The Effects of Hematocrit, Shear Rate, and Turbulence on Ultrasonic Doppler Spectrum from Blood

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Abstract—**Previous studies of ultrasonic scattering properties of blood using a pulse-echo experimental arrangement show that ultrasonic backscatter from blood is influenced by a number of factors including hematocrit, shear rate, and the nature of flow (*J. Acoust. Soc. Amer.*, vol. 75, p. 1265, 1984 and *J. Acoust. Soc. Amer.*, vol. 84, p. 1, 1988). Since the Doppler frequency spectrum from a Doppler flowmeter is derived from echoes backscattered by red blood cells in the flowing blood, it is also undoubtedly a function of these parameters. The effects of these parameters on Doppler spectrum from blood have been investigated using a pulsed Doppler flowmeter. The results agree well with those obtained in previous studies. One important conclusion of this study is that the assumption that the Doppler spectral power density at a frequency in Doppler spectrum is linearly proportional to the number of red cells flowing at that velocity used in many theoretical models developed to explain the Doppler phenomenon may be erroneous. An alternative is proposed. It is shown that conclusions derived from these theoretical models would remain valid by making this assumption.**

Introduction

DOPPLER ultrasound is used increasingly in medicine for measuring blood flow and diagnosing a number of cardiac and blood vessel diseases because it is noninvasive and can penetrate body tissues [1]–[4]. The most advanced ultrasonic scanners superimpose on a conventional *B*-mode gray-scale image a Doppler flow image in color indicating both the velocity of blood flow and the direction of the flow. They hold great promises in improving the diagnosis of heart disorders like tiny septal shunt, tumors and venous thrombosis [5]–[7]. Despite the proliferation of clinical applications of Doppler ultrasound, the effects of a few fundamental parameters on the Doppler signals obtained by Doppler devices are still poorly understood. One prominent example is an assumption that has been made in several theoretical treatments [1], [8]–[10], i.e. the power density or power contained in the frequency range from ω to $\omega + d\omega$ in Doppler spectrum is assumed to be proportional to the number of red blood cells, $n(v)$, traveling in the velocity range from v to $v + dv$, or

$$P(\omega)\, d\omega = \sigma_b n(v)\, dv \tag{1}$$

where σ_b is the backscattering cross-section of a red blood cell, based upon a single scattering model.

From this assumption, the mean Doppler frequency can be related to the mean velocity. In (1) ω and v are related by the Doppler equation

$$\omega = \frac{2\omega_0}{c} v \cos\theta \tag{2}$$

where ω_0 is the ultrasound frequency and θ is the angle between the Doppler beam and the direction of blood flow. The mean velocity is by definition

$$v_m = \frac{\int_0^\infty n(v) \cdot v\, dv}{\int_0^\infty n(v)\, dv}. \tag{3}$$

Substituting (1) and (2) into (3) the mean velocity can be rewritten as

$$v_m = \frac{c}{2\omega_0 \cos\theta} \cdot \frac{\int_0^\infty P(\omega) \cdot \omega\, d\omega}{\int_0^\infty P(\omega)\, d\omega}. \tag{4}$$

Since the mean frequency is defined as

$$\omega_m = \frac{\int_0^\infty P(\omega) \cdot \omega\, d\omega}{\int_0^\infty P(\omega)\, d\omega} \tag{5}$$

solving for ω_m gives the familiar Doppler equation

$$\omega_m = \frac{2\omega_0}{c} v_m \cos\theta. \tag{6}$$

Although it is quite obvious from this development that the assumption as stated by (1) is the physical basis of Doppler flowmetry, it validity has never been carefully examined. In fact, experimental results from several stud-

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ies [11]–[15] seem to suggest that this assumption based upon a single scattering model is flawed. Borders *et al.* [11] using a pulsed Doppler flowmeter showed that the Doppler power from red cells suspended in saline in frequency range from 5 to 27 MHz was linearly related to hematocrit up to 2% and decreased as the hematocrit was increased to beyond 10%. Furthermore, measurements on ultrasonic scattering from blood using a pulse-echo experimental arrangement performed in our laboratory [12]–[15] indicated that ultrasonic backscattering coefficient, defined as power scattered in the backward direction per unit incident intensity per steradian by a unit volume of scatterers, from red cell saline suspension or whole blood when red cell aggregation was prevented, increased almost linearly with hematocrit when hematocrit was low and reached a peak at approximately 13%, as predicted by theories [16]–[19]. In an attempt to verify these results using a Doppler device and to examine the validity of (1), the relationships between Doppler signal and hematocrit have recently been investigated with a mock flow loop.

In an earlier study [13], it was also observed that turbulent flow caused the scattering to increase. Later it was confirmed that the received Doppler power increased when turbulence was induced [20]. Recent studies on whole blood [14], [15] which differs from erythrocyte suspensions in saline in that red cells aggregate in whole blood if there are no external forces to disrupt it, demonstrate that ultrasonic backscatter from whole blood was shear-rate dependent. As the shear rate was increased or erythrocyte aggregation is inhibited, ultrasonic backscatter from whole blood decreased. However, due to limitations imposed by the capacity of the pump the maximal shear rate achievable was 22 s^{-1}, much lower than that observed in blood vessels [21]. These observations have also recently been verified with a pulsed Doppler flowmeter. Since Doppler measurements allowed the utilization of smaller tubing, it was possible to determine the relationship between Doppler spectrum from blood and shear rate to shear rates as high as 600 s^{-1}.

In this paper, these results will be reported along with a discussion of their significance. A modification of the assumption stated by (1) is proposed. It is shown that this modified assumption is theoretically more thorough and will not result in any changes in the fundamental concepts associated with Doppler flowmetry.

Materials and Methods

Materials

Fresh bovine and porcine blood collected from local slaughter-houses was used in this research. A solution of 1 g of EDTA per 10 mL of saline was added to whole blood at a concentration of 30 mL per liter of blood to prevent coagulation. The blood was passed through a fine sieve to filter out impurities. The concentrated erythrocytes were obtained by centrifuging the whole blood and removing the plasma and the top white layer. Whole blood of different hematocrits was obtained by reconstituting the concentrated erythrocytes with the separated plasma. The erythrocyte saline suspensions were prepared by washing the blood at least twice with 0.9% normal saline buffered to pH 7.4. The washed erythrocytes were then reconstituted with the buffered saline to the desired hematocrits. Blood samples were discarded whenever coagulation was observed.

Experimental Arrangement

The experimental arrangement used for this study is illustrated in Fig. 1. A nonfocused 10 MHz ultrasonic transducer of 0.3 cm diameter was used to transmit and receive signals. The pulsed Doppler flowmeter developed by Hartley [22] employed a carrier frequency of 10 MHz which was transmitted in four cycle bursts of 0.4 μs duration. A pulse of 0.3 μs duration was used to gate the returned echoes. The pulse repetition frequency (PRF) was 20 kHz. The transducer detected the reflected echoes from blood which were then quadrature-phase demodulated. The output from the flowmeter was an audible signal containing the Doppler shift information. This signal was amplified and high-pass filtered with the cutoff frequency at 100 Hz. Data was digitized by a Hewlett-Packard 54501A digitizing scope to 8 bits. An IEEE-488 interface board (Metrabyte model MBC-488), plugged directly into an expansion slot of a Compaq 386 personal computer, was used for data acquisition. Further processing of the Doppler signal was sometimes needed if the signal was weak or noisy. It was achieved by incorporating an audio amplifier and a bandpass filter between the Doppler flowmeter and the digitizer.

A square-wave electromagnetic flowmeter (Carolina Medical Electronics Inc., model 501) was employed along with a blood flow probe (In Vivo Metric, model K) to monitor the instantaneous flow rate within the vessel. The electrical signal representing the flow was low-pass filtered at 30 Hz and set at the 10 L per minute range. The flowmeter was calibrated by collecting a measured volume of blood over a known period of time. The corresponding voltage signal from the flowmeter was read off an oscilloscope. Several measurements at different flow rates were taken to ensure linear performance throughout the desired range of flow rates.

