AN IN VIVO ASSESSMENT OF STENOTIC DISEASE USING THE INSTANTANEOUS MEAN VELOCITY CURVES GENERATED AT SITES NEAR THE VESSEL WALL

by

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ABSTRACT -- Early investigations carried out in vitro have shown that the instantaneous mean velocity curves can be very useful to detect flow disturbances generated by stenotic models as small as 15% lumen area reduction. It is described here the results obtained in vivo using a minimum velocity tracker system connected to a multigated pulsed Doppler imaging system. This investigation has demonstrated that such method allowed the detection of flow disturbances which are sometimes totally missed by the non-invasive methods used as a means of comparison.

INTRODUCTION

The incidence of Transient Ischemic Attacks (TIA), even in the developed world still lacks a major evaluation. TIA is characterized by an acute loss of a focal cerebral or ocular function with symptoms lasting less than 24 hours which after adequate investigation it is presumed to be due to embolic or thrombotic vascular disease (Warlow et al, 1982). One of the great harzards of this disease is the significant risk of a later stroke occurence (Goldner et al, 1971). Embolism from the heart or from an atheromatous lesion on the vessel wall is now believed to be the common cause of TIA (Harisson, 1983). Another hazard of this disease is that there appears to be no correlation between degree of stenosis and severity of attacks.

In recent years a considerable number of non-invasive procedures has been developed aimed specifically at the assessment of disease at the carotid system. Among all these non-invasive procedures those based on ultrasonic techniques are the most likely to detect the flow disturbance produced by minor stenosis. However, even these techniques lack accuracy, though not sensitivity, in locating very small degree of stenosis (≤ 30% area reduction).

There are already some in vivo studies (animal experiments) describing (Khalifa et al, 1978; Brown et al, 1982; Bendick at al, 1982) methods for the detection of flow disturbances caused by vessel area reductions as small as 20%. However, the techniques which are based on Doppler instruments (Brown et al and Bendick et al) use a procedure whereby the position of the stenosis is already known. Thus, the major difficulty which is fiding the site most likely to present the enhanced flow disturbance is considerably reduced. This is not the case of investigations performed in human vessels. On the other hand, these latter studies, in addition to the ones produced by Calil et al, 1982, Calil et al, 1984b and Calil et al, 1985, have proved that the ultrasonic Doppler instruments suffer not from lack of sensitivity in detecting the presence of minor flow disturbances but from improper positioning of the ultrasonic beam within the regions where these disturbances are most likely to be detected.

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Mathematical studies (Lee et al, 1979; Liou et al, 1981) have shown the possibility of predicting the flow behavior around constrictions under very low flow conditions. In addition, practical studies (D'Luna et al, 1982; Khalifa et al, 1981) reported the development of axial vorticity components which can be detected if a suficiently sensitive method is used.

From all the studies about flow disturbances, the following conclusions can be drawn:

a) regardless of the cause of the stenotic development, once an obstruction has developed in an artery the flow of blood will be disturbed (Deshpande et al, 1976);

b) the distance over which flow distubances are transmitted is proportional to the Reynolds number of the flow local to the stenosis and to the degrees of oclusion (Young et al, 1973a and 1973b);

c) for small degrees of vessel lumen reduction, the flow disturbance is more significant in regions which are close to the obstruction (Casanova et al, 1978) and close to the vessel wall (Young et al, 1973b; Calil et al, 1982, 1984a and 1984b).

The present study describes the results produced during in vivo experiments to verify the accuracy of a method designed to improve the detection of flow disturbances produced by minor stenosis (≤ 30% area reduction). This method is based on multigated pulsed Doppler imaging device (MAVIS-Picker Int.) which connected to a Minimum Velocity Tracker System (MVTS) is able to extract, in a continuous way, the Doppler signals produced as close as possible to the vessel wall.

