The Assessment of Flow-Mediated Dilation (FMD) of the Brachial Artery

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Abstract

Brachial artery flow-mediated dilation (FMD) is a measure of endothelial dysfunction which is used to evaluate cardiovascular risk. A stand-alone video processing system based on a DSP board was developed in our lab to assess the brachial artery FMD from ultrasound images. In this paper the system is introduced and compared with the main methods and devices illustrated in literature.

The available systems were analysed and catalogued according to their main features: input data, accuracy, real-time capability, and complexity.

Our system was tested both on synthetic ultrasound images and in in-vivo FMD examinations so that its performances could be compared with those of the other methods.

1. Introduction

Brachial artery flow-mediated dilation (FMD) is a parameter which is used to assess endothelial dysfunction in humans. This evaluation is thought to be particularly important in subjects at risk of arteriosclerosis or other cardiovascular diseases. The assessment of brachial artery FMD from ultrasound imaging was developed and widely used because of its non-invasiveness and feasibility.

The examination requires the patients to be supine, at rest, in a quiet air conditioned room. A longitudinal section of the brachial artery is analysed; it is essential that the probe is held in the same position during the scan and, consequently, in many studies a stereo-tactic clamp is used. After a baseline measurement, a cuff, which can be placed either above or below the transducer position, is inflated to suprasystolic pressure to produce ischemia in the forearm. The cuff is deflated after some minutes (usually 5) thus causing a reactive hyperemia which in turn produces a shear stress stimulus that induces the endothelium to release NO, a vasodilator. FMD, which reflects endothelium dependent vasodilation, is calculated as the percentage increase in diameter from baseline to the maximum value which is obtained after the cuff deflation.

In the past, arterial diameters were generally measured manually using electronic callipers. Nevertheless, a manual procedure as described from guidelines [1] presents some drawbacks as it is time consuming, operator dependent and has limited reproducibility. Therefore, automated and semi-automated systems were developed to overcome these problems and to improve the evaluation of FMD from ultrasound data.

In our lab a method for the automatic assessment of the endothelial function from B-mode images of the brachial artery was developed. The system works in real-time and is based on a fast and robust edge detector which is used to locate the two borders of the artery. It was tested on synthetic ultrasound images and in in-vivo FMD examinations. In order to analyse both the advantages and problems of our system, a direct comparison with the other systems illustrated in literature is indispensable. A brief description of other kinds of techniques for the evaluation of arterial endothelial function is also reported.

2. Methods for the assessment of the endothelial function

Besides the assessment of Flow-mediated dilation, there are other methods to evaluate the in-vivo endothelial function. In [2] five main methodologies are identified and described: Venous Occlusion Plethysmography (VOP), Brachial Artery Flow-mediated Dilation (FMD), Iontophoresis in conjunction with Laser Doppler Imaging (LDI), Pulse-wave Analysis and Retinal Arterial Abnormalities.

However, though at least five different methodologies are known to assess the endothelial function, Flow-mediated dilation was the most widely used over the past decade. Guidelines for FMD have been well established since 2002 and this allowed a certain uniformity in studies. Besides, by using this non-invasive procedure, the presence of altered endothelium-dependent vasodilation has been observed in the brachial artery of patients with cardiovascular risk factors such as smoking [3][4], hypercholesterolemia[5], hypertension[6][7], diabetes[9] and

Automatic system VS manual measurement	Correlation coefficient *(diameter)*	Correlation coefficient *(%FMD)*	Bland-Altman analysis (±2 SD of difference) *(diameter)*	Bland & Altman analysis (±2SD of difference) *(%FMD)*
Woodman	----	----	+/-0.2mm	+/-4.2%
Sonka	0.99	----	----	----
Frangi	----	----	----	+/-2%
Our lab	0.99	0.94	+/-0.105mm	+/-2.62%
Kuvin	----	0.55	----	----

Table 1.
Comparative view of papers which performed Bland-Altman plots or regression analysis to test agreement with manual measurements.

hyperhomocysteinemia[10].

3. Methods for the assessment of Flow-mediated dilation

The systems that we considered are those developed by:

- Fan et Al [11]
- Beaux et Al [12]
- Woodman et Al [13]
- Newey et Al [14]
- Sonka et Al [15]
- Frangi et Al [16]
- our lab [17]
- Hoeks et Al [18]
- Brands et Al [19]
- Hiltawsky et Al [20]
- Kuvin et Al [21]
- Maltz et Al [22]
- Sorenesen et Al [23]

In this work we analysed and catalogued them according to their main features, which are input data, accuracy, real-time capability, and complexity, so that a useful comparative view of them is possible.

