AN AUTOMATED REAL TIME CAPILLARY VISCOMETER

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***Abstract*- This study describes how to establish a capillary viscometer (microviscosimeter) that uses an inline micro-flowmeter that can accurately measure whole blood effective viscosity in tubes of arteriolar diameter at physiologically nominal flow rates with all benefits of digital media. Total measurement time is 4 minutes. The data can be digitally handled. Currently this system is assembled at the Department of Anatomy, Istanbul Medical School, University of Istanbul. The system diagnoses elevated viscosity as a routine procedure providing valuable criteria for many clinical manifestations.**

***Keywords* - Capillary viscometer, microviscometer, blood viscosity**

I. INTRODUCTION

Viscosity as a hemorheological criteria has become far more important after the clinicians started to blame it for some pathological conditions. There is a bunch of study showing that the blood viscosity is apparently relevant with erythrocyte aggregation, endothelial damage, intimal thickening, coronary artery disease and diabetic ischemia.

Clinical manifestations of coronary and cerebrovascular disease are associated with an increased blood viscosity [1, 2]. Plasma viscosity is predictive of ischemic heart disease events in a free-living population [3] and progression to acute myocardial infarction in patients with unstable angina pectoris [4]. Abnormalities in blood rheology, including elevations of blood and plasma viscosity, are related to vascular complications in Diabetes Mellitus [5].

The rise in blood viscosity accounts for clinical manifestations of Polycythemia that have been observed in approximately 50 % of newborn infants with hematocrit values of 0.65 or greater**.** In neonates, hyperviscosity increases the risk of pulmonary hypertension, renal failure, necrotizing enterocolitis, cerebral ischemia, intracranial hemorrhage, and developmental retardation [6-10].

Currently, most of the researchers have used very conventional types of viscometers (cone-in-cone or cone-on-plate) or newer or developing systems such as ball or capillary types for measuring blood and plasma viscosity. Among all these type of viscometers, capillary type of viscometers seem to be more reliable than the others, because the blood flows in vessels that have similar geometry and size with capillary tubes of these instruments.

The capillary viscometer created by Kirby [11] is closer to the physiological system, because of the velocity-controlled nature of his instrument.

Kirby's system consisted of three parts; capillary tubes, transducers and amplifers, and a paper-chart recorder.

Kirby collects at least 38 data from paper chart by counting squares. Surely, this method is very slow, inaccurate and impractical. Also, it yields high observation error, limited number of data points, and low accuracy. To overcome the handicaps of this system's time consuming third part, we proposed a digital system.

II. METHODOLOGY

A. Theory

When fluid is flowing steadily through the entire system, the modified Hagen-Pouiseuille flow relationship holds throughout the flow system such that the effective viscosity in the test section is linearly related to the flow resistance in the reference section. Applied to the microviscometer, Hagen-Pouiseuille relation yields both μ_e (effective viscosity) and Q (flow rate) of the sample in place. Throughout the system these parameters are functions of measured pressure drops, system geometry (C), and the reference viscosity μ_R of the fluid (saline) in the reference section (1) and (2):

$$\mu_e = \left(\frac{R_X}{R_R}\right)^4 \left(\frac{L_R}{L_X}\right) \mu_R \frac{(P_0 - P_1)}{(P_1 - P_2)} = C\mu_R \frac{(P_0 - P_1)}{(P_1 - P_2)} \tag{1}$$

$$Q = \frac{\pi R_R^4}{8 L_R \mu_R}(P_1 - P_2) \tag{2}$$

Where Q is volumetric fluid flow rate, μ is viscosity, L is tube length, and tube radius is R.

By this means, effective viscosity and flow rate are continuous on-line output variables which can be directly obtained from PC records of only P_0 and P_1, both being gauge pressures relative to atmosphere pressure (P_2) [11].

B. Setup

The microviscosimeter consists of two tubes of polytetrafluoroethylene (PTFE; Zeus Industrial Products) with uniform internal diameters of 41 (μm), and lengths of 25 (mm) connected in series on either side of a small volume pressure transducer. An attached upstream reservoir contains the test fluid for input to the system. An attached downstream reservoir receives the system effluent. The upstream reservoir is connected to a variable pressure air

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Abstract

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4

supply, which drives the test solution through the system. Pressure relative to atmosphere is measured by pressure transducers at two points in the system Fig. 1.

C. Transducers

For data harvesting, one Ohmeda P23XL reusable dome pressure transducer was mounted between hand-made capillary sections. For air pressure measurement, another Ohmeda P23XL transducer was used. These transducers' pressure range is -30 to +300 (mm Hg), sensitivity is 5 (µV/V/mm Hg ±1%) and excitation voltage is 7.5 (V) DC.

D. Preamplifiers

The signals from the transducers were separately amplified using low-level DC preamplifiers because the pressure values that we measured were in a range of 20 (mV) to 2(V).

