New measures for assessment of impaired cerebral autoregulation

Dominique De Smet*, Joke Vanderhaegen**,
Gunnar Naulaers**, and Sabine Van Huffel*

* SCD, Dept. of Electrical Engineering, KULeuven, Belgium.
** Neonatal Intensive Care Unit, University Hospitals Gasthuisberg, KULeuven, Belgium.

Submitted for the Proceedings of the ISOTT 2007 conference in Uppsala, Sweden.

Abstract available at :
ftp://ftp.esat.kuleuven.be/SISTA/ddesmet/abstracts/0708-1.htm

Contact :
Dominique.DeSmet@esat.kuleuven.be

NEW MEASURES FOR ASSESSMENT OF IMPAIRED CEREBRAL AUTOREGULATION

Dominique De Smet, Joke Vanderhaegen, Gunnar Naulaers, and Sabine Van Huffel*

Abstract : Some preterm infants have poor cerebral autoregulation. The concordance between cerebral intravascular oxygenation (HbD) and mean arterial blood pressure (MABP) reflects impaired autoregulation. As HbD is not an absolute value, we developed mathematics to prove that the cerebral tissue oxygenation (TOI, which is absolute) may replace HbD. In the meantime, we attempt to theoretically predict the true level of autoregulation of a patient by defining a critical percentage of the signal recording time (CPRT). 20 preterm infants with need for intensive care were studied in the first days of life. HbD and TOI were obtained with the NIRO300 (Hamamatsu). Invasive MABP was measured continuously. All mathematics showed a strong similarity between HbD and TOI.

1. INTRODUCTION

The most important forms of brain injury in premature infants are partly caused by disturbances in cerebral autoregulation. As HbD reflects cerebral blood flow, autoregulation can be measured by studying the concordance between HbD and MABP, supposing the arterial oxygen saturation does not change appreciably.[1] As HbD is unfortunately not an absolute value, we focused our attention on another yet absolute-valued signal measured with the NIRO300 : the cerebral tissue oxygenation (TOI). We explored the relationship between HbD and TOI to prove that TOI may replace HbD. Figure 1 illustrates all mentioned signals.

* Dominique De Smet (Dominique.DeSmet@esat.kuleuven.be, Kasteelpark Arenberg no. 10 box 2446, B-3001 Heverlee, Belgium, tel. +3216321067, fax. +3216321986) and Sabine Van Huffel, SCD, Dept. of Electrical Engineering, KULeuven, Belgium. Joke Vanderhaegen and Gunnar Naulaers, Neonatal Intensive Care Unit, University Hospitals Gasthuisberg, KULeuven, Belgium.

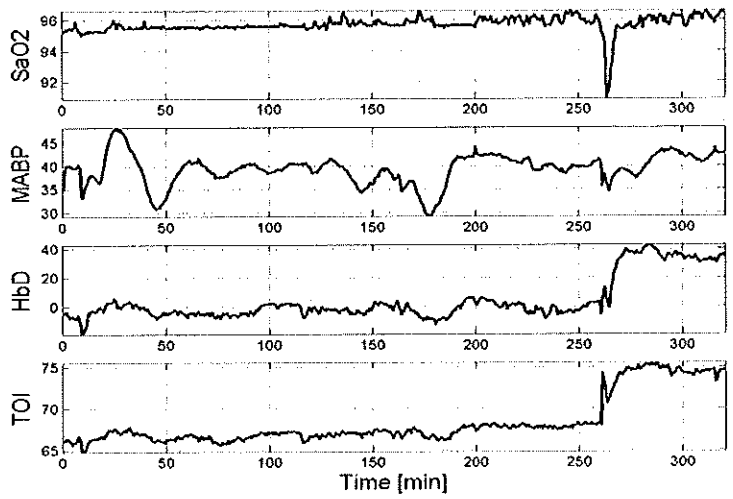


Figure 1. Signals from top to bottom : arterial oxygen saturation (SaO_2, in %), mean arterial blood pressure (MABP, in mmHg), cerebral intravascular oxygenation (HbD, in µMol/l), and cerebral tissue oxygenation (TOI, in %). All signals have been filtered to keep only the recording intervals during which the variation in SaO_2 around its mean does not exceed 5%. In this way the condition of constant SaO_2 is satisfied.

2. DATASETS

From 20 premature infants with need for intensive care, MABP, SaO_2, HbD, and TOI were measured simultaneously at the University Hospitals Leuven in the first days of life. The babies were characterized by a mean PMA of 28.7 weeks (24-39) and a weight ranging from 570 to 1470g. The recording time ranges from 1h30 to 23h35. HbD was calculated as the difference between the concentration changes of HbO_2 and Hb, and was acquired at the frequency of 6Hz, as is also the case for TOI. All these signals were assessed by Near-Infrared Spectroscopy. MABP (assessed by intravascular catheterisation) and SaO_2 were recorded at a sampling frequency of 10Hz. For this reason HbD and TOI were upsampled to 10Hz.

3. METHODS

3.1. Direct Concordance Methods

We considered two direct concordance methods (DiCo methods) widely used in the field of cerebral autoregulation : the correlation (COR) and coherence (COH) coefficients, but also a partial coherence coefficient (PCOH).[2] These methods applied to detect impaired cerebral autoregulation in neonates were described previously.[3] COR was scaled such that its value matches the interval [0,1] instead of [-1,1]. In this way the COR score may be more easily compared with the ones obtained with the other DiCo methods. Before computing COR, the signals were lowpass filtered to the frequency range of 0 –

0.01Hz.[1] COH measures the degree of linear dependence between the frequency spectra of two signals. In 2000, Tsuji et al.[1] applied this method to detect impaired cerebral autoregulation from continuous measurements. In 2001, Morren et al.[4] pursued Tsuji's work using the same methodology. Recently, Soul et al.[5] further optimized COH for continuous MABP and HbD. Nevertheless, we based our work on computing COH using the Welch's method as Morren et al.[4] described. The average of COH over the frequency band of interest (0 – 0.01Hz) was used as DiCo score for the considered signal duration.[1, 3-5] PCOH also measures the degree of linear dependence –in the frequency domain- between two signals, but after having eliminated in a least squares sense the contribution of other influencing signals.

3.2. The CPRT : A Synthesized Measure of Cerebral Autoregulation

The above defined DiCo scores are not handy enough for the physician to handle with. Because of time variability resulting from the continuous nature of the measurements, the DiCo score value describing the infant's cerebral autoregulation differs from one time instant to another one during the recording. Therefore, we define here a measure that synthesizes the level of autoregulation of a patient for the whole recording time. During the last years, some authors derived mathematics to synthesize in a single parameter the level of autoregulation of a patient. So did Tsuji et al.[1] when computing the mean COH of each patient for fixed periods of time. The higher this mean DiCo score, the worse the cerebral autoregulation of the patient. Last year, Soul et al.[5] proposed a pressure-passive index (PPI) : dividing first the signal recordings into consecutive epochs of constant duration,[4] they computed the percentage of epochs with significant low-frequency COH between MABP and HbD. If the mean COH was higher than a certain treshold value, then score 1 was assigned to the considered epoch, otherwise it received score 0. In this paper, we defined a similar parameter called CPRT (see Fig. 2), also based on the previously presented DiCo scores.

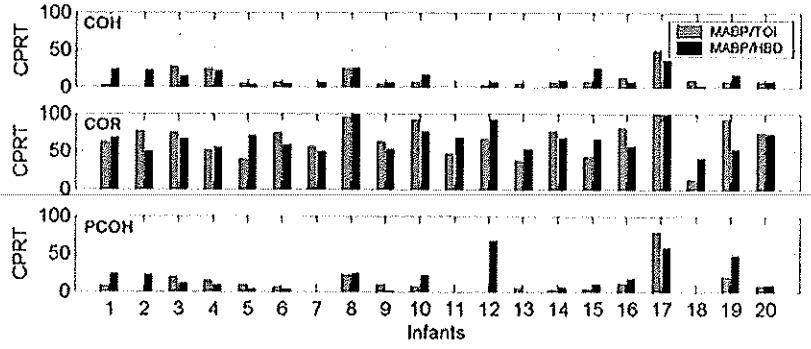


Figure 2. Illustration of the CPRT's related to each infant and for each score. For each DiCo method, a correlation coefficient (the CB-CPRT) was then computed from the interpolated CPRT curves related to both signal sets : it is equal to 0.81 for COH, 0.71 for COR, and 0.78 for PCOH.

The acronym CPRT stands for critical percentage of the recording time, i.e. the percentage of the recording time during which the DiCo score is greater than a fixed value, called critical score value (CSV). In this work the CSV will be set by default at half the maximum DiCo score value (i.e. 0.5). In contrast to the PPI, the CPRT is not computed from boolean scores over epochs -which means a loss of accuracy-, but from the DiCo scores. As seen previously, the DiCo scores are proportional to the autoregulation impairment. The proposed definition is moreover not limited to COH, but is applicable to all existing methods. We define the CPRT as

$$CPRT = \frac{\sum_i t_i}{t_{total}} \times 100$$

where the t_i's represent the durations of the parts of the DiCo score curve lying above the CSV, and t_{total} is the total recording time.

3.3. Similarity Measures

The aim of our work is to derive one or several similarity measures for proving that a continuously recorded signal –when studying cerebral autoregulation in neonates- may be replaced by another more handy one.

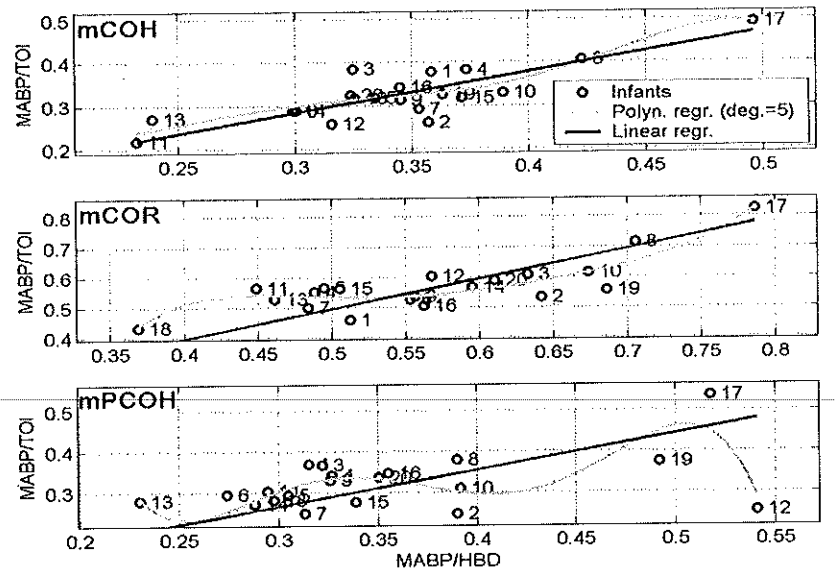


Figure 3. Multiple linear regression using least squares, achieved from the mean -over time- DiCo scores (mCOH, mCOR and mPCOH) of all patients. On the x-axis we considered the mean DiCo scores related to signal set MABP/HbD, and following the y-axis the ones of signal set MABP/TOI. The mean of the absolute values of the residuals is 0.027 for COH (corresponds to 2.7% of the full interval width [0,1] in which the DiCo scores belong), 0.043 for COR (4.3%), and 0.041 (4.1%) for PCOH. The MSE is 0.0013 for COH, 0.0031 for COR, and 0.0038 for PCOH. The figure also shows a polynomial regression of degree 5 of the data.

We particularly focused here on the replacement of HbD by TOI. Essentially we developed three similarity measures based either on a correlation coefficient between two curves, or on a multiple linear regression using least squares.

The first way was to compute the correlation between the interpolated DiCo score curves (CBS) related to both signals. These are the curves of the time-varying DiCo scores[3, 4] computed from MABP and HbD, and from MABP and TOI. As the CBS holds only for one infant, it has to be computed for all infants, afterwards a mean of the obtained CBS's (mCBS) is computed for each DiCo method.

The second way is based on the CPRT definition, and is done at the patient group level from the CPRT's. Figure 2 illustrates the CPRT's for all patients and for each DiCo method. For each DiCo method, we then computed a correlation coefficient between the interpolated curves related to signal sets MABP/HbD and MABP/TOI (CB-CPRT).

The last way to look at the similarity between HbD and TOI was achieved by computing a multiple linear regression, using least squares, from the mean DiCo scores of all patients (see Fig. 3). On the x-axis and y-axis, we considered the mean DiCo scores related to signal set MABP/HbD, and MABP/TOI respectively. We used two parameters to assess the regression efficiency. The first is the mean of the absolute values of the regression residuals r_i defined as

$$|\bar{r}| = \frac{\sum_{i=1}^{n} |r_i|}{n}$$

where n is the number of patients. The second parameter is the regression mean squared error (MSE), which is an estimator of the variance of the random disturbances.

