Abstract—Over the last ten years, monitors of depth of anesthesia have progressively been integrated in the clinical practice. Based on the analysis of the electroencephalogram (EEG), these monitors deliver an index that helps the anesthesiologist to determine the state of the patient during the surgery. Although they employ different kind of algorithms, spectral parameters are always taken into account to achieve the final indexes. In this work, a new spectral parameter based on the cumulative power spectrum is proposed. When compared to the Spectral Edge Frequency (SEF), a classic spectral parameter, the Cumulative Power Spectrum Index (CPSI) presents a higher correlation with reference indexes (AAI, BIS and CePROP) and a higher prediction probability of the state of the patient. Furthermore, when compared to the reference indexes, the CPSI shows similar performances in terms of correlation and presents a higher prediction probability than two of them (BIS and CePROP).

I. INTRODUCTION

During general anesthesia, clinical signs such as blood pressure, heart rate or involuntary movements may be used to detect an inadequate level of consciousness of the patient. Nevertheless, these signs are affected by the administration of other drugs like vasodilators, beta blockers or neural blocking agents, and are usually difficult to interpret in practice. For this reason, attention has been directed towards the study of the electroencephalographic signal (EEG) as a complementary source of information on the state of the patient.

Nowadays, several monitors of depth of anesthesia based on EEG analysis have entered into the clinical practice. The principal ones are the BIS monitor (Aspect Medical Systems, Inc., Newton, MA), which considers the phase coupling between different EEG frequency components [1], the AEP-monitor/2 (Danmeter A/S, Odense, Denmark), which analyzes the EEG response to an auditory stimulus [2],[3] and the Entropy monitor (Datex-Ohmeda, Helsinki, Finland), which studies the Shannon entropy of the EEG power spectrum [4]. All these monitors include spectral parameters in the computation of their index of depth of anesthesia.

Typically, while increasing the level of anesthesia, the EEG pattern progressively evolves from a low voltage fast wave to a high voltage slow wave. Starting from this observation, spectral parameters like the spectral edge frequency (SEF) [5], the frequency below which a fraction of the total EEG power is encountered, have been considered to reflect the decrease of the frequency content during general anesthesia.

Instead of focusing just on the global frequency shift, a new spectral parameter is proposed in this work to take into account the power distribution across the whole EEG frequency range in order to assess the depth of anesthesia.

II. MATERIALS AND METHODS

A. Databases

Two databases are used in this study, the first one to design the technique and the second one to assess its relevancy to evaluate the level of anesthesia.

Informed consent was obtained after approval of the Institutional Ethics Committee for all patients. The databases correspond to the monitoring of 17 and 20 patients, respectively, scheduled for ambulatory gynecologic or urologic surgery in the Ghent University Hospital, Belgium. The patients belonged to the ASA I group, (ASA, American Society of Anesthesiologists), which corresponds to the minor risk level of a 1-to-5 scale (increasing risk). Exclusion criteria included weight less than 70 % or more than 130% of ideal body weight, neurological disorders, and recent use of psycho-active medication, including alcohol.

The protocol followed for both databases is identical. All patients received continuous infusion of propofol, the most commonly used intravenous anesthetic, fixed at 300ml/h by a computer-assisted infusion device (RUGLOO [6]). The effect-site concentration CePROP (drug concentration in the central nervous system) was obtained using a three-compartment pharmacokinetic-dynamic model enlarged with an effect-site compartment [7],[8]. Effect-site concentration was computed to yield a time to peak effect of 1.6 min after the bolus injection [9],[10]. Propofol was infused via large left forearm vein. Before starting the drug administration, all
patients were asked to close their eyes and relax for two minutes. Infusion was continued until reaching deep anesthesia, when EEG presents a characteristic behavior called burst suppression consisting of periods of high amplitude (bursts) followed by periods of very low amplitude (suppression) [11]. Infusion was stopped when a burst suppression ratio of 80% or higher was achieved, but was interrupted in case of a mean arterial blood pressure lower than 50 mmHg.

The bispectral index BIS was computed from the frontal EEG (At-Fpzt) by the A-2000 BIS monitor. The smoothing time of the BIS monitor was set at 15s. The auditory evoked potential index AAI was calculated by the AEP-monitor/2, with the three electrodes positioned at mid forehead (+), left forehead (reference) and left mastoid (-). The haemodynamic data, the BIS and the AAI indexes were logged automatically every 10 s. Both A-2000 BIS monitor and AEP-monitor/2 provided a measure of the burst suppression ratio (BS), which represents the fraction of time where the EEG has small amplitudes. Raw EEG was recorded using the AEP-monitor/2. The sampling frequency was 900 Hz, with a resolution of 16 bits and a recording time between 10 and 15 minutes.

Since both databases do not include any assessment of the state of the patient by the anesthesiologists, commercial indexes BIS and AAI are used in this work as reference measures of the level of anesthesia. Furthermore, as these data correspond to the induction of the anesthesia, the increasing drug concentration in the central nervous system CePROP evolves in the same way as the depth of anesthesia and will be also considered as a reference of the level of anesthesia. When the analysis of the results requires a discretization of the state of the patient, thresholds on the AAI index scale are applied to define the different states.

The biphasic pattern characterizing the burst suppression state traditionally causes a rupture of the trend presented by simple indexes with an increasing level of anesthesia. Commercial indexes integrate a separate algorithm to detect and take into account this phenomenon. In order to allow a fair comparison with the spectral parameters, the EEG segments corresponding to the burst suppression state are discarded for all the statistical analysis done in this paper.

B. Analysis of the differences between states using cumulative power spectrum

A new parameter is defined in analogy to the Kolmogorov-Smirnov test employed in statistics to measure the goodness of fit. The Kolmogorov-Smirnov test evaluates the degree of agreement between the distribution of a set of samples and some specific theoretical distribution considering the distance between these two cumulative curves. The application of the same idea to the determination of the level of consciousness leads to define some cumulative curves from the EEG segments that, when compared to each other, present dissimilarities directly proportional to the difference of level of anesthesia associated to each EEG segment.

To perform this preliminary study, a subset of 30 EEG segments, chosen to cover the whole range of the levels of anesthesia, is extracted from the patients of the first database. The state of the patient associated to each segment is approximated by the value of the auditory evoked potential index (AAI).

The cumulative curves proposed for the comparison are derived from the power spectrum. Before applying the Fast Fourier Transform, each EEG segment is normalized. Then the power spectrum is divided by the average power spectrum of the whole subset of 30 segments. Since that subset covers the whole range of the possible states, the aim of this division is to subtract the common content and to emphasize the intrinsic information of each segment. Afterwards, the cumulative power is computed till a frequency Fmax and divided by the total power. The resulting function increases monotonically from 0 to 1 on the frequency range 0 Hz to Fmax. The cumulative curves obtained in this way are referred to as Modified Cumulative Power Spectrum (MCPS).

The area between two cumulative curves has been used to measure the divergence between them (Fig.1). The MCPS curves have been computed on 6-second segments considering \( F_{\text{max}} = 45 \) Hz. Fig. 2 presents the CPS curves for the 30 segments from the considered subset, with a level of grey proportional to the value of the associated AAI index. It can be observed that the data is organized according to the level of anesthesia. This reflects the fact that, at the same time as the AAI values decrease, a bigger fraction of the total frequency content is situated at the low frequencies.

C. Index of depth of anesthesia based on the cumulative power spectrum

A new index based on the technique of comparison of cumulative curves is proposed in this section. The 30 EEG segments previously mentioned are now used as a reference set to which every new EEG segment is compared. The new

Fig. 1. Area between the cumulative curves as a measure of divergence between two Modified Cumulative Power Spectrum (MCPS) curves.
index is deduced from the value of the AAI index of the reference segments that are the most similar to the new segment.

To measure the similarity, the average CPS curves corresponding to awake, sedated, slightly anesthetized and deeply anesthetized states are computed from the whole first database. The aim is to model a characteristic pattern in each state. Any EEG segment may then be described by the measure of the differences between its CPS curve and the four average CPS curves. These four differences are used as segment coordinates in a four-dimensional space. In this way, the segments of the reference subset that present the highest resemblance to the new segment are the ones that minimize the Euclidian distance to this segment.

Several ways of deducing the new index from the value of the AAI index of the closest reference segments are proposed: mean average of the 3 and 5 closest reference segments (Avg3 and Avg5), weighted average of the 3 and 5 closest reference segments using a weight inversely proportional to the distance of the related reference segment to the new segment (Dist3 and Dist5), linear interpolation from the 5 closest reference segments (Lin5) and linear interpolation from the orthogonal projection of the point corresponding to the new segment into the plane of the 3 closest reference segments (Lin3).

To determine the method with the best performance, the correlation between the new proposed indexes and the reference indexes of depth of anesthesia AAI, BIS and CePROP is computed (Table I). Because of the averaging, the estimates Avg3 and Avg5 would take their values in the ranges [5.3-96] and [8.2-92], respectively. A rescaling has thus been applied in order to cover the range [0-100]. The opposite problem occurs with the estimates Lin5 and Lin3, which present values out of scale. In this case, the value of the estimates is limited to the range [0-100].

The indexes achieved by interpolation present the lowest correlation coefficients. The indexes based on a simple averaging of the values of the closest neighbors present a higher correlation with the reference indexes AAI, BIS and CePROP than the indexes applying a weighting inversely proportional to the distance to these closest neighbors. In the best case, when averaging over the five closest neighbors (Avg5), the obtained values of the correlation coefficients are close to the ones presented by the reference indexes between themselves (|r_{Avg5/AAI}| = 0.819 while |r_{BIS/AAI}| = 0.833), or even higher (|r_{Avg5/BIS}| = 0.855 while |r_{AAIBIS}| = 0.833). Consequently, Avg5 is the cumulative power spectrum index (CPSI) considered in this study.

### III. RESULTS

The cumulative power spectrum index (CPSI), defined on the data of the first database, is validated using the patients of the second database. To evaluate its interest as a spectral parameter, it is compared to several variants of the Spectral Edge Frequency (SEF) [5]: SEF95, SEF90 and SEF50, also known as median frequency. For example, SEF95 represents the frequency below which 95% of the total EEG power is encountered.

The Pearson correlation coefficient is computed to measure the correlation presented by CPSI and the different SEFs with the reference hypnotic indexes AAI and BIS, and with the propofol effect site concentration CePROP. EEG segments with burst suppression are rejected. Values are shown in Table II.

CPSI always works better than the other spectral parameters, since it presents a higher correlation with the reference indexes than any SEFs. When comparing CPSI with reference indexes, it presents a higher correlation with AAI than BIS and CePROP (|r_{CPSI/AAI}| = 0.787 while |r_{BIS/AAI}| = 0.640 and |r_{CePROP/AAI}| = 0.619) and a higher correlation with BIS and CePROP than AAI (|r_{CPSI/BIS}| = 0.703 for |r_{AAIBIS}| = 0.640 and |r_{CePROP/AAI}| = 0.619). It may thus be considered a good compromise between these different indexes.

Then the prediction probability Pk [12] is computed. The Pk coefficient is a statistic commonly used in the field of anesthesia to measure how well an index predicts the state of the patient: a Pk of 1 represents a perfect prediction and 0.5 just chance. Table III presents the Pk values for the different indexes when three states are considered (awake, sedated and anesthetized). The definition of the three states is based on the AAI index value what implies a Pk value of 1.
for this index. Consequently, this result has not been included in Table III as it would lead to the erroneous conclusion that the AAI index gives a perfect prediction.

In this case CPSI presents the highest prediction probability value ($P_k = 0.8625$), above the value for the reference indexes and spectral parameters. Thus, CPSI provides the best prediction of the three considered levels of anesthesia for this second database.

### IV. Conclusion

In this work, a new spectral parameter for assessing depth of anesthesia based on cumulative power spectrum of the electroencephalogram (EEG) has been proposed. In a preliminary study, it has been verified that the difference of the level of anesthesia between two EEG segments can be expressed in terms of the comparison between their respective cumulative power spectrum curves. Then, using a first database, the Cumulative Power Spectrum Index (CPSI) has been developed in order to maximize the correlation with several references of the level of depth of anesthesia (AAI, BIS and CePROP).

The CPSI has been validated on a second database through a comparison with a family of spectral parameters corresponding to variants of the Spectral Edge Frequency (SEF). None of the variants of the SEF have shown higher correlation to reference indexes of depth of anesthesia than CPSI. While considering three distinct states of the patient defined by the value of the AAI index, the CPSI has also presented a higher prediction probability $P_k$ than the variants of the SEF.

Moreover, when compared to reference indexes, the CPSI presents a correlation that is similar to the correlation that the reference indexes present between themselves, and a higher $P_k$ than the reference indexes.

The CPSI may thus be considered as a promising spectral parameter in order to assess the level of anesthesia.

### REFERENCES