The flow conduit was a long cylindrical Tygon tube with an outer diameter of 0.635 cm, an inner diameter of 0.476 cm, and a length of 70 cm. The flow conduit was immersed horizontally in a tank filled with degassed water to facilitate the transmission of the ultrasound wave. The transducer was mounted so the ultrasonic beam propagation made a 60° angle with the flow conduit. Measurements were made via an acoustic window, which was located 65 cm downstream from the entrance of the conduit, to enhance the transmission and detection of ultrasonic signals. The blood flow was gravity driven by maintaining the blood level of a reservoir connected to the entrance of the conduit higher than that of a reservoir connected to the exit of the conduit. A calibrated roller pump

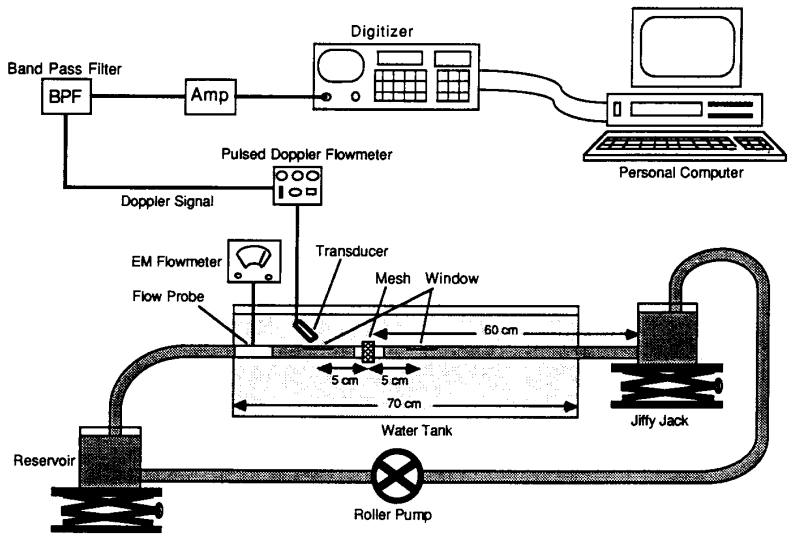

Fig. 1. Experimental block diagram.

with variable speed recirculated the blood from the exit reservoir to the entrance reservoir thereby preserving the height difference between the blood levels. With this arrangement the flow rate was proportional to the height difference of the blood levels of the reservoirs and the speed of the roller pump. Therefore it could be determined directly from the speed of the roller pump when the flow system was at steady state. Blood coming from the roller pump flowed directly into a reservoir placed at the entrance of the tube. Since the outlet of the entrance reservoir was situated near the bottom and air bubbles would tend to rise to the top because of their buoyancy, the likelihood that these air bubbles were introduced into the flow conduit was substantially reduced. The flow pulsations of the roller pump were thus eliminated and a steady flow was achieved and could be controlled by varying the height difference between the blood levels of the reservoirs.

For measurements on blood under laminar flow, the mesh screen upstream from the acoustic window, needed to generate turbulent flow, was removed.

In order to maintain laminar flow with a mean flow velocity v_m in a tube of inner radius R_i with a fluid dynamic viscosity μ and density ρ, the Reynolds number [23]

$$Re = \frac{2v_m R_i \rho}{\mu} \tag{7}$$

must be less than the critical value of about 2000. Assuming that blood behaves as a Newtonian fluid, theoretical studies [24], [25] have shown that for a flow arrangement such as that used in this study, the tube entrance must be sufficiently far away to insure that a fully developed parabolic profile (Poiseuille flow) is present at the location of insonation. The usual criteria used is that the entrance length

$$L_e > 2n' R_i Re \tag{8}$$

where n' is a constant and varies from 0.029 to 0.058. The maximum mean velocity that could be attained from this arrangement is approximately 60 cm/s. Assuming that $v_m = 60$ cm/s, $R_i = 0.238$ cm, a dynamic viscosity for whole blood of 3 to 5 cP, and a density of human blood of 1.093 gm/cm^3, the maximum value for the Reynold's number is approximately 1040 which is below the critical value of 2000. Substituting this value and $n' = 0.058$ in (8) the tube entrance length should be greater than 30 cm. Since the distance between the entrance of the conduit and the acoustic window was approximately 65 cm, it is safe to assume that a fully developed laminar flow was present at the location of insonation. The transverse velocity profile near the acoustic window was measured by the Doppler flowmeter. It was found to be approximately parabolic suggesting laminar flow.

In a fully developed laminar flow the velocity profile $v(r_i)$ is parabolic as given by

$$v(r_i) = \frac{P_G}{4\mu}(R_i^2 - r_i^2) \tag{9}$$

where P_G is the pressure gradient. The shear rate (S) increases from 0 at the center axis of the vessel to a maximum at the wall according to

$$S = \frac{P_G r_i}{2\mu}. \tag{10}$$

The mean shear rate across the conduit is given by [21], [23]

$$S_m = \frac{\int_0^{R_i} S 2\pi r_i \, dr_i}{\pi R_i^2} = \frac{8v_m}{3R_i}. \tag{11}$$

Since the mean shear rate is proportional to the average flow velocity, different mean shear rates could be obtained by adjusting the flow rate to the appropriate values.