INSTRUMENTATION

The description of the multigated pulsed Doppler device can be found in several reports (Fish 1975, Fish 1977, Calil et al 1982). Briefly, the system has an insonation frequency of 4.8 MHz at a pulse repetition rate of 4.8kHz. The reflected beam is divided into 30 adjacent gates of about 0.64 mm length. A probe position resolving system incorporated to an in built microcomputer offers the possibility of generating colour images of the blood haemodynamics on three different planes, i.e. anterior-posterior, lateral and cross-sectional plane. There are also several outputs which can supply extra information if further equipments (video system, flow direction indication system, audio output, etc) are connected. For this particular study we have made use of the output for a chart recorder which provides the instantaneous RMS velocity (by means of a in built zero crosser detector) from any one of the sampling gates, the Doppler signals (in quadrature) from all the 30 channels and the frequency to voltage converter output which is supplied for each one of the channels. The voltage level output from these converters is proportional to the blood velocity within the corresponding sampling gates.

THE TEST RIG AND THE MVTS

A detailed description of the test rig developed for the in vitro investigation as well as a Minimum Velocity Tracker System (MVTS) is done elsewhere (Calil et al, 1984b and Calil et al, 1985). In summary, it was designed and built a microcomputer system to keep a continous monitoring of the Doppler signals originating at sites located at the posterior or anterior vessel wall. The sampling gate located at either of these sites is automatically selected by the MVTS and the corresponding Doppler signal (in quadrature) is processed by a Phase Locked Loop system (Saïnz et al, 1976 and Sainz, 1977). The resulting directional instantaneous mean velocity is displayed in a graphic monitor

and a chart recorder. Figure 1 shows a schematic diagram of the connections between the pulsed Doppler system, the MVTS, the phase locked loop and the graphic display. The tape recorder and the PDP 11/40 microcomputer were used for a permanent storage of the Doppler signals (in quadrature) aiming at its processing to fast Fourier transform (Calil et al, 1984b).

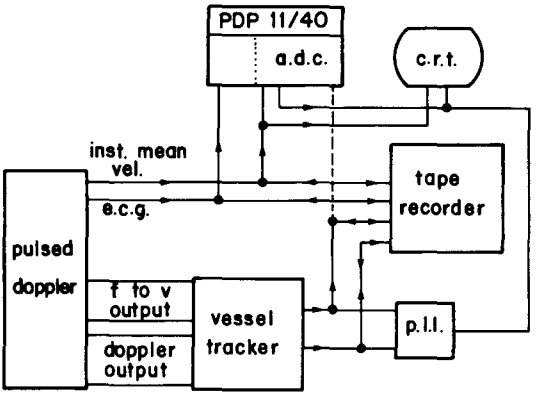

Figure 1. Schematic diagram of the connections between the pulse Doppler System and the MVTS.

The reason for developing the MVTS is that despite the great number of sampling gates (30 gates) it was very difficult to keep a continuous extraction of the Doppler signals, originating at the vessel wall using a manual selection of the gates. As the objective of this investigation was to isolate signals originating from fine layers of flow a single sampling gate had to be used. Biological movements such as patient breathing, handling of the probe by the operator and vessel pulsation have always the effect of moving the region under investigation out of the range of this single sampling gate. Thus the MVTS keeps a continuous search of the first or last sampling gate where the velocity of the flow layers is still detectable by means of the frequency to voltage converters, i.e. where the voltage level from the converter is above a set threshold point.

The results obtained during in vitro investigations as well as the assessment of the performance of the whole system are documented elsewhere (Calil et al, 1985). The conclusion taken from the in vitro studies using the instantaneous mean velocity (Calil et al, 1985) and the Fast Fourier Transform (Calil et al, 1984) processing methods have shown that if a careful investigation is performed, it is possible with a high degree of reliability to detect flow disturbances produced by constrictions which reduce the vessel lumen area by around 15% and above.

IN VIVO INVESTIGATIONS

Methods

As previously described, during a normal scanning procedure using the multigated Doppler system and the MVTS it was possible a constant monitoring of the Instantaneous Mean Velocity (IMV) produced by the phase locked loop. In

addition, for in vitro investigations it was displayed a second pulse wave signal generated by the in built zero crosser of the ultrasonic device. The corresponding waves produced by each one of the processing devices (Phase Locked Loop and zero crosser) were simultaneously displayed on the graphic monitor as shown in figure 2. Normally the pulse wave produced by the zero crosser was manually selected from a sampling gate located around the center stream.