4. Comparative analysis of the methods

Three main groups were determined according to the exploited input data:

i) B-mode images

The systems which evaluate the arterial diameter from ultrasound B-mode images are those developed by Fan et Al, Beaux et Al, Woodman et Al, Newey et Al , Sonka et Al, Frangi et Al, and our lab.

ii) RF-data

The systems which evaluate the arterial diameter from ultrasound rf-data are those developed by Hoeks et Al, Brands et Al., Hiltawsky et Al.

iii) other input data

The systems which evaluate the endothelial function from other kinds of signals (such as changes of the arterial pulse wave amplitude or of the transit times of artificially induced pulses after hyperemia) are those analysed by Kuvin et Al, Maltz et Al. In this group we have to also mention the study by Sorenesen et Al for the assessment of the brachial artery diameter with Cardiovascular Magnetic Resonance (CMR).

A comparison of the methods in terms of accuracy was particularly difficult due to the different methodologies used to validate the existing systems. For this reason, we decided to compare only those papers which used Bland-Altman plots [24] or regression analysis to evaluate the agreement of the proposed method with manual measurements. This comparison was further complicated by the fact that some studies report the analysis in diameter measurements, whereas others in %FMD values. Moreover, each study performed manual measurements with diverse precision and calculated the gold standard differently giving rise to likely repercussions on the results of the Bland Altman analysis.

However, the results shown in table 1 permit a global and important vision of the accuracy of the reported systems. Moreover, the full analysis we carried out with our system, which was performed on 120 images extracted from 20 in-vivo FMD examinations, allows its comparison with all the other methods. In regard to the results shown in table1, we have to point out that Kuvin et Al evaluated the ratio of the maximum arterial pulse wave amplitude relative to baseline and compared it with the corresponding FMD manual measurements. Moreover, Woodman et Al tested the agreement of diameter values assessed automatically and manually only on baseline measurements.

Some authors used regression analysis to evaluate the agreement of their methods with other gold standards. In Table 2 we briefly report these results. As regards these values, it has to be pointed out that Maltz et Al compared the maximum Pulse Transit Time versus the maximum diameter as a fraction of their respective baselines. Moreover, the diameter measurements obtained with Hoeks' system so as to compare it with Intravascular Ultrasound (IVUS) were not carried out on humans, and in the study of Cardiovascular Magnetic Resonance only baseline values were compared.

Automatic system	Gold standard	Correlation Coefficient *(diameter)*	Correlation Coefficient *(%FMD)*
Hoeks	IVUS	0.87	----
Maltz	Wall Track System	----	0.57
CMR	IVUS	0.87	0.87

Table 2. A comparative view of the papers which performed a regression analysis to test the agreement with a gold standard which is different from manual measurements.

In Table 3 the results obtained when detecting a small variation of diameter are shown; Hoeks et Al tested their system on a phantom (a moving target point) whereas the precision of our system was evaluated on a set of 100 synthetic images, which simulates five cardiac cycles, obtained using the software Field II [25].

	Precision
Our lab	8 μm
Hoeks	1 μm

Table 3. Precision of two systems

Real-time	**Post Processing**
Newey	Fan
Our lab	Beaux
Brands	Woodman
Hiltawsky	Sonka
	Frangi
	Hoeks

Table 4. Real-time capability of the systems

Another feature which differentiates the analysed techniques is the time needed to carry out the task; some papers presented real time implementations, while others adopted solutions based on data recording and post processing. We have summarised the real-time capability of the systems in Table 4.

5. Discussion and conclusions

In this work the problem of the automatic evaluation of the arterial diameter with the purpose of assessing its FMD from ultrasound images was considered. We listed the systems which are known in literature regarding this topic and we also mentioned other methodologies for the evaluation of the endothelial function.

From the comparative analysis of the existing methods the following conclusions can be drawn. Methods based on RF-data provide a higher spatial resolution. However, the precision of the systems based on B-mode image processing is also sufficient to correctly assess the FMD. Methods based on image processing do not require special ultrasound equipment since a standard video output signal is commonly accessible, whereas RF-data output is not always available. Real-time automatic systems, besides being fast, provide feedback which can be exploited to keep the probe in the correct position during the examination. Techniques based on other input data, such as Pulse Wave Amplitude and Pulse Transit Time are simple and permit easy measurements and training but their correlation with the gold standard does not seem to be very high. Cardiovascular Magnetic Resonance provides high quality images but, in comparison with ultrasound techniques, it shows a lower temporal resolution and it is limited by cost and equipment availability. Progress in this field and improvements in hardware, pulse sequences and image reconstruction algorithms seem to provide future prospects of real-time cardiac MRI [26].

The advantages of a real-time examination, the availability of visual information, and the possibility of using standard ultrasound equipment, make the use of real-time automatic systems, based on B-mode image processing, worthwhile despite a lower accuracy with respect to those based on RF-data and to those based on magnetic resonance imaging. Moreover, a simplification of the acquisition phase, with the use of an efficient clamp to sustain the probe, and the automation of the processing phase greatly reduce the complexity of the exam thus rendering it closer to the simplest techniques based on Pulse Wave Amplitude and Pulse Transit Time.

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