To produce a well-defined turbulent flow, a wire mesh screen was installed as depicted in Fig. 1 at a predetermined distance upstream from an acoustic window. The turbulence generated should be approximately isotropic [27] and follow the established decay laws [28]. The relative turbulence intensity is given by

$$\frac{\bar{v}^2}{v_m^2} = \frac{C_d}{k}\left[\frac{x}{M} - \left(\frac{x_0}{M}\right)\right]^{-1} \tag{12}$$

where v_m is the mean flow velocity, $\bar{v}^2$ is the mean of (velocity fluctuation)^2, k is a constant depending on the geometry of the screen, x is the distance downstream from the screen, M is the wire spacing, and (x_0/M) indicates the virtual origin of the turbulence where the energy is infinite. C_d for wire screens of round bars has been shown to be [27], [28]

$$C_d = \frac{d/M(2 - d/M)}{(1 - d/M)^4} \tag{13}$$

where d is the diameter of the wire. Different levels of turbulence intensity could be produced by either varying the flow rate v_m, the distance x, or the aspect ratio M/d of the screen. The wire mesh screen employed for this study had an M of 0.106 cm and a d of 0.023 cm. Hence the aspect ratio is approximately 4.61. Measurements were taken at the acoustic window and the screen was placed 5 cm upstream from the window. Using (12) and (13), the relative turbulence intensity induced by the wire screen was estimated to be 2.74%. In estimating the relative turbulent intensity, the constants k and (x_0/M) were assumed to be 101 and 10, respectively [27]. It should be noted that (8) was derived from measurements of turbulent motion behind screens placed in a laminar flow. The entrance length L_e before the screen was 60 cm which was greater than the minimum length estimated to be 30 cm, hence we could assume that the flow prior to the screen was laminar.

Experimental Procedure

The transducer was placed at an angle of 60° relative to the flow conduit near the acoustic window. In the face of difficulties in achieving insonation of the entire vessel, measurements were obtained from a sample volume placed near the center of the vessel. This was attained by utilizing the Doppler flowmeter to record the zero mean velocities associated with the near and far walls of the vessel and reading the corresponding range gate positions. The center of the vessel would then be situated half-way in between these two range gate positions. All measurements were performed at a temperature of 23° ± 1°C.

During ultrasonic measurements, the flow system was first filled with the separated plasma or the buffered saline. Extreme care was taken to avoid introducing air bubbles in the system. The hematocrit concentration was increased by adding a certain volume of concentrated erythrocytes. Following a waiting period of at least 5 min to allow the mixing of blood, the next measurement was performed. The hematocrit of the blood was determined immediately after the measurement by reading its value from a microcentrifuge tube. Measurements were performed on blood samples at different hematocrits typically from 2% up to 45%.

The relationship between the flow rate as determined by the electromagnetic flowmeter and the reading of the roller pump was calibrated for both whole blood and saline suspensions.

Data Acquisition

For both laminar and turbulent flow arrangements, the Doppler signals were digitized at a rate of 25.6 kHz. A 10 ms Hanning window (256 samples) was then applied and 1024 sample fast Fourier transform (FFT) computed. Zero padding was performed before FFT. The Hanning window was then slid over the Doppler signals and 500 consecutive spectra were evaluated. From these spectra, a mean Doppler spectrum was calculated as a function of frequency and its rms value was determined. Since the blood velocity in arteries can change quite significantly over a time interval as little as 10 ms, it is desirable to process the Doppler signal in a time interval of this order. Real-time spectrum analyzers for Doppler signal analysis generally produce a spectral estimate every 5–10 ms.