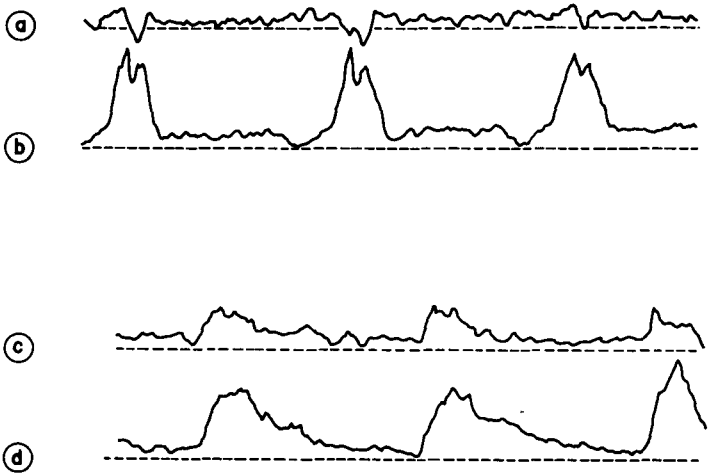

Figure 2. Instantaneous mean velocity curves obtained from: a) MVTS set to track posterior wall, b) centre stream using the zero crosser from MAVIS system, c) MVTS set to track velocities at sites at the anterior wall and d) same as b.

The fine resolution produced by the 30 gates makes possible the division of the anterior-posterior axis of a non-disturbed flow stream into several finite layers. Therefore, the pulse wave shape generated at each layer can be examined. We in common with others (van Merode et al, 1983) have found that in normal carotids the overall shape of the flow wave undergoes no abrupt changes as we move from gate to gate. Hence, if during a normal scanning procedure (in vivo) the waveshape generated by the MVTS becomes significantly different from the waveshape generated at the center stream, this is taken as an indication of flow disturbance at the vessel wall.

Having detected the flow disturbance, the next step in the clinical examination is to keep the probe at the suspected disturbed site and check if at the opposite wall the same distorted waveshape is being produced. Although the waveshape obtained from either wall would not be expected to be identical they would be expected to be substantially similar (except of course, close to the carotid bifurcation - Phillips et al, 1983). Subsequently, near sites up or downstream can also be examined to see wether the same effect is being produced. It is important to mention that during in vivo investigations we had no previous knowledge about the location of the constriction (if any). The technique thus, requires a constant observation of the instantaneous mean velocities (IMVs) displayed on the monitor. If during an imaging procedure any abnormality is observed on the pattern of the IMVs the operator returns the probe to the site where flow disturbances were observed, and a simultaneous recording of both IMVs (zero crosser and MVTS) is performed.

Experimental results (in vivo)

A number of 12 patients had been investigated using the MVTS in conjunction with the routine vascular assessment. It is important to point out that all the patients referred to the vascular laboratory had already presented some history of cerebral ischaemic attack.

For the assessment of the extracranial arteries the same standard vascular laboratory examination procedures described by Basket et al (1977) were used. These methods are the Temporal Artery Occlusion Test (Brockenbrough, 1970), the assessment of blood flow direction in the supra orbital artery (Muller et al, 1972), and the recording of the sonogram from the carotid system with subsequent calculation of the A/B ratio index (Basket et al, 1977). Two further procedures were also adopted: the carotid bruit auscultation and the multigated Doppler imaging of the carotid system.

In this study the intention was basically to qualify rather than quantify the flow disturbance generated by minor stenosis. However, on table 1 it is also indicated the mean values of the A/B ratios which were derived from at least 12 pulses. As a reminder, according to Basket et al (1977), the A/B index which are equal or smaller than 1.05 may be a significant indication of a severe carotid occlusion. On table 1 the incidence of carotid disease using each one of the methods is indicated by number 1 while the failure to detect the disease is indicated by zero.

