AN INTEGRATED SYSTEM FOR THE EVALUATION OF FLOW MEDIATED DILATION

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ABSTRACT

An integrated system capable of estimating either the stimulus (wall shear rate change) and the effect (diameter change) in Flow Mediated Dilation (FMD) ultrasound investigations is presented. The FMD integrated system consists of a modified ULA-OP research platform and a post-processing software. The ULA-OP provides a real-time visual feedback on the positioning of the ultrasound probe on the artery of interest. Both B-mode images and blood velocity profiles can be checked during the entire exam so that the operator continuously controls the morphology and the hemodynamics of the region of interest. In addition, ULA-OP is used to acquire the raw I/Q demodulated data. These are post-processed through a Matlab® platform to estimate the arterial diameter and the wall shear rate changes. Experimental examples are reported.

Index Terms— Ultrasound, Flow-mediated-dilation, endothelial function, ULA-OP, research platform

1. INTRODUCTION

Flow-mediated dilation (FMD) is widely used to assess the endothelial function by ultrasound. Blood flow in the brachial artery is restricted by a cuff for about 5 minutes. When the cuff is removed, the wall shear stress (i.e. the product of wall shear rate –WSR– by blood viscosity) increases, thus stimulating the release of a vasodilator, the nitric oxide, from the endothelial cells into the smooth muscle. By measuring the diameter change due to reactive hyperemia, possible endothelial dysfunctions can be detected [1].

Although FMD is thought to be evoked by shear stress, no direct measurements of the stimulus (WSR) yielding the FMD have been reported until 2011 [2]. This can be mainly attributed to the fact that the measurement of wall shear rate, i.e. the blood velocity gradient near the arterial walls, requires the simultaneous estimation of velocity in multiple sample volumes (SVs) located at different distances from the probe. The computational complexity of such multigate Doppler measurement adds to the inherent complexity of automatic diameter change measurement. The latter has been traditionally obtained from the analysis of B-mode echographic images. For this purpose, gradient-based elaborations [3], [4], artificial neural networks [5] or first order absolute central moment estimations [6] have been proposed. Such methods, however, have not been so far integrated together with a WSR measurement method in a single equipment dedicated to FMD.

In this paper, we report the description of an integrated system capable of estimating either the stimulus (WSR change) and the effect (diameter change) in FMD investigations. To reach this goal, the hardware of the ULtrasound Advanced Open Platform (ULA-OP) has been enriched with a specific acquisition system capable of storing the large amount of raw echo-data produced during this long examination. Furthermore, a Matlab® (The Mathwork Inc, Natick, MA) based software platform has been developed to analyze the data in order to evaluate the endothelial functionality.

2. METHOD

2.1. FMD integrated system

2.1.1. ULA-OP

The ULA-OP research platform [7], entirely developed by the Microelectronics systems design laboratory (MSDLab) of the University of Florence, contains, in two boards, all the electronics necessary to control linear/convex-phased array probes with up to 192 elements. The receiving (RX) section acquires the echo-signals from a selectable sub-group of elements, converts them to digital, beamforms them according to programmable apodization and delay coefficients. The radio-frequency echo-signal is quadrature-demodulated, low-pass filtered and processed in real time by software modules running on a digital signal processor

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(TMS320C6455, Texas Instruments, USA). ULA-OP is equipped with 1 GB of memory where data can be stored from all points of the RX chain, to be then downloaded to a PC.

Since an FMD exam may be long up to 15 minutes, a dedicated additional acquisition board has been developed to store all I/Q demodulated data over such a long time. This board includes a 16 GB compact flash memory card, and also permits to acquire auxiliary signals such as those produced by an ECG device or a tonometer.

2.1.2. Signal elaboration platform

The signal elaboration platform (SEP) has been organized as a collection of functional blocks implemented as Matlab classes. Each block is responsible of a specific task and works in cascade with the other blocks, i.e. the output of an upstream block forms the input for a downstream block.

Fig. 1 shows the flow chart and the links among the main functional blocks employed in an FMD elaboration. The *Data* class works as an interface between ULA-OP and SEP converting the data stored in a specific file into a Matlab two dimensional matrix. Since the acquired file could be very large and not fit the computer memory, the class is implemented to read a reduced set of data each time it is requested. The last read data, i.e. the *Data* class output, is the input of both *B-Mode* and *Profile* classes. The first one organizes the data in lines and frames, interpolates them along either axial and lateral direction, and filters them in time and in 2D spatial domain. Furthermore, the B-Mode class applies a logarithmic scale compression and converts the results in a color scale. The result is further elaborated by the *Diameter* class which extracts the vessel diameter and the position of both near and far wall [8].