Results and Discussion

Laminar Flow

A typical Doppler spectrum for porcine erythrocyte suspension at a hematocrit of 22% under laminar flow is shown in Fig. 2. The rms values of the Doppler spectra for porcine erythrocyte suspensions under laminar flow conditions (mean flow velocity ~30 cm/s) as a function of hematocrit are shown in Fig. 3. Each circle represents the average of five experimental measurements on different blood samples. The standard deviations of each measurement are also shown. The rms value seems to peak near 13% hematocrit. This observation is in good agreement with the results from pulse-echo measurements [12]–[15]. Fig. 4 shows examples of mean Doppler spectra at hematocrits of 3, 12, 22, and 35%. These measurements were repeated for bovine erythrocyte suspensions in saline and the aforementioned observations appear to be valid for bovine red cells as well.

The rms values of the Doppler spectra for porcine whole blood under laminar flow conditions as a function of hematocrit are depicted in Fig. 5. The circles and squares represent data averaged over five measurements on different blood samples taken at mean shear rates of 200 and 600 s^{-1} calculated from (11), respectively. The standard deviations are also included to indicate the extent of data fluctuation. For a mean shear rate of 600 s^{-1}, the rms values seemed to peak near 13% hematocrit. However, at a mean shear rate of 200 s^{-1}, a plateau was observed for hematocrits higher than 13% perhaps due to the presence of red cell aggregation at this shear rate which was not high enough to completely disrupt red cell aggregation.

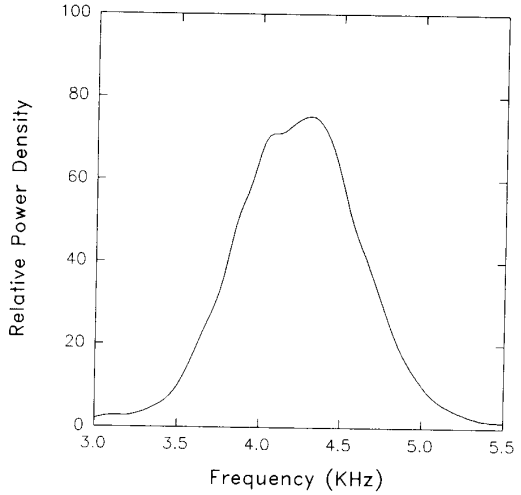

Fig. 2. Typical mean Doppler spectrum for porcine erythrocyte suspension of 22% hematocrit under laminar flow at mean velocity = 30 cm/s.

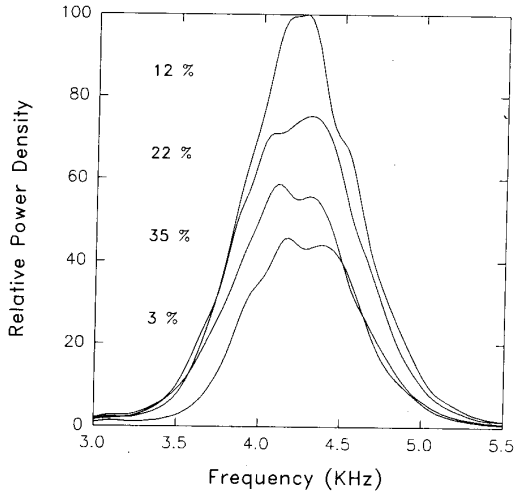

Fig. 4. Mean Doppler spectra for porcine erythrocyte suspensions of different hematocrit under laminar flow.

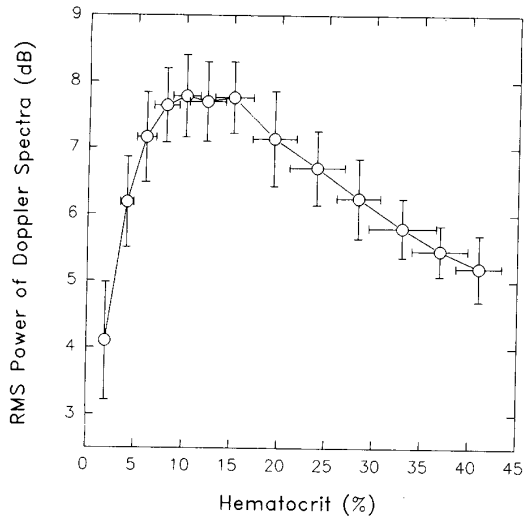

Fig. 3. The rms values of Doppler spectra for porcine erythrocyte suspensions under laminar flow as a function of hematocrit (mean velocity = 30 cm/s).