Patient number	Bruit	Supra Orbital	Sonogram	MAVIS Imaging	MVTS	FFT	A/B Ratio	Fig. no.
1	1	0	0	1	1	1	1.04	9.7.3
2	0	0	0	0	0	0	1.11	9.7.5
3	0	0	0	0	0	0	1.32	F1
4	1	1	1	1	1	1	0.95	F2
5	0	0	1	1	1	-	0.87	
6	0	0	1	0	0	1	1.02	F3
7	1	1	1	1	1	1	0.91	F4
8	0	0	1	1	1	0	1.51	F5
9	0	0	1	1	1	1	0.78	9.7.4
10	0	0	1	1	1	-	1.15	
11	0	0	0	1	1	1	1.09	9.7.2
12	0	0	0	0	1	-	1.42	9.7.1
2a	0	0	0	0	0	-	-	
12a	0	0	0	0	1	-	-	
N1	0	0	0	0	0	-	-	F6
N2	0	0	0	0	0	-	-	F7
N3	0	0	0	0	0	-	-	F8

Table 1. Comparison of the results obtained during the application of 5 different noninvasive methods for assessment of flow disturbances.

From the 12 patients shown by table 1 a group of three patients presented carotid bruits and among this group only two patients had supra orbital flow abnormality. These flow disturbances were also detected by the other procedures indicating severe disease. Among a group of 9 patients suggesting flow disturbances using MVTS, eight of them were confirmed by the multigated system

and seven by the sonogram.

In case of patient number 12, only the MVTS was able to detect the flow disturbance where the reversing effect on the IMVs (due to flow disturbance), which was displayed during the carotid ultrasonic scanning, could be clearly seen despite the non registration of the disturbance on the image of the ultrasonic device. Figure 2 shows the IMVs obtained from patient number 12. The top curve was recorded with the MVTS set to track the sites at the posterior wall while the third IMV curve (counting from top to bottom) was recorded from the MVTS set to track sites at the anterior wall within the same cross sectional plane. The second and fourth IMV traces are from the centre stream using the zero crosser from the ultrasonic device. What is shown in this figure is exactly what the operator is able to see on the monitor screen during a scanning procedure. Two of the patients (2 and 12) were recalled 3 months later (indicated by 2a and 12a). In case of the latter patient the same failure to detect the flow disturbance by the other noninvasive methods was observed. As a means of comparison, three suposedly normal subjects (age 18 to 30) where examined and the normal results are indicated by table 1 and figure 4.

One of the patients (11) who did not have a possible sonogram (indication of flow disturbance) was only positively selected by the multigated system (imaging of the carotid system) after a previous indication by the MVTS of an abnormal IMV pattern within a very small region at the internal carotid, as shown in figure 3.

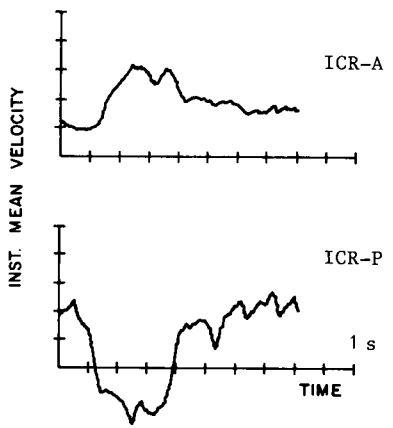

Figure 3. Instantaneous mean velocities (IMVs), using the MVTS, obtained at a region suggesting flow disturbance at the internal carotid right side posterior wall.

The tracking system, in this case, was programmed to sample the signals near the anterior and posterior wall. The results demonstrate a very distorted IMV from signals obtained within the internal carotid right side and posterior wall (ICR-P). During the sistolic-diastolic period there is a significant occurence of reverse flow indicated by the curve which is below the x-axis. As also shown by figure 3, there is no occurence of reverse flow (indication of a normal condition for the carotid system) at the opposite side - internal carotid right, anterior wall (ICR-A) - within the same cross sectional plane.