Preamplifiers are low-level D.C. Pre-amplifier (Grass Instrument Co. Model 7P1). The preamplifiers were high gain, low noise, low frequency, plug in DC preamplifier, with the specifications of CMRR: greater than 1000:1 and unity gain between 0.995 and 1. These preamplifiers give 6.2 (V) excitation voltage that is needed by transducers.

E. I/O Board

The output signals are carried to a personal computer (PC) through an AD/DA converter card (National Instruments, PCI-1200).

PCI-1200 Multifunctional I/O Board for PCI Bus Computers was used as A/D converter. This board is completely software configurable, 12-bit resolution and 100

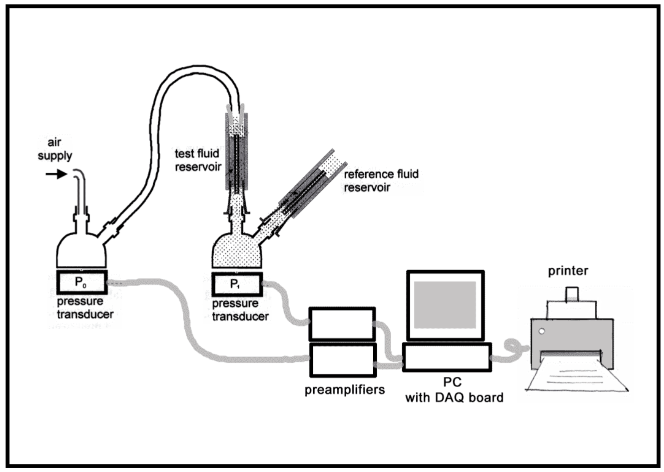


Fig. 1. Schematic diagram of the automated real time viscometer.

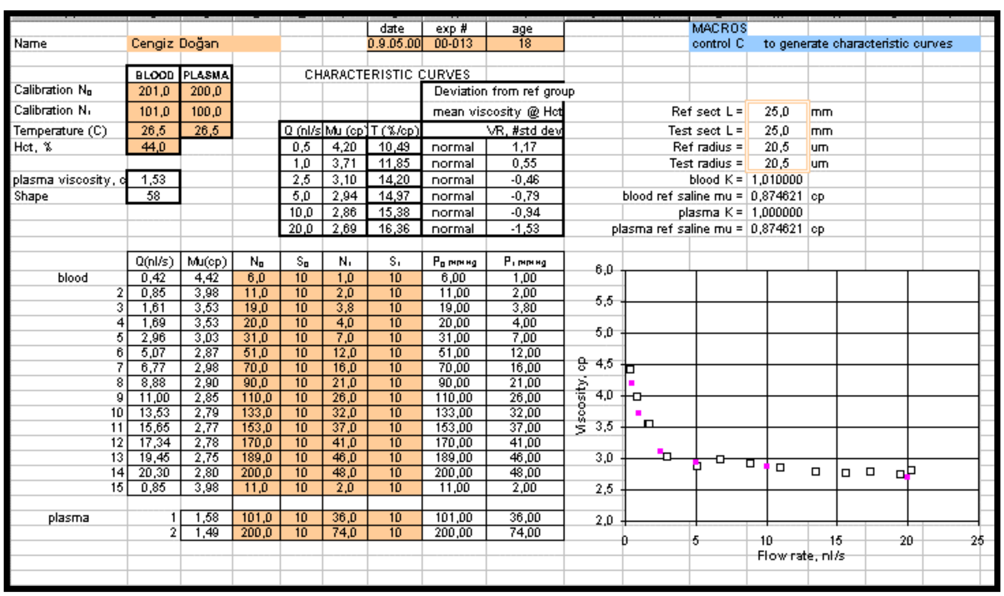
(KS/s) sampling rate. PCI-1200 is installed on a PCI expansion slot in the computer.

F. Software

LabView 5.01 (National Instruments) was used as software. An appropriate diagram and user interface was established.

III. RESULTS

Fig. 2 is an example for blood plasma viscosity report, corresponding to Case 1, a normal blood viscosity curve. Pressure values (P0 and P1) are found in mm Hg using data from transducers (N0 and N1) and sensitivity values (S0 and S1). Different sensitivity setting can be used to cope with the resolution requirements if needed. Q (flow rate) and µ (viscosity) were computed using the (1) and (2) respectively. On the right: the chart shows the relation between Q and µ values graphically. "Characteristic Curve" values (black dots on the chart) corresponding to the table on the top



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MACROS
control C to generate characteristic curves

	BLOOD	PLASMA
Calibration N_0	201,0	200,0
Calibration N_1	101,0	100,0
Temperature (C)	26,5	26,5
Hct, %	44,0	
plasma viscosity, c	1,53	
Shape	58	