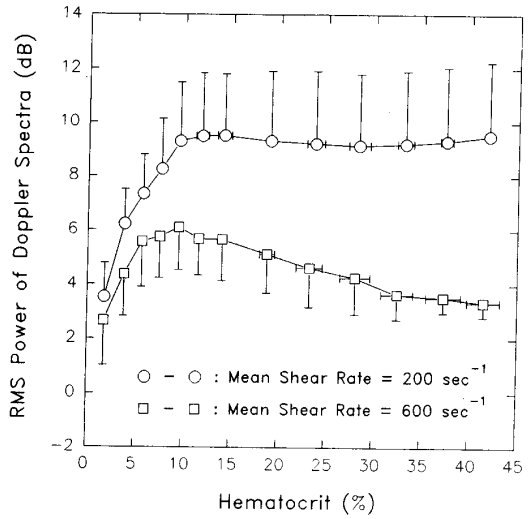

Fig. 5. The rms values of Doppler spectra for porcine whole blood under laminar flow as a function of hematocrit and mean shear rate.

Examples of mean Doppler spectra at mean shear rates of 200 and 600 s^{-1} for 12 and 37% hematocrit are shown in Figs. 6 and 7. It is intriguing to observe that the mean rms values increased with decreasing mean shear rates in spite of the relatively high mean shear rates involved in these experiments. It is known that shear rates greater than 50 s^{-1} are needed in normal human blood to reduce the red cell aggregation to a minimum [26], [31]. Although the value for porcine whole blood is unknown, these results seem to suggest that a much higher shear rate is needed to minimize the effect of red cell aggregation in porcine whole blood and are in agreement with previous observations indicating that red cell aggregation tendency in porcine blood is greater than that in human blood [30], [31]. Furthermore, the corresponding results for bovine whole blood, depicted in Fig. 8, which show little dependence of rms values of Doppler spectra on mean shear rate are in agreement with the fact that red cell aggregation tendency in bovine whole blood is minimal [30], [31].

These results clearly suggest that the assumption given by (1) may not be valid when hematocrit of the blood changes. For instance, an increase of the hematocrit from 20 to 40% according to (1) should result in an increase in Doppler signal strength since n increases as hematocrit increases. This is contradicted by data shown in Fig. 4. Here an alternative is proposed, i.e.,

$$P(\omega)\, d\omega = \eta_0\, dV \tag{14}$$

where η_0 is the backscattering coefficient and dV is the incremental volume of blood. η_0 is a function of red cell

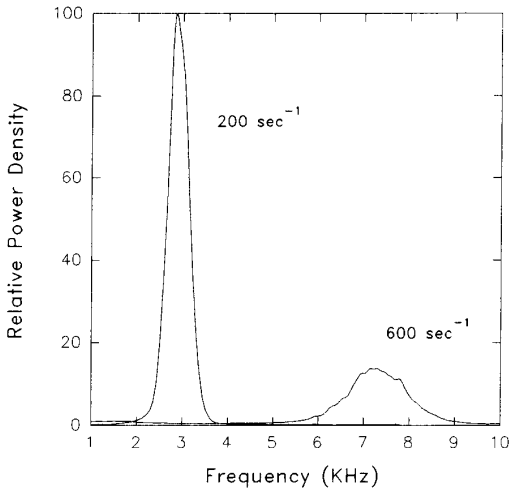

Fig. 6. Mean Doppler spectra for porcine whole blood of 12% hematocrit under laminar flow at different shear rates.

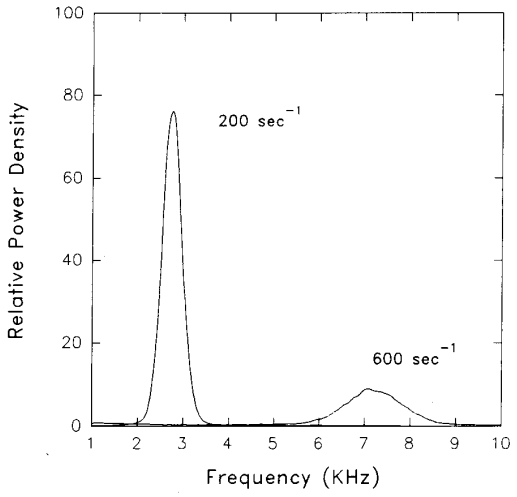

Fig. 7. Mean Doppler spectra for porcine whole blood of 37% hematocrit under laminar flow at different shear rates.

