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Emboli characterization in Blood Mimicking Fluid circulation using parametric modeling

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Abstract—Cerebral microemboli remain a high part of all vascular cerebral accidents in western world. Thus detection, sizing and nature (particulate or gaseous) evaluation are three important tasks which are necessary to understand embolism and to perform correct diagnostics and even therapy. The problem of detection has been widely reported in many works. Our aim was here to address the emboli characterization, sizing and nature evaluation. This characterization is based on EBR (Embolus to Blood Ratio). EBR values were computed with two signal processing approaches: Fourier technique and Parametric modeling. Emboli were simulated with acrylic particles ranging from 220 μm to 500 μm . With the smallest emboli, parametric approaches gave variance and standard deviation better than Fourier technique. In a second time, we use the same multi-frequency approach to find frequencies triplet which assumed the best differentiation between gaseous and particulate emboli over a high range of diameters.

I. INTRODUCTION

Transcranial Doppler ultrasound (US) is the most commonly used technique in order to detect and to track emboli in cerebral arteries circulation [1]. The number of emboli detected is often linked to a vascular pathology, or to its degree of severity, like carotid stenosis.

Detection techniques available on current Doppler pulsed wave (PW) devices are based on backscattered energy between an embolus and background red blood cells. Time-frequency distributions, like spectrogram, are commonly used in order to compute embolic Doppler signal energy. Recently, a new alternative has been developed : it consists in modeling Doppler signal through a white noise filter using a two order autoregressive (AR) model [2]. Emboli occurrences appear as a model change. This technique is extended here to emboli sizing. Several approaches concerning emboli discrimination have been investigated: Doppler signal processing and parameters extraction [3], solid and gaseous emboli backscattered radio-frequency signal spectrum analysis [4], or two frequencies emission technique [5].

After a brief description of the sizing method, which consists in computing EBR (Embolus to Blood Ratio) values at two different emission frequencies, the parametric approach is presented. Comparison with Fourier technique results is then performed. Results have been processed and compared in terms of bias and standard deviations. Finally, multi-frequency method is introduced to differentiate solid emboli from gaseous ones.

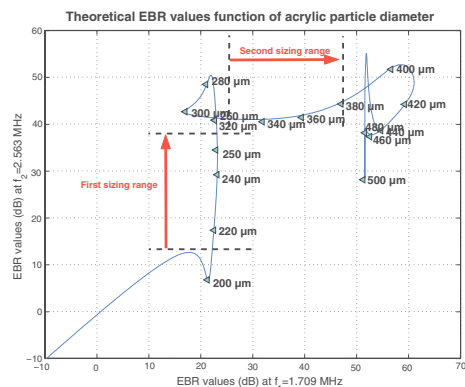


Fig. 1. Theoretical EBR_{f_2} function of EBR_{f_1}

II. EMBOLI SIZING TECHNIQUE

The technique used here has been suggested by previous studies [6], [7] and [8]. An EBR value, embolus to blood ratio, is introduced in eq.(1). It explicitly represents the acoustic impedance mismatch between embolus and the surrounding red blood cells.

$$EBR(f, r_e) = \frac{\sigma_e}{\eta V} \quad (1)$$

with σ_e is the embolus backscatter embolus cross-section, a quite complex function essentially of emission frequency, embolus acoustical properties: size, composition (density ρ and speed of sound c), computed supposing embolus spherically shaped. V is the volume of fluid flowing in Doppler sample volume, and η is the blood backscatter coefficient.

This frequency dependance of embolus backscatter cross-section is applied in order to solid emboli size. A two frequencies emission PW system is so used for computing EBR values of emboli of different sizes. This fact is illustrated, in figure 1, which represents EBR_2 ($f_2 = 2.563\text{MHz}$) function of EBR_1 ($f_1 = 1.709\text{MHz}$). Emboli mimicking particles here are acrylic ones.

This curve shows the reliability of this technique, specially for two ranges of acrylic particles diameter (220 to 260 μm) and (320 to 380 μm). At a given size within these ranges, a single (EBR_1, EBR_2) couple is allocated. Two energy estimators results are described below.