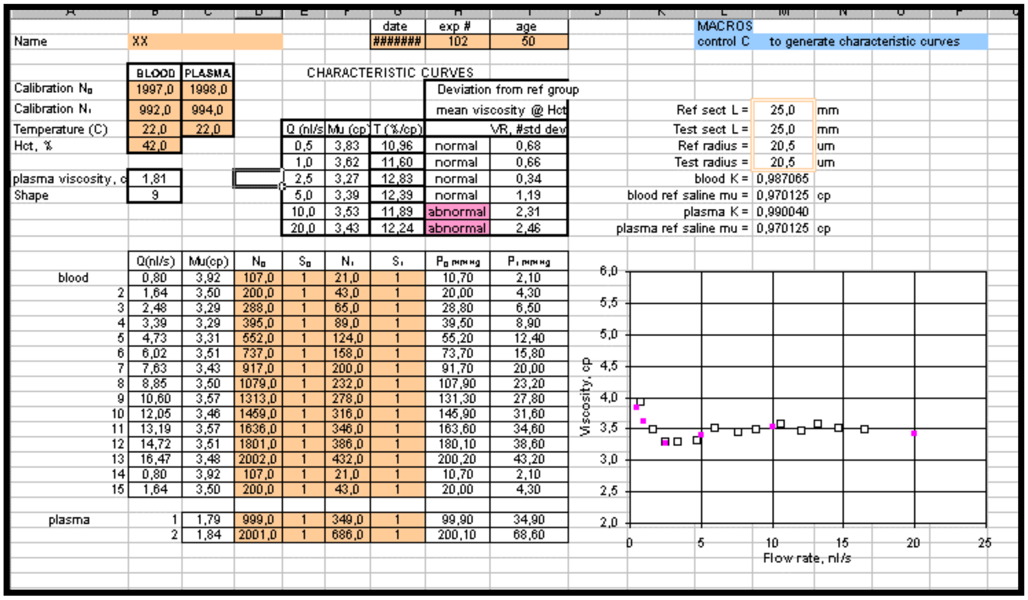
CHARACTERISTIC CURVES

Q (nl/s	Mu (cp	T (%/cp)	Deviation from ref group mean viscosity @ Hct	VR, #std dev
0,5	4,20	10,49	normal	1,17
1,0	3,71	11,85	normal	0,55
2,5	3,10	14,20	normal	-0,46
5,0	2,94	14,97	normal	-0,79
10,0	2,86	15,38	normal	-0,94
20,0	2,69	16,36	normal	-1,53

Ref sect L =	25,0	mm
Test sect L =	25,0	mm
Ref radius =	20,5	um
Test radius =	20,5	um
blood K =	1,010000	
blood ref saline mu =	0,874621	cp
plasma K =	1,000000	
plasma ref saline mu =	0,874621	cp

		Q(nl/s)	Mu(cp)	N_0	S_0	N_1	S_1	P_0 mmHg	P_1 mmHg
blood		0,42	4,42	6,0	10	1,0	10	6,00	1,00
	2	0,85	3,98	11,0	10	2,0	10	11,00	2,00
	3	1,61	3,53	19,0	10	3,8	10	19,00	3,80
	4	1,69	3,53	20,0	10	4,0	10	20,00	4,00
	5	2,96	3,03	31,0	10	7,0	10	31,00	7,00
	6	5,07	2,87	51,0	10	12,0	10	51,00	12,00
	7	6,77	2,98	70,0	10	16,0	10	70,00	16,00
	8	8,88	2,90	90,0	10	21,0	10	90,00	21,00
	9	11,00	2,85	110,0	10	26,0	10	110,00	26,00
	10	13,53	2,79	133,0	10	32,0	10	133,00	32,00
	11	15,65	2,77	153,0	10	37,0	10	153,00	37,00
	12	17,34	2,78	170,0	10	41,0	10	170,00	41,00
	13	19,45	2,75	189,0	10	46,0	10	189,00	46,00
	14	20,30	2,80	200,0	10	48,0	10	200,00	48,00
	15	0,85	3,98	11,0	10	2,0	10	11,00	2,00
plasma		1	1,58	101,0	10	36,0	10	101,00	36,00
		2	1,49	200,0	10	74,0	10	200,00	74,00

Fig. 2. Case 1: sample report demonstrating normal blood viscosity characteristics of a patient.



			date	exp #	age
Name	XX		#######	102	50

MACROS
control C to generate characteristic curves

	BLOOD	PLASMA
Calibration N_0	1997,0	1998,0
Calibration N_1	992,0	994,0
Temperature (C)	22,0	22,0
Hct, %	42,0	
plasma viscosity, c	1,81	
Shape	9	