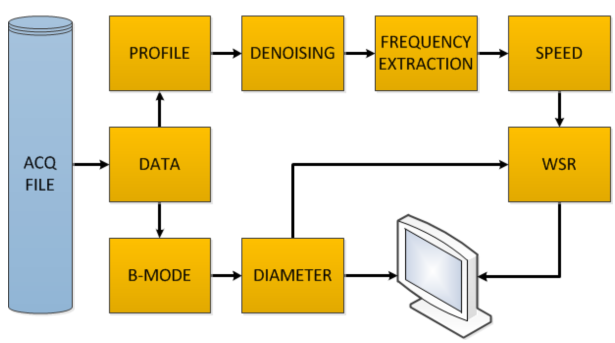

Fig. 1 Sketch of the main elaboration blocks of the signal elaboration platform.

The *Profile* class elaborates the last read data similarly to the ULA-OP real-time software. Multigate Spectral Doppler (MSD) profiles, containing the information about the distribution of blood velocities at different depths, are reconstructed through 256-point fast Fourier transforms (FFTs) [2]. These profiles are low-pass filtered in order to remove the low-frequency spectral components through a frequency domain mask. The *Denoising* class applies a threshold to the profile through a recursive estimation of its noise level. The availability of a complete spectrum for each investigated depth enables the extraction of the corresponding local Doppler mean frequency (f_{mean}) through a weighted average algorithm. This task is performed by the *Frequency Extraction* block. Subsequently, the *Speed* class, converts f_{mean} to blood speed according to the following equation:

$$v = \frac{f_{mean} \cdot c}{2 f_0 \cdot cos\theta} \qquad (1)$$

where c is the sound speed, f_0 is the transmitted central frequency and θ is the Doppler angle.

The *WSR* block has two inputs, i.e. the outputs coming from *Speed* and *Diameter*. In particular, a polynomial least-square fit is applied on the velocity points and the resulting velocity profile is used to evaluate the speed gradient with respect to the radius (shear rate). The positions of near and far walls estimated by the *Diameter* block are used to extract the corresponding shear rate (WSR).

3. RESULTS AND DISCUSSION

The ULA-OP and the SEP have been tested on the acquisitions from several healthy volunteers. Fig. 2 shows the output of the main elaboration blocks, as they are directly plotted by the graphic methods of the developed classes. In particular, Fig. 2a reports the B-Mode image of a brachial artery logarithmically compressed and represented in black and white color scale. The horizontal red lines on the image are the outputs of the *Diameter* class and represent the estimated position of near and far walls, respectively. Fig. 2b shows the raw multigate spectral Doppler profile elaborated by the *Profile* block. Here, the Doppler spectra from depths between 10 and 20 mm are coded in a color scale. The spectral profile is further denoised and plotted in Fig. 2c, where a white line representing the local Doppler mean frequency as evaluated by the *Frequency extraction* block is overlaid. In Fig. 2d both the estimated blood raw velocity (white line) and the corresponding polynomial least-square fit (red dashed line) are reported. Finally, the shear rate computed on both the estimated speed (white line) and on the polynomial fitting (red line) is reported in Fig. 2e. It highlights how noisy is the shear rate without applying a polynomial fitting. Two yellow dotted lines represent the near and far wall positions extracted by the *Diameter* class and used to evaluate the WSR as the closer shear rate peak.

Furthermore, in order to facilitate the use of the elaboration platform, a user friendly graphical interface has been developed (see Fig. 3). This allow the user to change all the elaboration parameters and to check the instantaneous values of both diameter and WSR over the entire exam. The user can also check whether the elaboration chain is correctly working by looking at the B-Mode image, the MSD profile and at the speed estimation and fitting.

In Fig. 4 a typical FMD elaboration result is reported. The upper plot shows the WSR averaged between the near and far wall WSR values, the middle plot reports the diameter changes and the lower one shows the blood pressure. The graph are splitted in two time intervals, the first corresponding to the acquisition before the cuff restriction (baseline) and the second, 5 minutes long, starting one minute before releasing the cuff. The red lines report the values averaged on each cardiac cycle. These graphs allow extracting the main parameters needed to investigate the endothelial function, i.e. the WSR peaks, the area under the curve of WSR, the percentage diameter distension and the delay occurring between WSR peak and diameter peak.