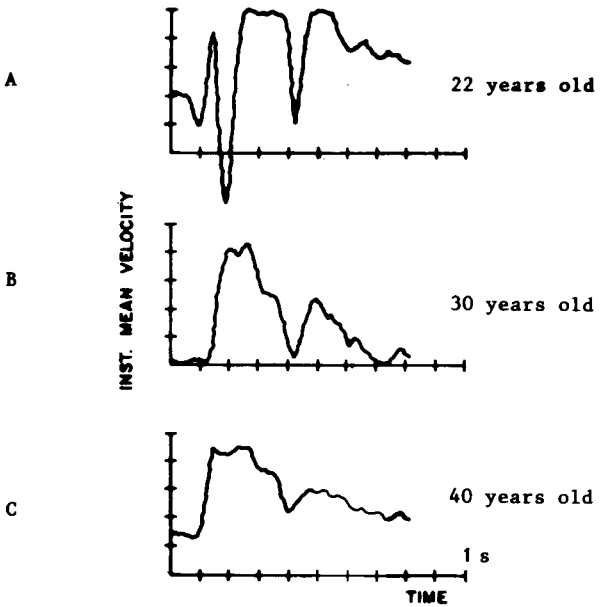

Figure 4. (A) Site CCL-A (Common Carotid Left-Anterior Wall)
(B) Site CCL-P (Common Carotid Left-Posterior Wall)
(C) Site CCL-A (Common Carotid Left-Anterior Wall)

DISCUSSION

Due to lack of space it is not possible to show all the results obtained during the in vivo investigations. However, the IMVs from all the patients listed on table 1 with a positive indication of the presence of flow disturbance by the MVTS presented the same characteristic reversing effect during the systolic-diastolic period.

Investigations reported previously using pulsed Doppler systems in carotid arteries in healthy and young patients (Phillips et al, 1983), presented sonograms which can be interpreted as being characteristic of flow disturbance. During the acceleration phase of the systolic-diastolic interval, a short period of reverse flow was presented. This observation could be due to the highly elastic properties of the arterial wall system of young people. Investigations carried out using the MVTS in a young subject (22 years old) have also shown some differing IMV patterns along, the carotid arteries, from the ones obtained in older non-symptomatic patients (30 and 40 years old). While the younger subject presented an IMV with a short incidence (about 40 ms) of reverse flow with a fast return to forward flow (figure 4 A) in older individuals (figures 4 B and 4 C) did not indicate such a distortion. On the contrary, a high degree of similarity has been shown along the arterial system at both opposite vessel wall. Further studies however, will be necessary to assess the waveforms from young subjects, despite the improbability of any symptomatic disease at such age.

Although it may be possible the correlation of the shape of the IMV curve

obtained in vitro with the degree of area reduction such method can be very unreliable if transferred to the in vivo situation. In the latter case variables such as distance from the stenosis when the samples were taken, the vessel impedance, the geometry of the stenosis and the variability of the cardiac pulses may become strong factors contributing towards the inaccuracy of the results. Furthermore, the properties of blood differ from the blood analogue used during our in vitro studies. However, despite these reservations, the in vivo application of the MVTS has demonstrated that similar effects are seen as those observed in our model studies though their exact quantification has yet to be investigated in more depth.

Unfortunately, at present, it was not possible to quantify the accuracy (sensitivity/specificity - Sumner, 1981) of the MVTS in terms of angiographic results since they are considered the "gold standard technique". Such a comparison was not possible since the investigations were searching for disturbances caused by small stenosis and therefore such symptomatic patients ethically should not and would not be recommended for an invasive and risky investigation such arteriography.

However, the results obtained in both types of investigation, in vitro and in vivo, lead to optimistic speculation that the velocity waveformas from sites near and at the vessel wall may provide valuable clues leading towards the early detection of arterial disease.

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DETERMINAÇÃO IN VIVO DE DOENÇA ESTENÓTICA UTILIZANDO AS CURVAS DA VELOCIDADE MÉDIA INSTANTÂNEA GERADAS EM REGIÕES PRÓXIMAS DA PAREDE DA ARTÉRIA

RESUMO-- Investigações efetuadas anteriormente "in vitro" demonstraram que o registro da velocidade média instantânea do fluxo sangüíneo arterial, obtida por meio de instrumentação ultrasônica "Doppler", podem ser indicadores bastante úteis na detecção de perturbações de fluxo geradas através de modelos de estenoses. Os modelos testados foram desenhados para reduzir o lúmen arterial de até 15%. São descritos aqui os resultados obtidos "in vivo",usando-se um sistema rastreador de velocidades mínimas, o qual é conectado a um instrumento ultrasônico Doppler pulsátil de múltiplos canais.Esta investigação demonstrou que este sistema permite a detecção de perturbações do fluxo sangüíneo, as quais não são percebidas por outros métodos não invasivos usados como comparação.