CHARACTERISTIC CURVES

Deviation from ref group mean viscosity @ Hct

Q (nl/s	Mu (cp)	T (%/cp)	VR, #std dev	
0,5	3,83	10,96	normal	0,68
1,0	3,62	11,60	normal	0,66
2,5	3,27	12,83	normal	0,34
5,0	3,39	12,39	normal	1,19
10,0	3,53	11,89	abnormal	2,31
20,0	3,43	12,24	abnormal	2,46

Ref sect L =	25,0	mm
Test sect L =	25,0	mm
Ref radius =	20,5	um
Test radius =	20,5	um
blood K =	0,987065	
blood ref saline mu =	0,970125	cp
plasma K =	0,990040	
plasma ref saline mu =	0,970125	cp

		Q(nl/s)	Mu(cp)	N_0	S_0	N_1	S_1	P_0 mmHg	P_1 mmHg
blood		0,80	3,92	107,0	1	21,0	1	10,70	2,10
	2	1,64	3,50	200,0	1	43,0	1	20,00	4,30
	3	2,48	3,29	288,0	1	65,0	1	28,80	6,50
	4	3,39	3,29	395,0	1	89,0	1	39,50	8,90
	5	4,73	3,31	552,0	1	124,0	1	55,20	12,40
	6	6,02	3,51	737,0	1	158,0	1	73,70	15,80
	7	7,63	3,43	917,0	1	200,0	1	91,70	20,00
	8	8,85	3,50	1079,0	1	232,0	1	107,90	23,20
	9	10,60	3,57	1313,0	1	278,0	1	131,30	27,80
	10	12,05	3,46	1459,0	1	316,0	1	145,90	31,60
	11	13,19	3,57	1636,0	1	346,0	1	163,60	34,60
	12	14,72	3,51	1801,0	1	386,0	1	180,10	38,60
	13	16,47	3,48	2002,0	1	432,0	1	200,20	43,20
	14	0,80	3,92	107,0	1	21,0	1	10,70	2,10
	15	1,64	3,50	200,0	1	43,0	1	20,00	4,30
plasma	1		1,79	999,0	1	349,0	1	99,90	34,90
	2		1,84	2001,0	1	686,0	1	200,10	68,60

Fig. 3. Case 2: sample report demonstrating abnormal blood viscosity characteristics of a patient at optimal and fast flow rates.

center are also presented in the same graph. These values are the set reference points that are always 0.5, 0.1, 2.5, 5.0, 10.0, 20.0. These related N values at these reference Q points are always computed for comparison purposes. On the top left, in addition to saline calibration measurement values (as N0 and N1) both for blood and plasma, the temperature of environment and Hematocrit (Hct) values of the case are shown. On the top right, geometrical values of the test and reference sections, blood and plasma K (vascular resistance), µ (viscosity) values of blood and plasma reference saline are also shown.

In Fig. 3, Case 2 shows abnormal blood viscosity values at the flow rates of 10.0 (nl/s) and 20.0 (nl/s).

IV. Discussion and Conclusion

The measurement of flow rate is often problematic for lack of small-scale precision flow meters with rapid time response.

Kirby at al. developed a rapid response viscometer using two 41 (µm) tubes connected in series that measures blood viscosity more rapidly and reliably than the conventional and other capillary type of microviscometers [11]. But still this system needed long procedure to get usable data, and very long hours for manual data input. In his system a strip-chart record was used. After visual analysis of the chart, all data were carried to an Excel work sheet for calculation.

For collecting data, instead of ink-writing strip chart, only a PC with appropriate software that is faster, and more reliable was used. Additionally, with this system the laboratory was kept tidier, and all data could be stored in digital media that could be reproducible and electronically transferable.

Creating a handy and reliable viscosimeter will be very helpful for both researchers and clinicians who try to investigate the relation between elevated blood viscosity and various disorders. Blood viscosity information is also valuable in monitoring the patient's body reaction to medical treatment.

Using microtubes with the 41 (µm) diameter simulates a living tissue arteriolar vessel. In the body, physiological nominal flow rate in that size arteriole is about 12 (nl/s). Although this flow rate is not always steady, in this setup the range of physiological flow rate was represented more than necessary that was 0.1 to 25 (nl/s).

Measurements in capillary part are done in as quickly as almost 3 minutes. To analyze data and print the report another 1 minute is required.

The software based analysis system enables us a more flexible research platform for future research.

The automated real time physiological viscometer is currently assembled in a laboratory room at the Department of Anatomy, Istanbul Medical School - University of Istanbul, under the name of "Viscosity Laboratory". This is a clinical laboratory accepting patients from Istanbul Medical School Hospitals and Cerrahpasa Medical School Hospitals.

Currently, this system has been successfully used in 45 patients to diagnose viscosity level as valuable criteria since December 2000.

Future works will include several promising developments; such as automated air pressure control, and more compact design.

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