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Reliability Evaluation of Emboli Detection using a Statistical Approach

D. Kouamé, J-M. Girault, A. Ouahabi, and F. Patat

Abstract— Cerebral emboli detection is a problem of considerable practical importance for monitoring vascular pathologies. If in most practical in vivo or in vitro experiments, big-size emboli detection seems comfortable, small-size emboli detection remains a challenge. The aim of this paper is to evaluate the performances of micro-emboli detections using statistical tools. We first introduce for this purpose a specific decision information through Autoregressive (AR) modeling. To overcome the problem of empirical detection threshold choice and quantify the reliability of the emboli detection, the chosen decision information makes it possible to link the threshold with the probability of false alarm (PFA). We then extend this approach to classical detection methods based on nonparametric analysis in order to perform comparisons, by using computer simulation of embolic signal. It is shown that reliable detection is not possible by the classical approaches when the Embolus-to-Blood Ratio (EBR) is lower than 10dB since in this case the PFA is by far above 10%, whereas our approach can detect small-size emboli with EBR as low as 5 dB since the PFA is then below 5%. In vivo measurements are finally performed in order to validate our approach.

Keywords— Emboli, Information Decision, Parametric, Probability of False Alarm, Probability of Non Detection.

I. INTRODUCTION

AN embolus can be considered as non-liquid particles or particles aggregates such flat, gas bubble, or any other stranger body, carried by blood flow. Emboli can stop the blood flow in the narrow area of vessels or slow it and thus yield thromboembolic complications. A micro-embolus is embolus of which size is sufficiently small for not stopping the blood flow in the main arteries of an organ, but which can obstruct micro-flow around these arteries. Micro-emboli investigation is quite recent because of the limitations of conventional commercial apparatus. Micro-emboli and therefore emboli detection has several interests: preventing cerebral vascular accidents, finding the cause of the emboli and validating the effectiveness of the treatments. The main technique used to detect emboli is the recording of transcranial ultrasound Doppler, *e.g.* [1]. Typical material for emboli detection is the Doppler signal. Embolic signature in blood flow is then assumed to be a non predicted high intensity transient signal (HITS) superimposed on the Doppler signal backscattered by the blood. Concerning detection, most of existing systems use an intensity measurement via the classical Fourier spectrogram. An embolic signal is detected when this intensity is above a reference one. This raises two main problems. The first one, is the well-known limitations of the Fourier analysis that is the conflict between time and frequency

resolutions and the necessary compromise between them. This has a practical consequence; due to the trade-off between the time and the frequency resolutions, two (or more than two) close emboli can hardly be detected. Therefore, this can have bad effects in situations where the number of detected emboli has to be counted. The second one is the choice of the reference intensity level. Its choice is empirical and is lied on *a-priori* experiments. Worst, the reliability of the detection is never evaluated.

The aim of this paper is to present a detection procedure using a parametric modeling. This approach is compared to classical ones through computer generated Doppler signal. *In vivo* experiment is investigated to validate our approach.

II. BACKGROUND

Emboli detection will be presented in a context of fault detection in a random process or signal. We will therefore introduce the general framework.

A. Binary Hypothesis Testing

Consider we have to make a decision related to the existence (or not) of a target in the process. Given some basic hypotheses, a criterion is selected upon which the decision is made. In this situation, we have to distinguish two sets : the first one is the set of (here, two) hypotheses, say H_0 representing the fact that there is no target and H_1 that a target is present. The second set is the set of decisions, say D_0 , "decide no target is present" and D_1 "decide a target is present". And depending on the hypothesis, four cases have to be considered concerning the decision.

A_{00} : Decide H_0 when H_0 is true,

A_{01} : Decide H_1 when H_0 is true,

A_{11} : Decide H_1 when H_1 is true,

A_{10} : Decide H_0 when H_1 is true.

The cases A_{01} and A_{10} correspond to errors in the decision. The case A_{01} is referred to as false alarm and the case A_{10} is referred to as non detection. Since a decision may be affected by any one of these errors, we evaluate the reliability of a decision by the probability of false alarm (PFA) and the probability of non detection (PND).

