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RESEARCH ARTICLE

APPLIED MATHEMATICAL MODELS OF TWO PHASE HUMAN PULMONARY BLOOD FLOW IN VENULES WITH SPECIAL REFERENCE TO LUNG CANCER

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ABSTRACT

Aim of present study was to apply a mathematical model of two phase human blood flow in pulmonary Venules, keeping in view the nature of pulmonary blood circulation during lung cancer. We have applied Herschel Bulkley model in Bio- fluid mechanical setup and we have used with respect to clinical data in case of Lung Cancer for hemoglobin versus blood pressure. In this examination overall presentation was in tensorial form and the solution method adopted was analytical as well as numerical. The role of hematocrit is clear in the determination of blood pressure drop in case of pulmonary disease Lung Cancer.

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INTRODUCTION

The human lungs are divided in two lobes and right lung has three lobes. The lung can be rather obviously grouped into a number of almost distinct non-respiratory functions related mostly to protection (Jason and Bates, 2009). The human lungs perform just like purification station for blood (Guyton and Hall, 2006). Human circulatory system was divided systemic circulation and pulmonary circulation. Because in this proposed research work based on human pulmonary blood circulation so we have focused only human pulmonary blood circulation. Human Pulmonary blood circulation is a sub system of human circulatory system. According to Upadhyay and pandey we have concedered two phase blood which is one of the red blood cells and other is plasma.
Lung cancer is the second most common cancer, the most important cause of cancer related mortality in both men and women. Each year more people die of lung cancer (Moses *et al*., 2014). According to the World Health Organization (WHO) reports that over 1.1 million people die of lung cancer each year. This data increases every year. WHO has identified lung cancer as one of the major problems facing the world in this new century (Tina M. St. John, 2003). We have collected clinical data in case of Lung Cancer for hemoglobin versus blood pressure for in this study. We have selected a frame of reference for mathematical modeling of two phase blood flow of the state of a moving blood· It was in view the difficulty and generality of the problem of blood flow and selected generalized three-dimensional orthogonal curvilinear co-ordinate system, briefly prescribed as E3 , called as 3-dim Euclidean space, It is interpret the quantities related to blood flow in tensorial form which was comparatively more realistic, The biophysical laws thus expressed fully hold good in any co-ordinate system , which was compulsion for the truthfulness of the law (Upadhyay, 2000). The flow of blood was affected by the presence of blood cells. This effect was directly proportional to the volume covered by blood cells. Let the volume portion covered by blood cells in unit volume be$X$, X is replaced by H */100*, where H was the hematocrit the volume percentage of blood cells. The hematocrit is normally about three times the hemoglobin concentration (reported as grams per deciliter) (Berkow, Robert, 1997). Then the volume portion covered by the plasma will be ($1-X$).

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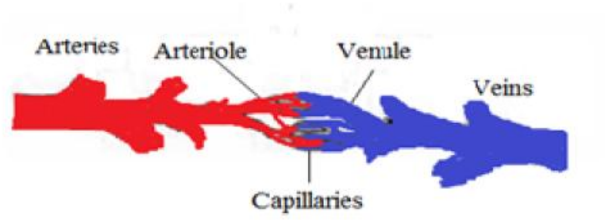


Fig.1. Pulmonary blood flow in vessels

If mass ratio of cells to plasma is r then clearly: $r = \frac{X\rho_c}{(1-X)\rho_p}$.

Where ρ_c and ρ_p are densities of blood cells and plasma respectivily. Usually this mass ratio is not a constant. Even then this may be supposed to constant in present context (Upadhyay, 2000).

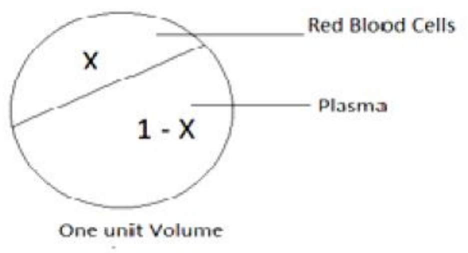


Fig. 2. Blood volume

Mathematical Model / