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NON-INVASIVE ESTIMATION OF WALL SHEAR RATE IN HUMANS BY MEANS OF ULTRASOUND

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1. Introduction

In both arteries and arterioles the wall is not only subjected to pressure, acting perpendicular to the vessel wall, but also to stress tangential to the surface of the wall in the direction of flow. This shear stress, being shear rate times the local viscosity where shear rate is defined as the velocity gradient relative to the vessel radius (dv/dr), strongly influences function and structure of the endothelial cells lining the artery wall. Shear rate or shear stress makes the endothelial cells to align with flow (NEREM [8]), induces the production of, for example, endothelium-derived relaxing factor (EDRF) (RUBANYI *et al.* [11]), being nitrous oxide, and prostacyclin (FRANGOS *et al.* [3]), and activates K^+ channels (OLESEN *et al.* [9]). Most of the information about the effect of shear rate or stress on endothelial cell function has been obtained in *in vitro* studies, hampering conclusions regarding the role of shear rate or stress in vascular disorders as atherosclerosis. To obtain insights into this role of shear rate or stress, one needs to have at one's disposal a method to assess wall shear rate *in vivo*. To assess wall shear rate reliably one must be able to determine the low blood flow velocities close to the wall accurately. Accurate determination of the low, near wall velocities is hampered by contamination due to the high power signals reflected by the slowly moving artery walls. Suppression of these artery wall reflections is generally achieved by static high-pass filtering, ignoring the time-dependent aspect of these reflections. This type of filtering also eliminates the scattering as induced by the blood cells flowing at low velocity near the vessel wall.

In the present study we introduce adaptive vessel wall filtering to suppress artery wall signals while maintaining most of the flow velocity information near the artery wall, allowing the estimation of shear rate relatively close to this wall.

2. Principle of adaptive filtering

To determine the blood flow velocity distribution in a blood vessel the velocities along the ultrasound beam are generally assessed at discrete time-intervals in subsequent sample volumes as in multi-gate pulsed Doppler systems (Hoeks *et al.* [7], Reneman *et al.* [10]). In these systems the sample volumes are fixed in size and place. Therefore, tracking of the artery wall during its displacement in the cardiac cycle is not possible, resulting, among others, in contamination of the low velocity scattering signals near the wall by the low frequency high power reflections from the artery wall. Separation of these reflections and the scattering is difficult to achieve with static high-pass filtering, generally used in these systems, but can largely be attained with adaptive vessel wall filtering.

To be able to apply adaptive vessel wall filtering, taking into account the time-dependent aspects of artery wall reflections, the system must be able to track the artery wall. To this end the velocities along the ultrasound beam are determined more or less continuously, basically using overlapping sample volumes. The difference between regular and adaptive blood flow velocity estimation along the ultrasound beam is depicted schematically in Fig. 1. In adaptive vessel wall filtering the power of

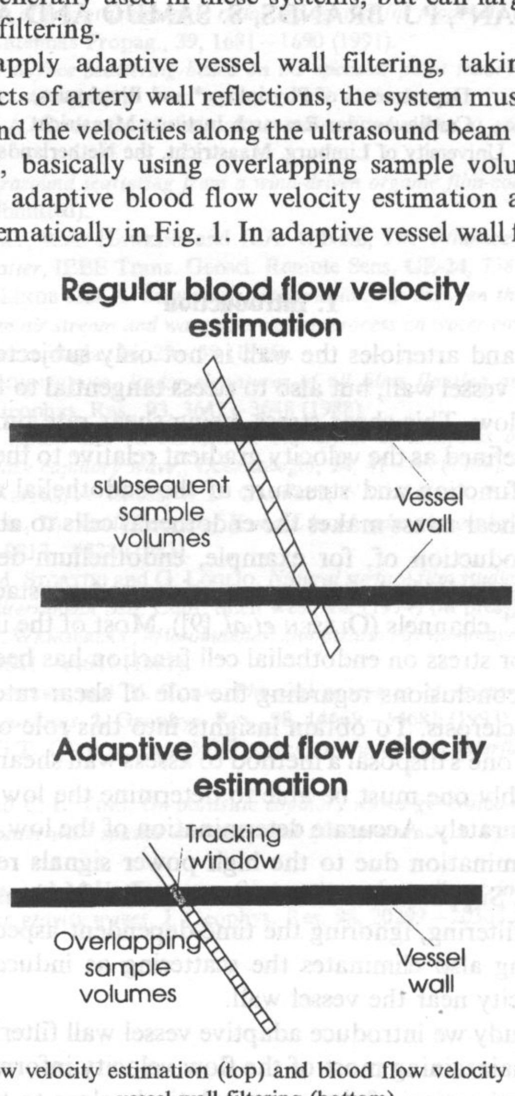

Fig. 1. Regular blood flow velocity estimation (top) and blood flow velocity estimation using adaptive vessel wall filtering (bottom).

the reflections induced by the artery wall is suppressed by shifting the temporal frequency distribution of the reflections to zero frequency, the shift being given by the estimated mean frequency of the reflected signals. Subsequently high-pass filtering with a low cut-off frequency is used to suppress the reflections centered around zero frequency; the bandpass filter apparently adapts its central frequency to the mean frequency of the slowly moving artery wall. The principle of adaptive vessel wall filtering is depicted schematically in Fig. 2. After adaptive filtering the RF signal, containing reflections, scattering and noise, is converted to a signal consisting of scattering and noise alone.