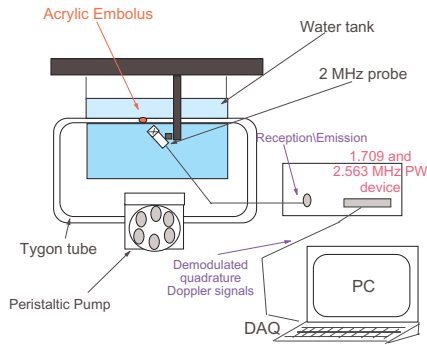


Fig. 2. Experimental set-up

III. EXPERIMENTAL RESULTS

A. Experimental set-up

In order to verify sizing technique, an *in vitro* set-up was made. It consists of a fluid, BMF (blood Mimicking Fluid) mainly consisting of $5 \mu\text{m}$ orgasol particles, moving in a tygon tube with a peristaltic pump, which allows to generate pulsatile flow. Emboli were introduced by acrylic particles ranging from $220 \mu\text{m}$ to $500 \mu\text{m}$. The same experimental conditions were used for each measure: insonification angle around $\pi/6$. Flow speed (near 7 to 10 cm.s^{-1}) is lower than those met in cerebral circulation, in order to avoid bubbles generated by the pump and the tube joins. The PW doppler device is a two frequencies 1.709 MHz and 2.563 MHz emission one. Emission power can be adjusted. Sample volume length and depth were fixed to 4 and 45 mm respectively, for all measures. The experimental set-up is represented in figure 2. The quadrature demodulated Doppler signals (for the two frequencies at two depths) were sampled at pulse repetition frequency (PRF) 6.4 kHz using a data acquisition board (DAQ).

B. Fourier Approach

Energy estimation using Fourier approach is very common. It consists of power density calculations in frequency domain. As Doppler signal is strongly non-stationary, spectrogram technique is used. The EBR value is defined as, eq.(2):

$$EBR = 10 \log_{10} \left(0.5 * \frac{P_{E+B}}{P_B} \right) \quad (2)$$

where P_{E+B} and P_B are respectively power backscattered by embolus in blood, and blood only. The figure 3 represents Fourier-based EBR values compared with theoretical ones, at each emission frequency.

Table I exhibits results (mean and standard deviation) obtained with Fourier approach at the two frequencies versus theoretical ones in brackets.

For acrylic sizes up to $400 \mu\text{m}$, bias (over 10 dB) can be mainly explained by signal saturations (magnitude out of dynamic range of PW device). Relatively significant bias

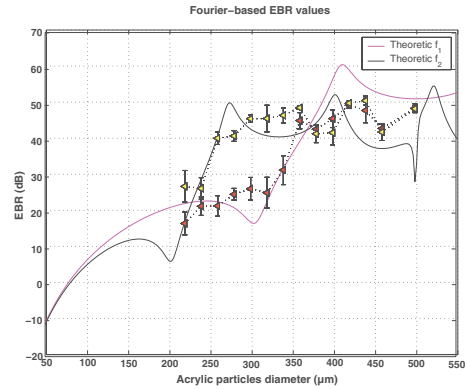

 Fig. 3. 1.709 MHz and 2.563 MHz Fourier-based and theoretical EBR values function of acrylic particles diameter

TABLE I

FOURIER EVALUATED EBR MEAN AND STANDARD DEVIATION FOR ACRYLIC PARTICLES

Size (μm)	mean(theoretic) at $f_1; f_2$ (dB)	std (f_1, f_2) (dB)
220	16.99 (25.77); 27.28 (20.65)	3.13 ; 4.41
240	21.76 (26.43); 26.71 (32.51)	2.56 ; 3.01
260	21.85 (26.25); 40.66 (44.61)	2.87 ; 1.74
280	25.09 (24.63); 41.27 (52.22)	1.61 ; 1.51
300	26.60 (20.68); 46.05 (42.42)	3.15 ; 0.99
320	25.52 (26.11); 46.11 (44.57)	4.25 ; 3.68
340	31.81 (35.35); 47.01 (44.30)	4.01 ; 2.08
360	45.54 (42.92); 49.11 (45.22)	2.23 ; 0.44

appeared close to small particles sizes, specially at emission frequency f_2 . For example, for $220 \mu\text{m}$ diameter acrylic particles, computed EBR values were higher than theoretical ones (around 10 dB for the two frequencies). Other energy computing approach was also introduced.

C. Parametric Approach

As previously enounced, Doppler signal can be modelled by a two order AR model. This signal can be expressed by eq.(3):

$$y_d(n) = - \sum_{i=1}^p a_i(n) y_d(n-1) + u(n) \quad (3)$$

with p is the model order, a_i is AR coefficients and $u(n)$ is a white noise. Power spectral density is then obtained from parameters a_i . The figure 4 represents EBR parametric estimated values compared with theoretical ones, at each emission frequency. Parametric approach results between 220 and $360 \mu\text{m}$ were shown on table II. Unlike fourier computed values, EBR ratios, corresponding to 220 up to $320 \mu\text{m}$ acrylic particles, presented low standard deviations (around $2-3 \text{ dB}$) and bias was not as important as previously at emission frequency f_2 .