B. Probabilities Evaluation

Now, assume that the made decision is based on single observations of the process or the received signal represented by random variable X and that the possible values of X constitute the observation set denoted O . The set O is then divided into two subsets O_0 and O_1 such that if values of X belong to O_i the decision is D_i , with $i = 0, 1$. The probability density functions of X corresponding to

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each hypothesis are denoted $f_{X|H_0}(x|H_0)$ and $f_{X|H_1}(x|H_1)$, where x is a particular value of the random variable X . Denoting $P(D_i|H_j)$ the probability of deciding D_i when H_j is true, it follows that,

$$P_{ij} \stackrel{\text{def}}{=} P(D_i|H_j) = \int_{O_i} f_{X|H_j}(x|H_j) dx$$

With these definitions we have:

$$PFA = P_{01} = 1 - P_{00} \quad (1)$$

$$PND = P_{10} = 1 - P_{11} \quad (2)$$

In practice each hypothesis is characterized by a decision information (DI) and belonging to the O_0 or O_1 is represented by a threshold, say λ . For example if DI has unit variance centered gaussian variable, and H_0 is " $DI \leq \lambda$ ", $PFA = 1 - P(DI \leq \lambda)$; that is the probability of false alarm is directly related to the threshold. In this particular case, $\lambda = \text{erf}^{-1}(PFA)$ where erf^{-1} is Inverse function of the integral of the unit variance centered Gaussian distribution.

III. METHODS

In the following part of the paper we will consider complex signal, since the Doppler signal is complex (analytic). Three methods will be analyzed here. The parametric Autoregressive method (AR), the short time Fourier Analysis (STFA) and Wigner Ville distribution (WVD).

A. Short Time Fourier Analysis

The STFA is the most common analysis tool in the field of emboli detection. It consists in estimating on short time analyzing w windows the spectrum $S(n, f)$ of a signal x . It is defined in discrete (time (n) and frequency (f)) form by :

$$S(n, f) = \sum_{k=-\infty}^{\infty} x(k) w^*(k-n) \exp(-2\pi j f k)$$

where $*$ denotes the complex conjugate notation. The decision information is then

$$DI_F = \max_t |S(t, f)|^2$$

The typical problem of resolution of this approach has given rise to methods with better resolutions.

B. Wigner Ville Distribution

Emboic Doppler signal is a band limited pulse modulated signal. So two dimensional (time (t) frequency (f)) processing techniques are more appropriate for its analysis. Typical techniques are the so-called Cohen class distributions [2] defined for a signal x by :

$$D(t, f, Q) = \int_{-\infty}^{+\infty} \int_{-\infty}^{+\infty} Q(u, \tau) x(t+u+\tau/2) x^*(t+u-\tau/2) \exp(-j2\pi f \tau) du d\tau$$

where Q is a function which defines the distribution and its properties. Note that the short time Fourier Spectrogram is a special case of these distributions. The Wigner Ville Distribution, another particular case of these distributions [3] is one of the most commonly used. It has been used recently by [4] for emboli detection. For a signal x , it is defined in discrete form by :

$$W(n, f) = \sum_{k=-\infty}^{+\infty} x(n+k) x^*(n-k) \exp^{-j4\pi f k}$$

The decision information is then

$$DI_W = \max_t |W(n, f)|$$

From the previous definitions, DI_F and DI_W can be assumed to follow a Chi-square probability density function.

C. Parametric Autoregressive method

This method consists, unlike the previous methods, in working not directly on the signal, but on a model of the signal. Consider a discrete time complex signal x . Assuming that it is the output of an AR model, it can be expressed by :

$$x(n) = -a_1(n)x(n-1) - a_2(n)x(n-2) - \dots - a_p(n)x(n-p) + \eta(n)$$

where the $a_i(n)$ are complex coefficients defining the AR model, p is order of the model (number of coefficients) and $\eta(n)$ is a complex white noise. This model is referred to as AR(p) model. For convenience the previous expression is commonly expressed in matrix form as :

$$x(n) = \varphi^T(n) \theta(n) + \eta(n) \quad (3)$$

where

$$\varphi^T(n) = [-x(n-1), \dots, -x(n-p)], \text{ and}$$

$$\theta(n) = [a_1(n), \dots, a_p(n)].$$

Modeling the signal x as an AR process then corresponds to obtain from x , the vector $\hat{\theta}(n)$ which is an estimate of the vector $\theta(n)$. This estimation can be performed using for example the Recursive Least Squares (RLS) algorithm. Its principle consists in minimizing a cost function representing the quadratic mean difference between $x(n)$ and $\hat{x}(n) = \varphi^T(n) \hat{\theta}(n)$. A forgetting factor can be used in order to mainly account for the latest data in the estimation process; see for example [5]. This leads to obtain each time n , using intermediate variable $G(n)$ (Covariance matrix), the expression of the estimates as:

$$\begin{aligned} e(n) &= x(n) - \varphi^T(n) \hat{\theta}(n-1) \\ G(n) &= \frac{G(n-1)}{\lambda} \left(1 - \frac{G(n-1) \phi(n) \phi(n)^T G(n-1)}{\lambda + \phi(n)^T G(n-1) \phi(n)} \right) \\ \hat{\theta}(n) &= \hat{\theta}(n-1) + G(n) \phi(n) e(n) \end{aligned}$$