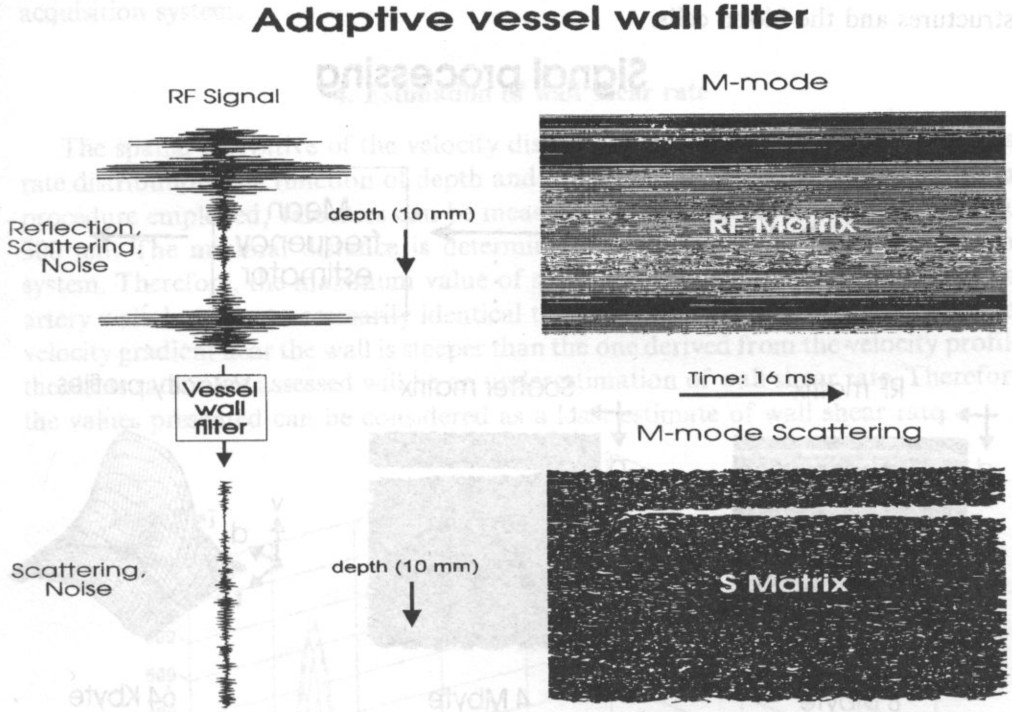

Fig. 2. Principle of adaptive vessel wall filtering.

In adaptive vessel wall filtering the cut-off frequency is fixed but can be set at a rather low value, because the centre frequency of the vessel wall signal is shifted downward to zero and the bandwidth of the vessel wall signal is marginal (all parts of the structure move at the same instantaneous speed). The main restriction for the cut-off frequency is the length of the time-window considered. A low cut-off frequency of, for example, a second order high-pass filter has the advantage that effective suppression of at least 36 dB is reached within a short frequency range. The same type of filter used in a conventional approach, where the cut-off frequency is related to the anticipated highest Doppler frequency of the wall, would require a substantially larger transition zone, resulting in a cut-off frequency 3 octaves higher than the maximum frequency.

The mean velocity at each site in the artery is assessed off-line by means of an RF-domain velocity estimator (HOEKS *et al.* [4, 5]; DE JONG *et al.* [2]), providing velocity profiles (Fig. 3). The details of adaptive vessel wall filtering and mean velocity estimation have been described elsewhere (BRANDS *et al.* [1]). Off-line processing of the acquired RF-signals has the advantage that all the data can be retained on tape, remaining them available to test and implement new algorithms for signal processing; for example, to estimate artery wall displacement and shear rate. Moreover, the processing procedure requires sequential analysis of the velocity of the structures and the blood cells.