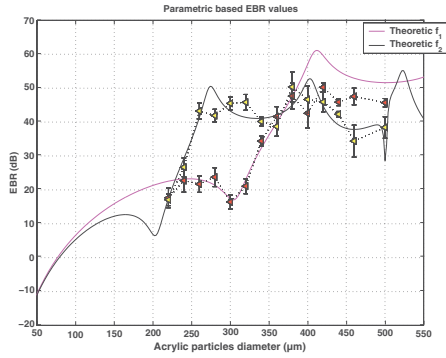


Fig. 4. 1.709 MHz and 2.563 MHz Parametric evaluated and theoretical EBR values function of acrylic particles diameter

TABLE II
PARAMETRIC EVALUATED EBR MEAN AND STANDARD DEVIATION FOR ACRYLIC PARTICLES

Size (μm)	mean(theoretic) at (f_1, f_2) (dB)	std (f_1, f_2) (dB)
220	17.58 (25.77); 17.01 (20.65)	2.88 ; 1.69
240	22.67 (26.43); 26.61 (32.51)	3.39 ; 2.75
260	21.63 (26.25); 43.19 (44.61)	2.42 ; 2.38
280	23.71 (24.63); 41.86 (52.22)	2.78 ; 1.85
300	16.37 (20.68); 45.46 (42.42)	2.06 ; 1.87
320	21.04 (26.11); 45.77 (44.57)	2.20 ; 2.33
340	34.33 (35.35); 40.10 (44.30)	1.45 ; 1.30
360	41.53 (42.92); 38.13 (45.27)	2.99 ; 2.88

IV. EMBOLI DIFFERENTIATION

A. Two frequencies technique

As previously mentioned, the two frequencies PW device allowed us to estimate solid emboli sizes. This technique is now applied in order to differentiate gaseous emboli from solid ones. The parameter introduced here was $\Theta_{EBR}(f_1, f_2)$ which was expressed by eq.(4):

$$\Theta_{EBR}(f_1, f_2) = EBR(f_1) - EBR(f_2) \quad (4)$$

An important criteria of differentiation seems to be the evolution of the $\Theta_{EBR}(f_1, f_2)$ sign. Doppler signals attributed to 200 μm air bubbles occurrences were recorded with the same two frequencies PW device. $\Theta_{EBR}(f_1, f_2)$ values were dressed in table III, they were always positive.

Backscattered Doppler signals of red blood cells aggregates, fat and gaseous emboli were then simulated. The first fre-

TABLE III
 $\Theta_{EBR}(f_1, f_2)$ FOURIER AND PARAMETRIC VALUES FOR AIR BUBBLES

Fourier	$\Theta_{EBR}(f_1, f_2)$ mean value (dB)	std (dB)
	12.40	2.71
Parametric	$\Theta_{EBR}(f_1, f_2)$ mean value (dB)	std (dB)
	15.80	2.92

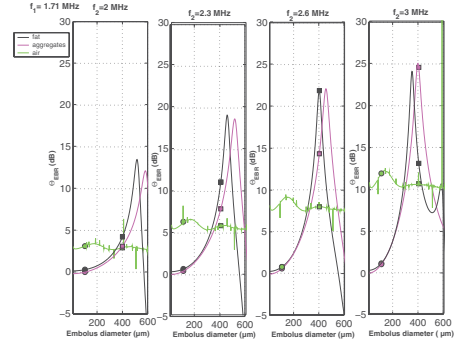


Fig. 5. $\Theta_{EBR}(f_1, f_2)$ function of emboli diameters and second frequency

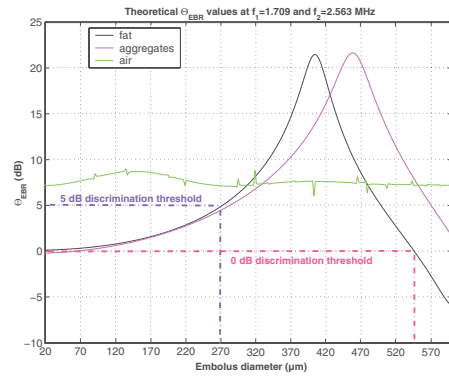


Fig. 6. $\Theta_{EBR}(f_1, f_2)$ function of emboli diameters at $f_1=1.709$ MHz and $f_2=2.563$ MHz

quency was fixed at $f_1 = 1.709$ MHz. Emboli sizes varied from 10 to 600 μm . Evolutions of Θ_{EBR} for these three emboli types where shown in figure 5, with, for example, four frequency f_2 2, 2.3, 2.6 and 3 MHz. Simulations were performed with a 10 mm sample volume. Even if $\Theta_{EBR}(f_1, f_2)$ was always positive for air bubbles, this is not true in case of fat and aggregates: Θ_{EBR} was only negative for aggregates smaller than 40 μm , and for fat emboli up to 550 μm at $f_2 = 2.3$ MHz. This parameter sign is not sufficient to discriminate solid and gaseous emboli. Nevertheless, if a threshold (around 5 dB and not zero as previously) is established and the two emission frequencies were $f_1=1.709$ MHz and $f_2=2.563$ MHz, Θ_{EBR} between gas and solid emboli difference could be made if diameters didn't exceed 270 μm , in figure 6. Three frequencies approach was so suggested.