concentration, red cell acoustic characteristics, and flow behavior [12]–[15], [18], [19], η_0 can always be written as the product of σ_b, the backscattering cross-section; n, red cell volume concentration; and W, the packing factor as defined by Twersky *et al.*, [18], [19], which takes into consideration the interaction among cells as the cell concentration is increased. W is a function of cell concentration or hematocrit in this case. If red cells can be approximated as spherical particles, $W = (1 - H)^4/(1 + 2H)^2$ for laminar flow where H is hematocrit. Assuming that the variation of red cell concentration as a function of both time and space is negligible at a fixed hematocrit, both n and W can be treated as constants. Then the power density of a Doppler spectrum is linearly proportional to the volume of red cells flowing with a velocity within $v + dv$, $dV(v)$, or

$$P(\omega)\, d\omega = \sigma_b n_0 W(H)\, dV(v) \qquad (15)$$

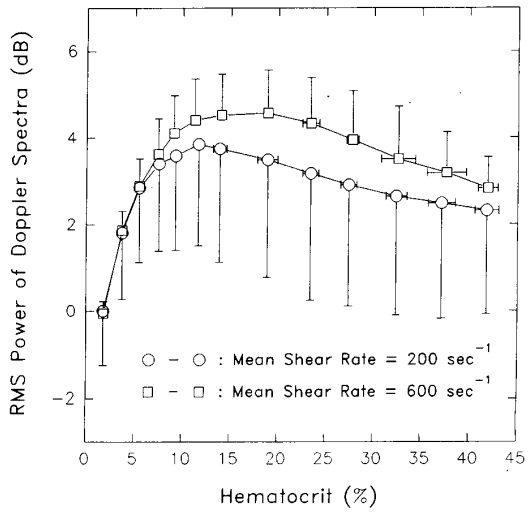

Fig. 8. The rms values of Doppler spectra for bovine whole blood under laminar flow as a function of hematocrit and mean shear rate.

where n_0 is the average number of red cells per unit volume. Thus, $H = n_0 v_{rbc}$ where v_{rbc} is the red cell volume. Equation (6) results by substituting $n(v)\, dv = n_0\, dV(v)$ and (15) into (3) and (5). Therefore, (15) is indifferent from (1) at a fixed hematocrit and the effect of hematocrit on Doppler spectrum is included in $W(H)$ if hematocrit changes. This alternative assumption would not alter any conclusions previously derived from using (1) but is more vigorous than (1).

Turbulent Flow

In a previous study using a pulse-echo arrangement [12] the scattering peak was observed to occur near hematocrits greater than 20%. It was postulated that this discrepancy may be caused by the presence of turbulence. Later studies on the effect of flow disturbances on the backscatter of blood [13] confirmed this hypothesis. The present study was undertaken to interrogate the effect of turbulent flow on the magnitude of Doppler spectrum. Fig. 9 shows examples of mean Doppler spectra for porcine erythrocyte suspension of approximately 20% hematocrit for a mean velocity of 30 cm/s under laminar and turbulent flow. The Doppler shift frequency for turbulent flow is lower than laminar flow because the pulsed Doppler flowmeter sensed only the flow in the center stream where the flow profile was blunter for turbulent flow [21]. The rms values of Doppler spectra for porcine erythrocyte suspensions under laminar and turbulent flow conditions as a function of hematocrit are shown in Fig. 10. The filled and open circles represent the average of five measurements on different blood samples for the turbulent and laminar flow, respectively. The standard deviations are shown for both the Doppler and hematocrit measurements. Both flow velocities were approximately 30 cm/s. The controlled turbulence was introduced by inserting a mesh screen with an aspect ratio of 4.61 in the conduit.

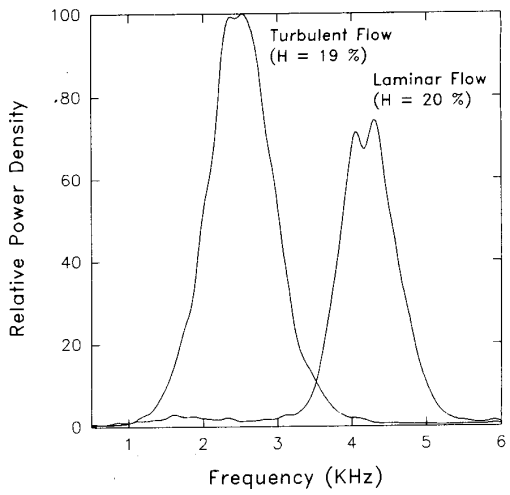

Fig. 9. Typical Doppler spectra for porcine erythrocyte suspensions of approximately 20% hematocrit flowing at mean velocity of 30 cm/s under laminar and turbulent flow.