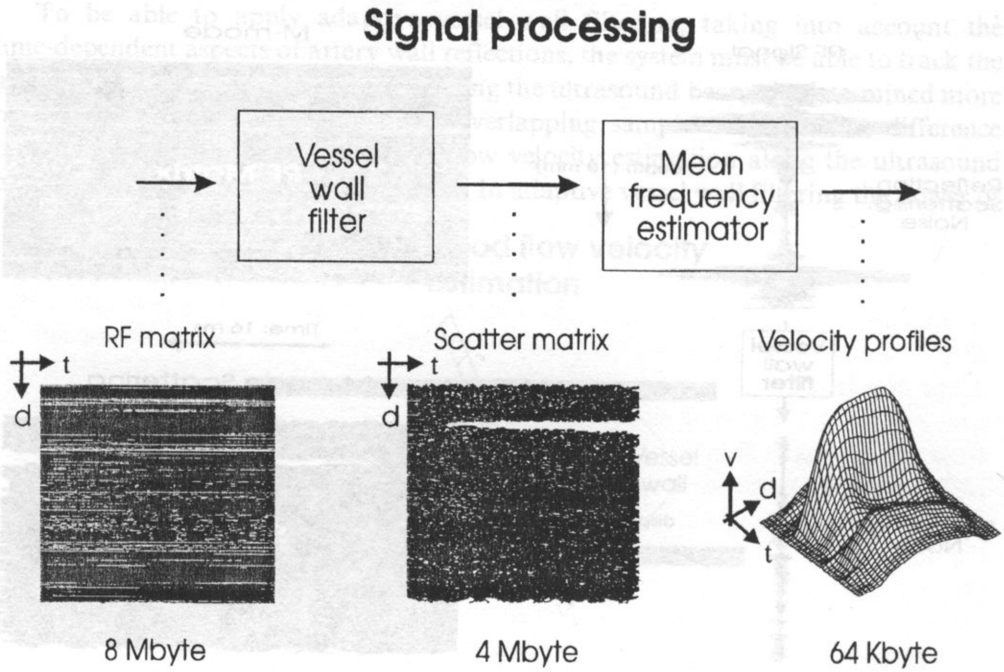

Fig. 3. Schematic representation of signal processing in the ultrasound system.

3. Measurement system

The measurements are basically performed with the M-mode of an echo system (ATL-Mark V), with an emission frequency of 5 or 7.5 MHz, connected to a data acquisition and a computer system. The acquisition system samples and stores the RF-signals in real-time. It has a sample frequency (synchronously with the emission trigger of the attached echo system) with a maximum of 50 MHz, an acquisition memory of 4 Mword (1 word is 10 bit) and a dynamic range of 60 dB (10 bit). Data acquisition is enabled by a footswitch and starts synchronously with a trigger derived from the R-wave of an ECG-signal. The acquisition of each RF-signal received starts after a selected delay with respect to the emission trigger, allowing free selection of the range of interest. The echo system is connected to the acquisition system by three signals: 1) the RF-signal after amplification and bandpass filtering according to the quality factor of the ultrasound transducer used; 2) a trigger to indicate the moment of ultrasound transmission; 3) a sample clock synchronous with the emission trigger and with a frequency of at least four times the emission frequency ($f_s = 20$ MHz). The latter is necessary to retain the phase information in the sampled RF-signals. If the echo system does not provide the required clock signal, it can be regenerated by the acquisition system.

4. Estimation of wall shear rate

The spatial derivative of the velocity distribution in an artery provides the shear rate distribution as a function of depth and time (Fig. 4). With the adaptive filtering procedure employed, velocities can be measured as close to the artery wall as about 300 μm. The minimal distance is determined by the axial resolution of the echo system. Therefore, the maximum value of shear rate can be determined close to the artery wall, but is not necessarily identical to wall shear rate. For example, when the velocity gradient near the wall is steeper than the one derived from the velocity profile, the shear rate value assessed will be an underestimation of wall shear rate. Therefore, the values presented can be considered as a least estimate of wall shear rate.