4. CONCLUSION

In this work, an integrated system for FMD application, consisting of a hardware and a software part, has been presented. The hardware of an existing scanner (ULA-OP) has been upgraded to acquire the large amount of data, which is needed for FMD exams. Furthermore, a Matlab based software platform consisting of several elaboration blocks has been developed and proved to be capable of extracting diameter and wall-shear-rate from B-Mode images and MSD-profiles. The WSR, in particular, is directly estimated from the velocity profile gradient, avoiding assumptions concerning the flow nature.

The approach followed in the design of the SEP blocks, i.e. based on object-oriented programming and on a specific task for each block, allows changing or updating each part of the processing chain. For example, different algorithms [4], [8] for arterial diameter detection have been tested simply developing two classes differing only in one method. In the same way the flow speed can be evaluated starting from the mean spectral frequency or by extracting the maximum spectral frequency. The integrated FMD system will be adopted in a multicenter study as part of the SUMMIT Project granted by UE.

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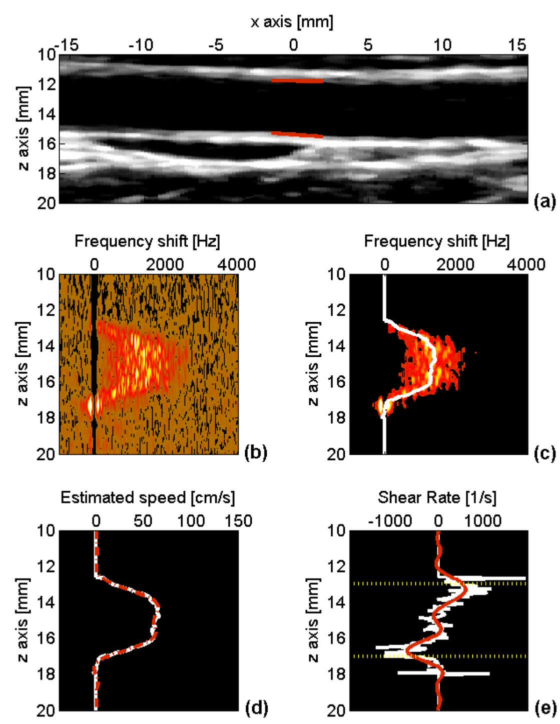

Fig. 2 Output of the main elaboration blocks, how they are plotted by the graphic methods of the developed classes. (a) B-Mode and Diameter extraction; (b) multigate spectral profile; (c) denoised profile and mean frequency extraction (white line); (d) speed estimation (white line) and fitting (red line); shear rate considering the unfitted speed (white line) and the fitted one (red line).