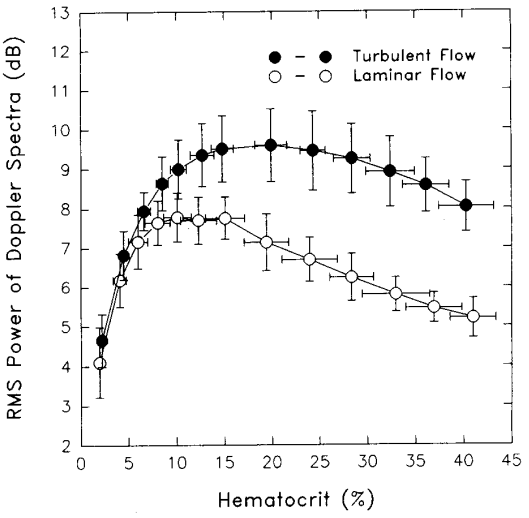

Fig. 10. The rms values of Doppler spectra for porcine erythrocyte suspension under laminar and turbulent flow as a function of hematocrit.

The mesh tend to hemolyze the red cells. However, care was taken to minimize the duration of the experiments to insure minimal hemolysis. Fig. 10 shows that the rms peak for the turbulent flow has shifted to a higher hematocrit of approximately 20%. In addition, it was observed that the rms values for turbulent flow were appreciably higher than the values for laminar flow. This phenomenon is most pronounced for hematocrits greater than 10%. A word of caution is warranted here. Since significant hemolysis of red cells could occur as a result of prolonged exposure of the red cells to the mesh screen, red cell stroma might deposit on the screen to cause a change in the apparent aspect ratio of the screen. The mesh screen should therefore be inspected frequently during prolonged experimentation to avoid such growth from happening.

It should be stressed that presently it is not yet entirely clear which mechanisms are responsible for the increase in backscatter of erythrocytes under turbulent flow conditions. On one hand, Angelsen [32] theorized that, by assuming that blood behaves essentially as an isotropic continuum, the scattering arises from fluctuations in the mass density and compressibility of the blood. It was postulated that turbulence will increase these fluctuations, since local acceleration in the velocity field due to the presence of turbulence will cause a separation between cells and surrounding medium due to their different mass densities. Consequently, an increase in these fluctuations would result in increased scattering. Twersky *et al.* [18], [19], on the other hand, based upon a discrete scatterer model, showed that scattering from a volume of smaller scatterers is proportional to the particle number fluctuation in that volume. Turbulence which decreases correlation among the scatterers and increases particle number fluctuation increases scattering. Similar conclusion was recently obtained by Mo, Cobbold *et al.* [33] using a hybrid approach.

Conclusion

Results previously obtained with a pulse-echo type experimental arrangement on the relationships between ultrasonic scattering properties of blood and several important factors in Doppler blood flowmetry, namely, hematocrit of the blood, shear rate, and the nature of the flow have been validated by results collected by a pulsed Doppler flowmeter. These results indicate that the magnitude of Doppler signal can be affected by the hematocrit of the blood flowing in a blood vessel, shear rate if the shear rate is not sufficiently high to completely disrupt erythrocyte aggregation, and flow disturbance. In fact, the results suggest that an increase in hematocrit can result in a reduction in Doppler signal strength. This observation contradicts a common belief as implied in (1) that the Doppler signal strength is proportional to the number of red cells. We propose in this paper a modified assumption which assumes that the Doppler signal strength is proportional to the volume of blood. It is also shown that this assumption would not alter any previously reached conclusions in Doppler flowmetry. These results also suggest that flow disturbance causes not only spectral broadening but an increase in magnitude of the Doppler signal from blood.

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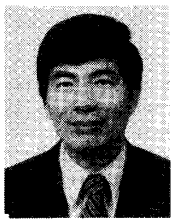

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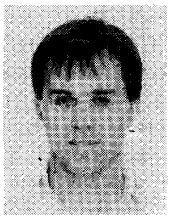

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Chee C. Lim, photograph and biography not available at the time of publication.