B. Three frequencies technique

Now, an approach was to simultaneously emit three frequencies. It was, also, to verify that $\Delta\Theta_{EBR}$ value sign, defined as eq.(5), is different with gaseous emboli (> 0) that for solid ones (< 0).

$$\Delta\Theta_{EBR} = \Theta_{EBR}(f_1, f_2) - \Theta_{EBR}(f_2, f_3) \quad (5)$$

Similar simulations, but now with three frequencies, were made with air bubbles, red blood cells aggregates, and fat

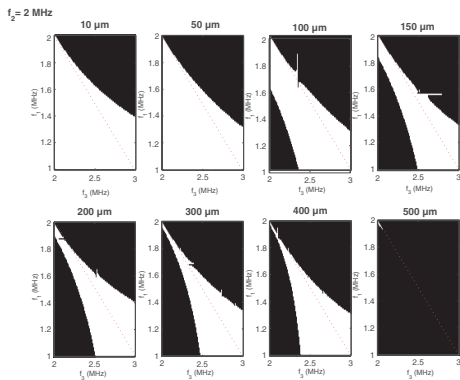


Fig. 7. $\Delta\Theta_{EBR}$ domains for air bubbles and fat emboli

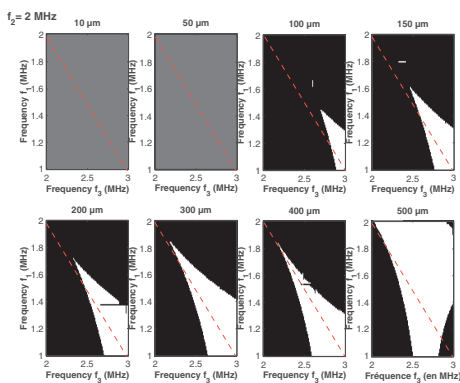


Fig. 8. $\Delta\Theta_{EBR}$ domains for air bubbles, fat and aggregates

emboli. Frequency f_2 is fixed at 2 MHz. Frequencies f_1 and f_3 were varied between 1 and 2 MHz, and 2 and 3 MHz respectively. Emboli diameters range was contained between 10 and 600 μm . A binary representation was achieved in order to distinguish domains where $\Delta\Theta_{EBR}$ is positive for gaseous emboli and negative in case of solid ones. Figures 7 and 8 displayed these domains, respectively, by considering only fat, and red blood cells aggregates and fat for solid emboli. These figures showed $\Delta\Theta_{EBR}$ sign evolution, for example, for emboli diameters equals to 10, 50, 100, 150, 200, 300, 400 and 500 μm . Regions, where $\Delta\Theta_{EBR}$ values were positive, colored white, or black in case of negative $\Delta\Theta_{EBR}$ values. When the total domain colored gray, $\Delta\Theta_{EBR}$ sign was identical for all computed (f_1, f_2, f_3) triplet, and any differentiation were possible.

The frequencies triplet (f_1, f_2, f_3) , optimally chosen in order to have $\Delta\Theta_{EBR}$ negative and positive values for fat and air bubbles along a large size range, was, for example, 1.71, 2 and 2.32 MHz, in figure 7. Furthermore, these frequencies values must be relatively close to each other, so that a good transducer sensitivity was conserved. Nevertheless, if aggregates were taken account, in figure 8, conclusions were notably different. Thus, frequencies (f_1, f_3) domain, which correspond to positive $\Delta\Theta_{EBR}$ values for air bubbles and negative for fat and aggregates, was smaller than previously. Frequency triplet

previously introduced was true now only for aggregates up to 250 μm . Nevertheless, Clinical investigations were led to emboli sizes between 20 and 300 μm . An other frequencies couple (f_1, f_3) must be introduced for smaller aggregates discrimination (up to 50 μm) 1.35 and 2.8 MHz. Compromise must be made between emboli size range discrimination and probe sensibility.

V. CONCLUSION

It was actually admitted that embolism consequences were correlated to embolus composition. That's why emboli differentiation and sizing remain promising researches. Approaches used in our study are multi-frequencies emission. The ability by a two frequencies PW device, associated with a good energy estimator, of sizing was proved. Nevertheless, this sizing was possible only on particular diameter ranges, if embolus composition was known. Parametric estimated EBR values presented less bias and standard deviation against theoretical than Fourier-based ones, specially in the two size ranges previously defined. Simulations showed practical attraction of multi-frequencies emission, concerning emboli differentiation. We have seen that the parameter $\Delta\Theta_{EBR}$ could be a discriminative factor in emboli discrimination, if emission frequencies were well chosen. Nevertheless, experimental measures must be performed.

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