$e(n)$ is referred to as the prediction error. The superscript T denotes complex transposition. From these expressions one can make the following remark. When the model (3) efficiently fits the signal, the prediction error is asymptotically a white noise. Since the autocorrelation function (AF) of a white noise, equals zero at any lag except at initial lag ($n=0$), the AF of predicting error is therefore an indicated DI for this parametric method. Indeed, when an embolus crosses the measurement volume, the predicting error will no more be asymptotically a white noise, and its AF at lag 1 (for example) will differ from zero. The AF at lag 1 can be expressed by:

$$C_N \stackrel{def}{=} C(1) = \frac{1}{N} \sum_{k=1}^N e(k)e(k-1)$$

This can be estimated recursively each time n using a forgetting factor α ($0 < \alpha \leq 1$) by :

$$C_n = \alpha C_{n-1} + (1 - \alpha)e(n)e(n-1)$$

Here $\lambda = 0.95$ and $\alpha = 0.9$. Due to the previous remark, C_n will be almost zero for a normal Doppler signal, and the presence of an embolus will be characterized by an abrupt change. Then here:

$$DI_A = |C_n|$$

Moreover, for a unit-variance centered gaussian random signal $g(k)$, the random signal $v(k) = g(k)g(k-1)$ has the "cosh probability density function" [6]

$$P(x) = \frac{1}{\pi} \int_0^{\infty} \exp[-|x| \cosh(u)] du, x \neq 0$$

Provided the additive noise - it is the case in most practical experiments - in the model (3) is gaussian, DI_A can be assumed to have the cosh probability density function.

IV. RESULTS

A. Simulation Results

As it can be seen on fig.1 and fig.2 theoretical and estimated distributions obtained by a non embolic Doppler signal are similar. This validates the hypotheses made previously.

TABLE I

| $PFA = PND \leq 10\%$ | | | |
|-----------------------|--------|--------|--------|
| Methods | DI_F | DI_W | DI_A |
| $EBR_{min}(dB)$ | 12 | 10 | 4 |
| $PFA = PND$ | 10% | 7 % | 3% |

EBR_{min} for each method (DI_F, DI_W, DI_A) using simulated signals.

Therefore, since the theoretical evaluation of the distributions from real data is cumbersome (estimation of the parameters of distribution by fitting the experimental and

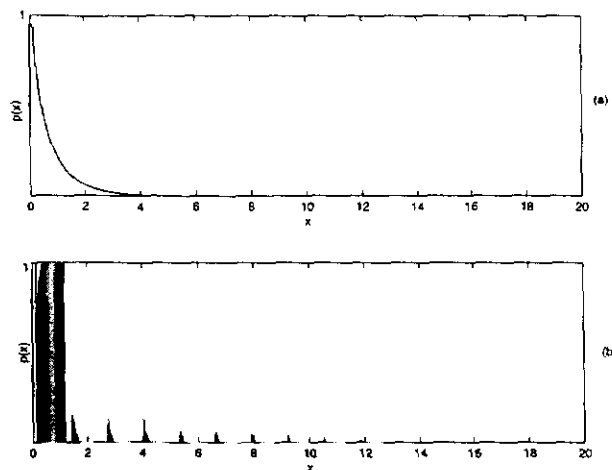


Fig. 1.

Cosh-Distribution Theoretical curve for a unit-variance centered normal random variable (a) and estimated curve (b) using DI_A from a normal Doppler signal using 100 realizations.

the theoretical curves), and does not bring additional information, we use estimated distributions instead.

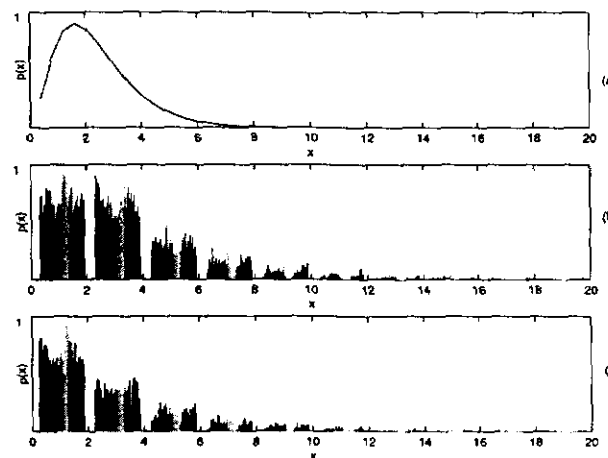


Fig. 2.

Chi-square Distribution Theoretical curve (a) and estimated curve (b) using DI_W and (c) using DI_F from a normal Doppler signal using 100 realizations.

