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Ultrasonic Doppler Measurement of the Attenuation, Scattering and Blood Hematocrit in the Human Artery

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The goal of this work was to develop a clinically applicable method for noninvasive acoustic determination of hematocrit in vivo based on the Doppler Ultrasound.
The value of hematocrit (HCT) was determined from the pulse-echo measurements of acoustic attenuation at 20 MHz. The measurements in blood in vivo were implemented using 128 gate pulse Doppler flowmeter. The Doppler signal was recorded in the brachial artery and attenuation coefficients were calculated from the appropriate ratios between the received echo amplitudes.
The method proposed appears to be promising for in vivo determination of hematocrit, as 5% error is adequate to monitor changes at patients in shock or during dialysis.

Key words: *ultrasound, Doppler, blood, hematocrit*

1. Introduction

At present the only noninvasive method for estimating the blood hematocrit is based on the measurement of speed of sound [7] or near infrared spectroscopy [13] and is mainly used during patient's dialysis. Other applications include patients in the posttraumatic shock, open-heart surgery and anemia. We propose a novel approach to solve this problem. The instrumentation developed is based on the measurement of absorption of ultrasonic

wave in blood independently of the overall attenuation outside the blood vessel. The instrument consists of a 128 gate pulsed Doppler operating at 20 MHz and DSP signal-processing unit.

Time gating of the receiver makes it possible to record echoes returning from a specific depth. The delay of the receiving gate in relation to the transmitted impulse is directly proportional to the distance between the measured volume and transducer surface. Approximately speaking, the measurement volume has the form of a cylinder whose axis overlaps with the symmetry axis of the ultrasound transducer. The cylinder length depends on the duration of the switched-on receiver gate, while the cylinder diameter equals the diameter of the ultrasound beam. Using higher ultrasound frequencies makes it possible to reduce the measurement volume, both its length and diameter.

2. Ultrasonic Attenuation in Blood

When a wave propagates through a medium, its energy is reduced as a function of distance. The energy may be diverted by scattering or absorbed by the medium and converted to heat. The pressure p of a plane wave propagating in the z direction is given by equation:

$$p = p_0 \mathrm{e}^{-\alpha z} \tag{2.1}$$

where p_0 is the pressure at $z = 0$ and α is the pressure attenuation coefficient. The total coefficient α is a sum of the attenuation coefficients α_i caused by independent energy losses in the medium:

$$\alpha = \sum_i \alpha_i. \tag{2.2}$$

The blood consists of plasma in which are suspended blood cells, mostly red, erythrocytes. Thus the total attenuation coefficient α in blood can be expressed as:

$$\alpha = \alpha_1 + \alpha_2 + \alpha_3 \tag{2.3}$$

where α_1 is an attenuation coefficient caused by acoustical absorption in blood cells, α_2 relates to absorption in plasma and α_3 is caused by scattering on the cell-plasma boundaries. Total ultrasonic attenuation in blood depends on frequency and is equal to [6]:

$$\alpha = \alpha_0 f^{1.2} \tag{2.4}$$

where $\alpha_0 = 0.021\,\mathrm{Np/cm} = 0.18\,\mathrm{dB/cm}$ [3, 6] and f is the ultrasonic frequency, in MHz. Other authors published $\alpha_0 = 0.014 \ldots 0.018\,\mathrm{Np/cm} = 0.12 \ldots 0.16\,\mathrm{dB/cm}$ and frequency exponent is equal to 1.19... 1.23, [5].

To estimate relation between attenuation coefficient α and hematocrit HCT, ratios between coefficients $\alpha_1 \ldots \alpha_3$ must be found. Coefficient α_3 is related to the acoustical scattering on the red blood cells only. Those cells consist more than 99% of all blood cells in quantity and volume. For the ultrasonic frequencies $f = 2 \ldots 20\,\mathrm{MHz}$, used for medical diagnostics, wavelength is equal to $\lambda = 750 \ldots 75\,\mu\mathrm{m}$. Average size of the red blood cell $d = 8\,\mu\mathrm{m}$ is much less than ultrasonic wavelength. The mismatches in density and compressibility between the cell and the plasma are fairly small. In that case the Born approximation is valid. With the above assumptions, the Green's function approach gives the differential scattering cross-section $\sigma_d(\gamma)$ [12]:

$$\sigma_d(\gamma) = \frac{V_c^2 \pi^2}{\lambda_0^4} \left[\frac{\kappa_e - \kappa_o}{\kappa_o} + \frac{\rho_e - \rho_o}{\rho_e} \cos\gamma \right]^2 \quad \mathrm{cm^2/sr} \tag{2.5}$$

where V_c is the volume of the red blood cell, λ_0 is an acoustical wavelength, κ_e, ρ_e and κ_o, ρ_o are the compressibility and mass density of the red blood cell and surrounding plasma, respectively, γ is the angle between the incident and the scattered wave vectors. For the human blood $V_c = 87\,\mu\mathrm{m}^3$ called mean corpuscular volume (MCV), $\kappa_e = 34.1 \times 10^{-7}\,\mathrm{cm/N}$; $\kappa_o = 40.9 \times 10^{-7}\,\mathrm{cm/N}$; $\rho_e = 1.092\,\mathrm{g/cm^3}$; $\rho_o = 1.021\,\mathrm{g/cm^3}$ [11, 12].

The angular scattering coefficient $\sigma_s(\gamma)$ is given by:

$$\sigma_s(\gamma) = \sigma_d(\gamma)(N_c/\Omega)W \quad 1/\mathrm{cm} \cdot \mathrm{sr} \tag{2.6}$$

where N_c is the total number of the red blood cells in the insonified volume Ω. For the human $N_c/\Omega = 5 \times 10^6\,1/\mathrm{mm^3}$ [9]. W is the packing factor and can be viewed as a measure of orderliness in the spatial cells arrangement. There is non-linear dependence of W versus hematocrit HCT with maximum at HCT $\cong$ 25% [11]. This model is valid for not aggregated blood cells. However aggregation occurs for HCT>25% and increase of scattering coefficient is compensated by decrease of packing factor W.

The total scattering σ can be expressed as:

$$\sigma = \int_{4\pi} \sigma_s(\gamma)\,\mathrm{d}\gamma \tag{2.7}$$

where $\mathrm{d}\gamma$ is the differential solid angle.

Thus, from Eqs. (2.5), (2.6), (2.7), for the human blood, the total scattering is given by:

$$\sigma = \frac{V_c^2 \pi^2 N_c N}{\Omega \lambda_0^4} \int_{4\pi} \left[\frac{\kappa_e - \kappa_o}{\kappa_o} + \frac{\rho_e - \rho_o}{\rho_e} \cos\gamma \right]^2 \mathrm{d}\gamma$$

$$= \frac{3.7352 \times 10^{-10}}{\lambda_0^4} \int_{4\pi} [-0.1663 + 0.0650 \cos\gamma]^2 \, \mathrm{d}\gamma$$

$$= \frac{3.7352 \times 10^{-10}}{\lambda_0^4} \times 0.3669 = \frac{1.3704 \times 10^{-10}}{\lambda_0^4}. \quad (2.8)$$

The scattering attenuation coefficient α_3, in dB/cm, calculated from equation (2.8) is equal to:

$$\alpha_3 = -10 \log(1 - \sigma(f)) = -10 \log(1 - 2.7070 \times 10^{-7} f^4) \quad (2.9)$$

where f is the ultrasonic frequency in MHz.

