75.8] for \( m_{TF} \) and 85.8 [85.2,86.1] for \( \sigma^2_{TF} \).

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**Tab. 6** Mean [95% CI] of area under the curve (AUC) of the receiving operating curve (ROC), sensitivity (\( Sen \)) and specificity (\( Spe \)) of the \( TFRE_q \) feature for all the studied distributions and all q values. \( TFRE_{so} \) values for before and after the LOC have also been included. CI of AUC are the same as the mean and thus are not included.

<table>
<thead>
<tr>
<th></th>
<th>( Sen(%) )</th>
<th>( Spe(%) )</th>
<th>AUC</th>
<th>( TFRE_{so} ) (pre-LOC)</th>
<th>( TFRE_{so} ) (post-LOC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CWD</td>
<td>61.52 [61.35,61.69]</td>
<td>68.90 [68.64,69.16]</td>
<td>0.69</td>
<td>-9.26 ± 1.18</td>
<td>-8.51 ± 1.13</td>
</tr>
<tr>
<td>MBD</td>
<td>61.07 [60.86,61.27]</td>
<td>67.17 [66.66,67.69]</td>
<td>0.69</td>
<td>-11.38 ± 1.25</td>
<td>-10.59 ± 1.21</td>
</tr>
<tr>
<td>EMBD</td>
<td>63.01 [62.91,63.11]</td>
<td>69.33 [69.04,69.62]</td>
<td>0.71</td>
<td>-17.64 ± 1.24</td>
<td>-16.77 ± 1.20</td>
</tr>
<tr>
<td>Spec. (Han)</td>
<td>62.29 [61.90,62.67]</td>
<td>69.92 [69.69,70.14]</td>
<td>0.72</td>
<td>-17.15 ± 1.23</td>
<td>-16.22 ± 1.13</td>
</tr>
<tr>
<td>ZAM</td>
<td>62.44 [62.16,62.73]</td>
<td>69.41 [68.92,69.90]</td>
<td>0.70</td>
<td>-16.73 ± 1.22</td>
<td>-15.91 ± 1.15</td>
</tr>
</tbody>
</table>

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**Tab. 7** Time-extended TF features of the ICG signals before and after the LOC using the spectrogram kernel with a Hanning window. All changes are statistically significant. Features have arbitrary units.

<table>
<thead>
<tr>
<th></th>
<th>( m_{TF} )</th>
<th>( \sigma^2_{TF} )</th>
<th>( k_{TF} )</th>
<th>( \gamma_{TF} )</th>
<th>( c_{TF} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>pre-LOC</td>
<td>486.5 ± 340.5</td>
<td>(3.6 ± 5.3)·10(^{-3})</td>
<td>16.1 ± 2.8</td>
<td>319.0 ± 100.9</td>
<td>9.8 ± 1.5</td>
</tr>
<tr>
<td>post-LOC</td>
<td>275.0 ± 168.4</td>
<td>(1.0 ± 1.5)·10(^{-3})</td>
<td>15.0 ± 2.4</td>
<td>278.0 ± 87.1</td>
<td>9.5 ± 1.3</td>
</tr>
</tbody>
</table>
tended TF features decrease after LOC for the spectrogram. This also occurs for the rest of kernels.

3.4 Energy Concentration

ECOME values for all TFD kernels before and after LOC are plotted in Figure 4 and these are higher after the LOC than before it. All changes have proven to be statistically significant. In average, Sen is 75.3 [73.2,77.4], Spe is 51.6 [49.9,53.3] and AUC is 0.72 for all kernels.

3.5 Sub-Bands Energy-based Features

The spectrum of the TFDs has been divided into 138 different frequency bands. The MBD and the ZAM distribution are the ones with the largest number of statistically significant frequency bands, with 114 and 116, respectively. The rest of kernels provide less significant bands: EMBD (106), CWD (100) and the spectrogram with a Hanning window (91). The spectral content of the TFD bands is always greater before the LOC than after the LOC. AUC is in almost all cases above 0.6 but both Sen and Spe are not larger than 60% at the same time. Figure 5 shows how the energy in some of the frequency bands changes between before and after the LOC. Moreover, this figure also shows how most energy is concentrated between 1 and 4 Hz. The very low frequency from 0 to 0.05 Hz is also prominent, due to the non-zero signal mean.

4. Discussion

TFDs have been analyzed using five different kernels and information has been extracted using several features based on SVD decomposition, entropy, extended time-domain, concentration and sub-bands energy. All features decreased after the LOC. The EMBD kernel offered the largest quantity of features with statistically significant differences (156). In total, 129 were found for CWD, 129 for MBD, 147 for the spectrogram and 146 for ZAM distribution. After EMBD, kernels such as the spectrogram and the ZAM distribution also offer a large amount of significant features but ZAM usually introduces more cross-terms than other distributions.

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**Fig. 4**  Pre and post-LOC ECOME values for the CWD (A), the EMBD (B), the MBD (C), the spectrogram with a Hamming window (D) and the ZAM distribution (E). Changes between pre and post LOC values are always statistically significant (p<0.05).

**Fig. 5**  Mean and standard deviation of the energy of some bands for the pre-LOC (blue) and post-LOC (red) periods. The kernel used for this figure is the MBD. * indicates that the change is statistically significant (p<0.05).
The robustness of the spectrogram is generally related to the lack of undesirable artifacts present in other TFDs since the non-linearity is introduced in the final step of the spectrogram computation. Nonetheless, the spectrogram does not satisfy the instantaneous frequency criterion of the quadratic class of TFDs and hence it does not allow the exact extraction of the signal IFs from its dominant peaks.

Among all the features which have been analyzed, TFRE is the most successful. For all kernel types and for any q value, TFRE values decrease after the loss of consciousness and both their sensitivity and specificity are always above 60%. Moreover, the AUC is always above 0.6. The increase in the TFRE is theoretically related to the decrease of predictability or the increase of disorder. From a biological point of view, this would imply that the ICG signals are more deterministic after the LOC. Regarding the sub-bands energy-based features, these show that most of the ICG energy is concentrated between 1 and 4 Hz, since their values are higher than in the rest of frequency band. Nevertheless, sensitivity and specificity of the features should be improved in the future for such features to be adequate for clinical applications.

Our study presents some limitations which must be considered. The pharmacological effects of the drugs infused in the patients may vary depending on the target concentrations. This is especially true when analysing signals after the LOC. This fact does not reduce the validity of results but should be taken into account especially in future works for which information from depth-of-anaesthesia monitors should be included.

5. Conclusion

In conclusion, this work presents a collection of various features which can be obtained from TFDs. Different kernel TFDs have been calculated and their results have been compared. When analyzing signals representing different anesthetic states, the TF Rényi entropy is the most prominent feature. Regarding the various kernels which have been analyzed, the EMBD is the most successful for the extraction of features showing statistically significant differences in different anesthesia points.

Author Contribution

J Escrivá Muñoz did the data base analysis and writing of the manuscript, and P Gambús collected the cases for the data base; EW Jensen and M Válleurdú act as academic advisors in the corresponding author’s PhD program.

Conflict of Interest

J Escrivá Muñoz and EW Jensen work for Quantum Medical, SL.

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