4. EXPERIMENTAL RESULTS

Since the concordance between the signals might vary as a function of time, a sliding window approach was used (the DiCo scores were calculated over 30-minute epochs).[4] Before applying COH and COR, we first filtered all signals to keep only the recording intervals during which the variation in SaO_2 around its mean did not exceed 5%.[3] In this way the condition of constant SaO_2 was satisfied. This procedure was not followed for PCOH, as SaO_2 was the signal of which we took off the influence on MABP and HbD/TOI. For further information on the operating conditions, we refer the reader to the literature.[3, 4] The mCBS is equal to 0.76 for COH, 0.63 for COR, and 0.70 for PCOH. The CB-CPRT is equal to 0.81 for COH, 0.71 for COR, and 0.78 for PCOH. As a scaled correlation coefficient belonging to interval [0,1] was considered to compute mCBS and CB-CPRT, the obtained results are very positive. The mean of the absolute values of the residuals r_i is 0.027 (corresponds to 2.7% of the full interval width [0,1] in which the DiCo scores take their values) for COH, 0.043 (4.3%) for COR, and 0.041 (4.1%) for PCOH (see Fig. 3). The MSE is 0.0013 for COH, 0.0031 for COR, and 0.0038 for PCOH. The linear regression shows also that TOI is similar to HbD as the regression parameters are low.

5. CONCLUSION

First, a new synthesized measure of cerebral autoregulation -the CPRT- was presented. In opposition to previously defined measures, it is applicable to all existing DiCo methods, and generates a measure of the autoregulation impairment proportional to the time-varying DiCo score between the signals of interest. A larger follow-up study is however needed to evaluate statistically the CPRT efficiency with respect to the infant clinical outcomes. Secondly, the measures presented to study the similarities between signal sets MABP/HbD and MABP/TOI show very positive results, which brings us to claim that TOI -which is, in opposition to HbD, an absolute signal- may be used for the calculation of cerebral autoregulation in neonates.

6. ACKNOWLEDGEMENTS

The research was supported (1) by Research Council KUL : GOAAMBioRICS, CoE EF/05/006 Optimization in Engineering, IDO 05/010 EEG-fMRI, several PhD/postdoc & fellow grants; (2) by Flemish Government : FWO : PhD/postdoc grants, projects, G.0407.02 (support vector machines), G.0360.05 (EEG, Epileptic), G.0519.06 (Noninvasive brain oxygenation), FWO-G.0321.06 (Tensors/Spectral Analysis), G.0341.07 (Data fusion), research communities (ICCoS, ANMMM); and IWT : PhD Grants; (3) by Belgian Federal Science Policy Office IUAP P5/22 (Dynamical Systems and Control : Computation, Identification and Modelling); (4) by EU : BIOPATTERN (FP6-2002-IST 508803), ETUMOUR (FP6-2002-LIFESCIHEALTH 503094), Healthagents (IST-2004-27214, FAST (FP6-MC-RTN-035801), and (5) by ESA : Cardiovascular Control (Prodex-8 C90242).

7. REFERENCES

1. M. Tsuji, J. Saul, A. du Plessis, E. Eichenwald, J. Sobh, R. Crocker; and J. Volpe, Cerebral intravascular oxygenation correlates with mean arterial pressure in critically ill premature infants, Pediatrics 106 (4), 625-632 (2000).
2. J. Leuridan, and B. Rost, Multiple input estimation of frequency response functions : diagnostic techniques for the excitation, ASME Paper Number 85-DET-107, 5 pages, (1985).
3. D. De Smet, S. Van Huffel, J. Vanderhaegen, G. Naulaers, and E. Dempsey, Detection of autoregulation in the brain of premature infants, EMBS/BSMBEC, Proc. of IEEE/EMBS Annual Benelux Symposium and of Belgian Day on Biomedical Engineering, 215-218 (2006).
4. G. Morren, P. Lemmerling, S. Van Huffel, G. Naulaers, H. Devlieger, and P. Casaer, Detection of autoregulation in the brain of premature infants using a novel subspace-based technique, EMBS, Proc. of the 23rd Annual Intern. Conf. of the IEEE (2), 2064-2067 (2001).
5. J. Soul, P. Hammer, M. Tsuji, J. Saul, H. Bassan, C. Limperopoulos, D. Disalvo, M. Moore, P. Akins, S. Ringer, J. Volpe, F. Trachtenberg, and A. du Plessis, Fluctuating pressure-passivity is common in the cerebral circulation of sick premature infants, Pediatric Research 61 (4), 467-473 (2007).