The frequency dependence of the ultrasonic attenuation coefficient α and the scattering attenuation coefficient α_3 are presented in Fig. 1 and in Table 1. Even for the highest frequency $f = 20$ MHz, the scattering coefficient α_3 is at least two orders less than total scattering coefficient α and may be neglected. Then ultrasonic attenuation in blood is caused only by acoustical absorption

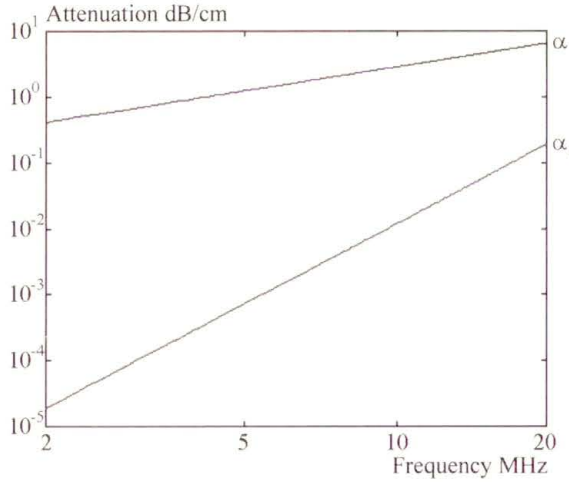

FIGURE 1. Total attenuation coefficient of the human blood α and scattering attenuation coefficient α_3 for frequencies $f = 2 \ldots 20$ MHz. Calculated from equations (2.4) and (2.9).

TABLE 1. Calculated and measured values of the total attenuation and scattering attenuation coefficient in blood.

Frequency	2 MHz	5 MHz	10 MHz	20 MHz
Attenuation coefficient α calculated from (4) (dB/cm)	0.41	1.24	2.85	6.55
Attenuation coefficient α measured [2] (dB/cm)	0.4	1.3	3.0	–
Backscattering coefficient $\sigma_s(\gamma = \pi)$ calculated from (6) (1/cm·sr)	6.31×10^{-7}	2.47×10^{-5}	3.95×10^{-4}	6.31×10^{-3}
Backscattering coefficient σ_s $(\gamma = \pi)$ measured [11] (1/cm·sr)	–	2.0×10^{-5}	5.4×10^{-4}	–
Total scattering σ calculated from (8) (1/cm)	4.33×10^{-6}	1.69×10^{-4}	2.71×10^{-3}	4.33×10^{-2}
Scattering coefficient α_3 calculated from (9) (dB/cm)	1.88×10^{-5}	7.35×10^{-4}	1.18×10^{-2}	1.92×10^{-1}

in the blood cells and plasma:

$$\alpha = \alpha_1 + \alpha_2. \tag{2.10}$$

The size of the red blood cells is at least one order smaller than length of ultrasonic wave. Absorption depends on the total volume of plasma and the sum of the cells volume. The attenuation coefficient α can be expressed as:

$$\alpha = \frac{V_K}{V}\alpha_K + \frac{V_O}{V}\alpha_O \tag{2.11}$$

where α_K, V_K and α_O, V_O are the absorption coefficient and volume of the red blood cell and plasma, respectively. V is a sum of V_K and V_O. The hematocrit HCT value is given by equation:

$$\mathrm{HCT} = \frac{V_K}{V}. \tag{2.12}$$

Equations (2.10) and (2.11) yield:

$$\alpha = \mathrm{HCT}\alpha_K + (1 - \mathrm{HCT})\alpha_O \tag{2.13}$$

or:

$$\alpha = \alpha_O + \mathrm{HCT}(\alpha_K - \alpha_O). \tag{2.14}$$

Those equations present linear relation of the attenuation coefficient to the hematocrit.

3. Doppler Attenuation Measurement

The attenuation was measured in-vitro from the spectrum of the Doppler signal. In Fig. 2 the initial measurement system is shown. It provides for a measurement of flow velocity at two different depths. In practical terms, this means using two receivers, in which the gate delay has a constant difference, corresponding to the constant distance between measurement volumes Q_1 and Q_2. The power of the backscattered Doppler signal from the first and the second gate was determined from equations (2.1) and (2.2), respectively,

$$P_{Q1} = P_T T \eta_1, \tag{3.1}$$

$$P_{Q2} = P_T T \eta_2 \mathrm{e}^{-4\alpha z} \tag{3.2}$$

where P_T denotes the transmitted acoustic power, T is equal to total loss of the signal between the transducer and the gate Q_1, η_1 and η_2 denotes the backscattering coefficients of red blood cells in the gates Q_1 and Q_2 respectively, α is equal to the total acoustic attenuation and z the axial distance between the two gates (see Fig. 2).