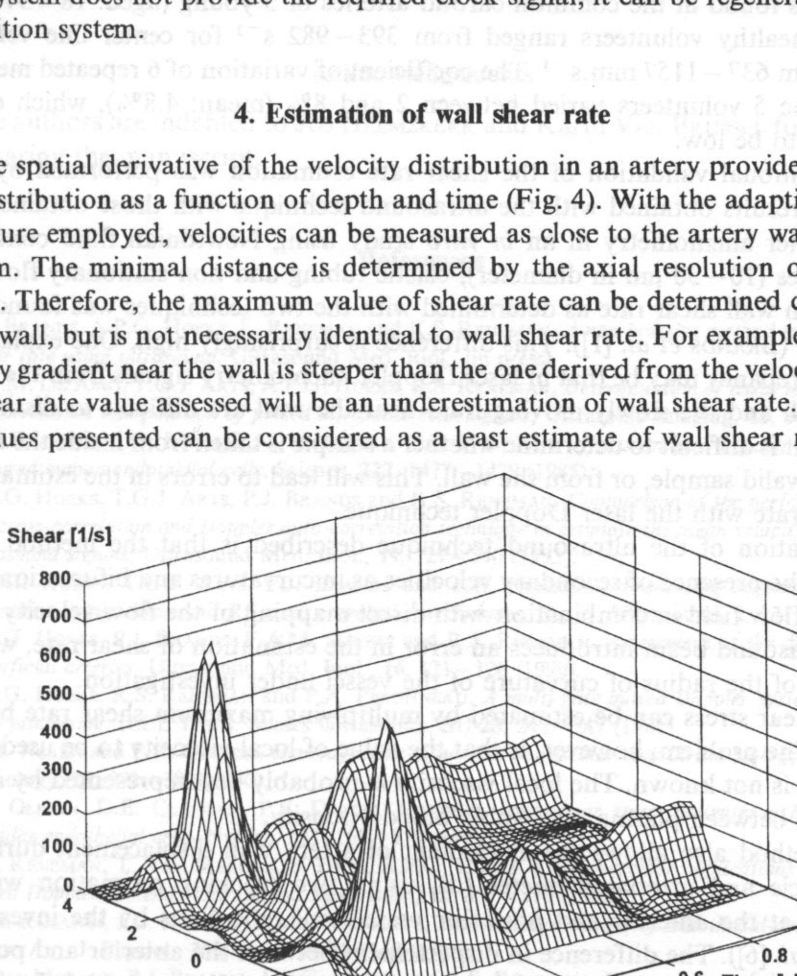

Fig. 4. The time dependent shear rate distribution as derived from the time dependent velocity distribution in the common carotid artery of a young presumed healthy volunteer.

The blood flow velocity in a blood vessel is a vector with an axial, a lateral (radial) and an azimuth component, the estimated velocity being a projection of the vectorial components on the ultrasound beam. The azimuth component may be ignored when the line of observation passes through the axis of the vessel, which is generally aimed at. The lateral component will act oppositely on the anterior and posterior sides of the lumen. Therefore, to estimate wall shear rate resulting from only the axial blood flow velocity component, shear rates at the anterior and posterior vessel walls have to be averaged.

The maximum shear rate values — the average of the anterior and posterior wall values — as found in the common carotid arteries of 5 young (aged: 18–34 years) presumed healthy volunteers ranged from 393–982 s^{-1} for center line velocities ranging from 637–1157 $mm.s^{-1}$. The coefficient of variation of 6 repeated measurements in the 5 volunteers varied between 2 and 8% (mean: 4.8%), which can be considered to be low.

An additional validation of the shear rate estimation was performed by comparing the results obtained with the ultrasound technique with those obtained with laser Doppler anemometry in an *in vitro* study using Newtonian fluid containing microspheres (10–30 μm in diameter), elastic tubing and non-stationary flow. The difference in wall shear rate as determined with the two techniques was found to be about 11% (BRANDS *et al.* [1]). This difference is surprisingly high. One explanation for the discrepancy may be that in laser Doppler anemometry signals from the slowly moving wall and the slowly moving fluid near the wall are difficult to distinguish. Therefore, it is difficult to determine whether a sample is taken from inside the tubing, and thus a valid sample, or from the wall. This will lead to errors in the estimation of wall shear rate with the laser Doppler technique.

A limitation of the ultrasound technique described is that the method is less reliable in the presence of secondary velocities as in curvatures and bifurcations. This secondary flow field in combination with direct mapping of the flow velocity vector on the ultrasound beam introduces an error in the estimation of shear rate, which is a function of the radius of curvature of the vessel under investigation.

Wall shear stress can be estimated by multiplying maximum shear rate by local viscosity. The problem, however, is that the value of local viscosity to be used in this calculation is not known. The local viscosity is probably best represented by a value somewhere between plasma and whole blood viscosity.

The method also allows the assessment of artery wall displacement during the cardiac cycle and arterial diameter (d), using two tracking estimation windows positioned at the anterior and posterior vessel wall reflections by the investigator (HOEKS *et al.* [6]). The difference in displacement between the anterior and posterior wall provides the change in arterial diameter during the cardiac cycle (Δd). In this way information can be obtained about artery wall distension (Δd) along artery bifurcations (e.g. VAN MERODE *et al.* [12]) and the strain ($\Delta d/d$) the wall is exposed to. Moreover, insight can be obtained into the relation between distension, blood flow velocity and wall shear rate, if any.

5. Conclusions

By means of adaptive vessel wall filtering velocities in arteries can be measured as close to the wall as about 300 μm, allowing the estimation of wall shear rate. The shear rate values, being the maximum value obtained, can be determined reliably in humans (coefficient of variation of 6 measurements in 5 volunteers varies from 2–8%), but is an underestimation of wall shear rate when the velocity gradient near the wall is steeper than the one derived from the velocity profile. The method described is less accurate in the presence of secondary velocities, limiting its use in arterial bifurcations.

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