The simulation results have been obtained by using artificial embolic Doppler signals with a 10 dB Signal-to-Noise-Ratio (SNR). These signals are based on pusaltil Doppler signal simulation [6],[7],[8]. In order to evaluate the reliability of detecting micro-emboli detection, the different methods are compared using the so-called embolus-to-blood-ratio (EBR). EBR is the ratio between the energy backscattered by the embolus embedded in the blood (P_{E+B}) and

the one backscattered by the blood without embolus (P_B). The EBR values used go from 3 to 20 dB. For each EBR, 100 realizations of the embolic Doppler signal are first computed and then the PFA and the PND are evaluated. The Characteristics Operational Receivers curves, are curves giving PFA versus PND. In our study, we choose to give the same importance to PFA and PND. From the values of PND and PFA, the minimum EBR can be evaluated. Table I shows the results of the minimum EBR (detectable) emboli a with reliability of $PFA = PND < 10\%$. As it can be seen, in these conditions, classical non parametric methods have a minimum detectable embolus with an EBR up to twice higher than the parametric one. This table also underlines the fact the reliability of the detection using classical methods vanishes when the EBR is less than 10 dB, that is, micro-emboli detection is not possible with these approaches, whereas it is with the parametric one.

B. Experimental Results

The different methods have been tested using in vivo data recorded on patients. The recording signals - 2 MHz-emitting-frequency and 6 KHz-PRF-Transcranial Doppler have been first performed with MDX-4 TCD-8 DWL Elektronische Systeme GmbH. The *a-posteriori* estimated SNR is lower than 10dB. The recorded signals (400 signals) have been classified in high EBR ($EBR \geq 20dB$) and low EBR($EBR < 10dB$). For high EBR, all the methods give reliable detections. The results shown on fig.3 are obtained with $EBR \approx 3$ dB. For these values, Fourier method gives $PFA = PND = 39\%$, Wigner-Ville approach gives $PFA = PND = 25\%$ and parametric approach give $PFA = PND = 19\%$. One can notice that although the low SNR degrades the performance of all methods, the better reliability is achieved with parametric method.

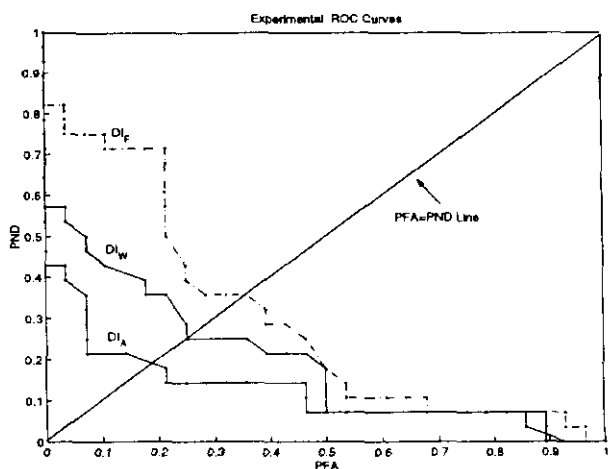


Fig. 3.

Experimental in vivo ROC curves of each of the different Decision Information DI_F for Fourier, DI_W for Wigner Ville and DI_A for parametric predicting error Autocorrelation

Another fact underlined by this experimental study is that when two or more emboli cross the measurement volume, the classical approaches hardly detect the second and following. This is illustrated by Table II. The results indicated in Table II show that in the experimental conditions mentioned above, the Fourier method detects reliably 44 % of emboli (the other being not detected or considered as false alarm) which crossed the measurement volume alone, 0 % of them crossed the measurement volume with another one. Wigner-Ville method detects reliably 75 % of emboli which crossed the measurement volume alone. Among them 20% and 6% crossed the measurement volume with respectively another one and two others. The results are respectively 81% 25% and 12% for parametric method.

TABLE II

| Number of embolus | DI_W | DI_A | DI_F |
|-------------------|--------|--------|--------|
| 1 | 75 % | 81 % | 44 % |
| 2 | 20 % | 25 % | 0 % |
| 3 | 6 % | 12 % | 0 % |

Percentage of a single, two and three detected emboli in the measurement volume during in vivo recordings.

V. CONCLUSION

In this paper we have evaluated the reliability of the emboli detection of classical nonparametric (Fourier and Wigner-Ville) and parametric AR method. It has been shown using simulated signal that detection performed by the classical approaches is by far worse than parametric one. Indeed, when the Embolus-to-Blood Ratio (EBR) is lower than 10dB, the PFA is high (above at least 10%), whereas the parametric approach can detect small-size emboli with EBR as low as 5 dB since the PFA is then below 5% when the SNR is at least 10%. These results are validated by in vivo experiments.

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