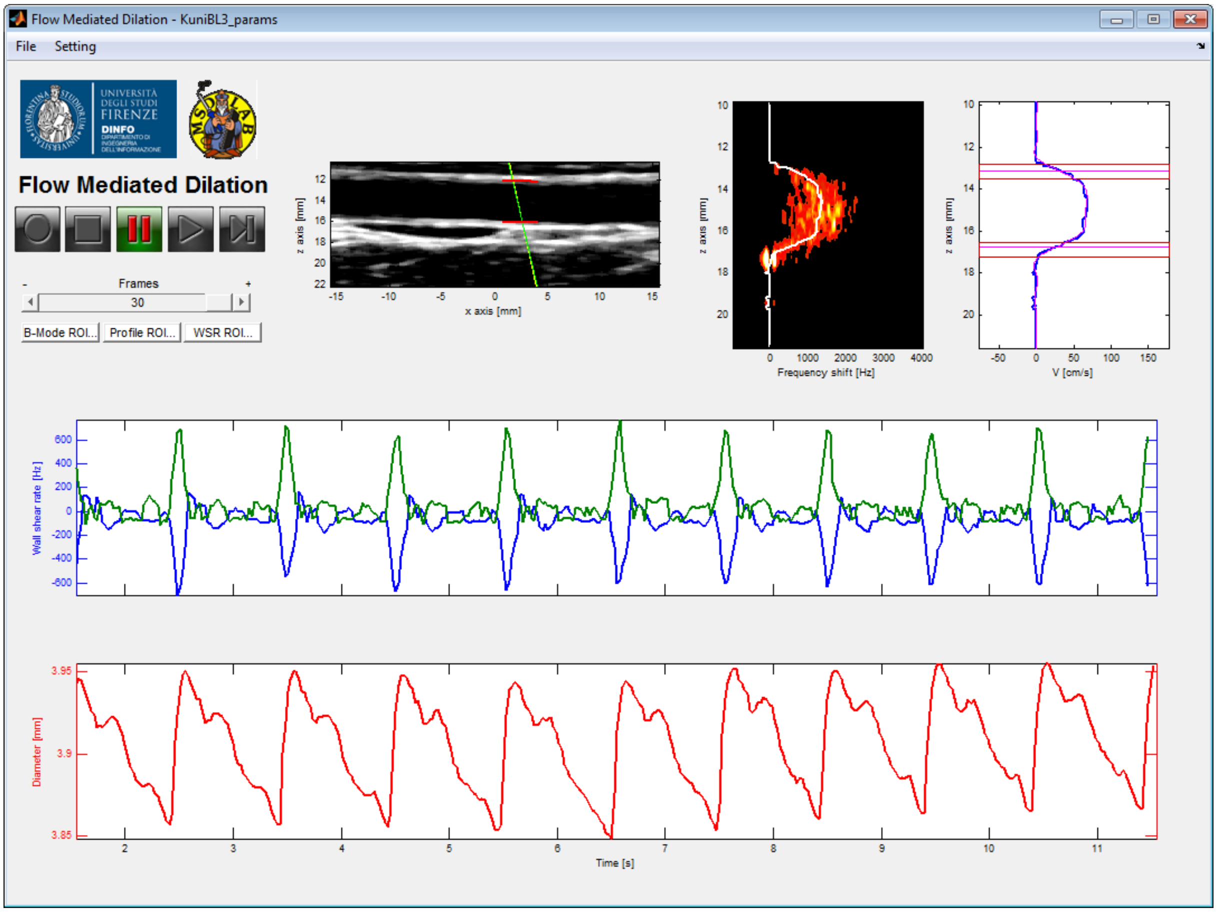

Fig. 3 Signal elaboration platform main interface.

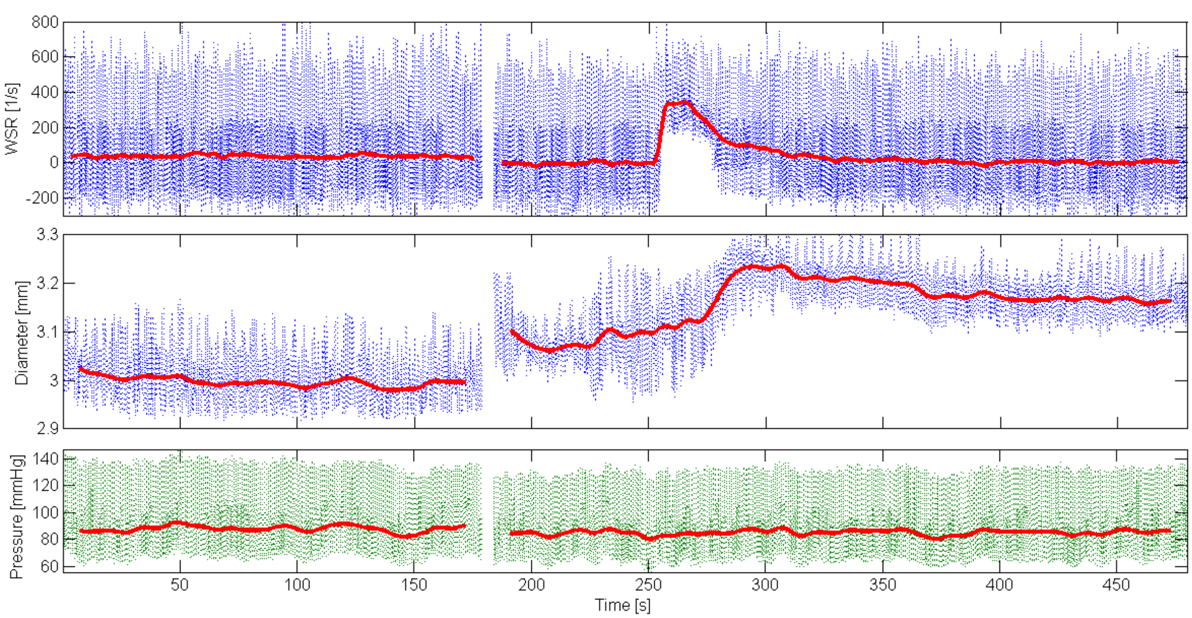

Fig. 4 A typical FMD elaboration result. The average WSR between near and far wall (top), the estimated diameter (middle) and the blood pressure (bottom). In each case the red line corresponds to the result of a low pass filter.