The backscattering coefficient depends on hematocrit, cell aggregation and concentration of roleaux [8]. The cell aggregation changes with spatial shear rate, acceleration and turbulences [4]. The backscattering coefficient depends on the angle between the flow direction and the transducer axis [1].

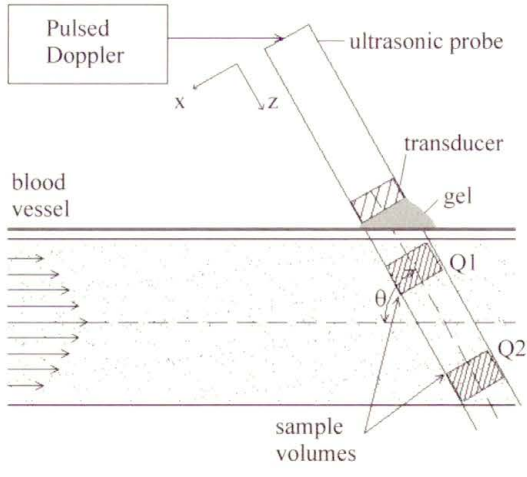

FIGURE 2. The principle of operation of the initial, two gate Doppler hematocrit meter

When the gates (sample volumes) are positioned symmetrically to the center of the vessel, it can be assumed, that:

$$\eta_1 = \eta_2. \tag{3.3}$$

Then, from (3.1) and (3.2) attenuation coefficient can be determined as:

$$\alpha = \frac{\ln(P_{Q1}/P_{Q2})}{4z}. \tag{3.4}$$

The hematocrit value based on pulse-echo measurements and Eq. (2.14) can be then expressed as [10]:

$$\mathrm{HCT} = 11.2(\alpha - 3.66). \tag{3.5}$$

As mentioned earlier, 20 MHz Doppler signal was chosen to maximize the sensitivity of the hematocrit meter. The 3 mm diameter, 20 MHz transducer was made of Lithium Niobate crystal and special attention was paid to ensure symmetric distribution of the generated field.

4. Measurements in-vitro

To further examine the Doppler approach, a multigate system with 128 gates was constructed. The tested porcine blood of various hematocrit flew within a plexiglas tube of internal diameter equal to 6.4 mm. A peristaltic pump forced either continuous flow with constant velocity 15 cm/s or pulsatile flow with cyclic velocity variation between -16 cm/s and $+68$ cm/s. The distance between the axis of the tube and the transducer surface was 4.0 mm. In this way, the sampling volumes were located symmetrically. The value of hematocrit was determined from the ratios of the power Doppler spectra from the two sets of measurements corresponding to laminar and pulsatile flow. The porcine blood assays ranging from 3%...72% HCT. For each hematocrit sample 100 sets of Doppler spectra were recorded, each set being related to all of 128 gates across the vessel. After the spectra were acquired, the data were processed using MatLab™ software (The MathWorks, Natick, MA, USA). For each spectrum recorded in each gate, the power of the flow signal was calculated and Doppler power profile DPP (the distribution of the Doppler power across the vessel diameter) was obtained. The DPP data were used to calculate the value of hematocrit. The averaged linear regression was calculated from the DPP curve. The slope of the regression line

divided by 2 is equal to the attenuation coefficient. The DPP data were used to calculate the value of hematocrit. Next, all measurements were averaged to yield the final value of hematocrit. The results are presented in Fig. 3.

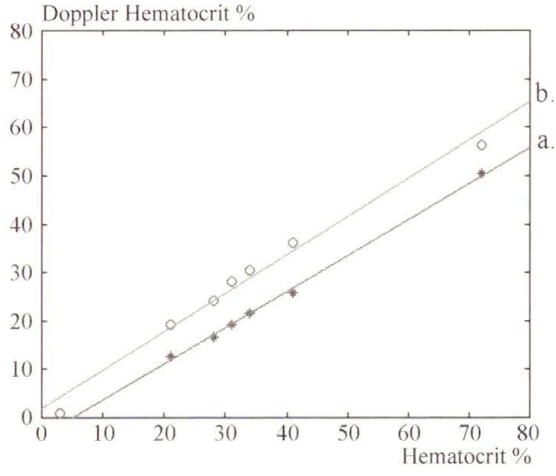

FIGURE 3. Comparison of the results obtained using conventional hematocrit centrifuge and multigate Doppler method for porcine blood; a. constant velocity blood flow; b. pulstile flow

The correlation coefficient was $R = 0.999$ for continuous flow and $R = 0.992$ for pulsatile flow. The standard deviation was SD = 0.065 dB/cm and SD = 0.239 dB/cm respectively. The absolute accuracy of Doppler measurements were ±15% HCT for continuous flow and ±4.9% HCT for pulsatile flow.

5. Measurements in-vivo

In vivo measurements of hematocrit were performed on radial artery in 9 volunteers. The hematocrit values varying from 36.4% to 47.4%. For each volunteer 250 sets of Doppler spectra were recorded, each set being related to all of 128 gates across the vessel. The recording was done over a period of 2.5 s; that corresponded to 2 heart cycles. After the spectra were acquired, the data were processed and Doppler power versus depth was calculated. The hematocrit value in vivo was calculated from the Eq. (3.5). The results are presented in Fig. 4.

The correlation coefficient was $R = 0.986$, $n = 9$. The absolute accuracy of Doppler in-vivo measurements in brachial artery were not more than

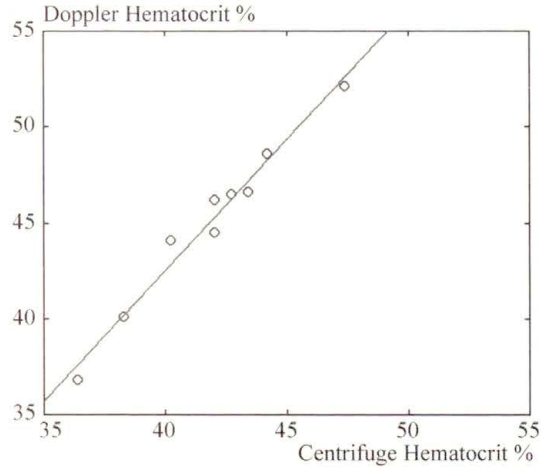

FIGURE 4. Comparison of the results obtained using centrifuge and multigate Doppler method in vivo in the brachial artery.

4.7% HCT. The determined error was always positive, the Doppler measurement was always overestimated.

6. Summary

The goal of this work was to develop a clinically applicable method for non-invasive acoustic determination of hematocrit in vivo based on the Doppler Ultrasound.

The value of hematocrit (HCT) was determined from the pulse-echo measurements of acoustic attenuation at 20 MHz. The measurements in blood in vivo were implemented using 128-gate, 20 MHz pulse Doppler flowmeter. The Doppler signal was recorded in the brachial artery and attenuation coefficients were calculated from the appropriate ratios between the received echo amplitudes.

The attenuation coefficient of ultrasonic wave in vitro was determined from the measurements of porcine blood samples with hematocrit varying between 3% and 72%. The in vitro experiments indicated that the attenuation coefficient increased linearly with hematocrit. The correlation coefficient was $R = 0.999$ for the continuous blood flow and $R = 0.992$ for pulsatile flow. The in vivo measurements were performed in the brachial artery in 9 volunteers. The absolute accuracy of in vivo measurements was determined to be within $\pm 5\%$ HCT.

The method proposed appears to be promising for in vivo determination of hematocrit as 5% error is adequate to monitor changes at patients in shock or during dialysis. The multigate system largely simplifies the placement of an ultrasonic probing beam in the center of the blood vessel. Current work focuses on enhancing the method's applicability to arbitrary selected vessels and reducing the HCT measurement error to well below 5%.

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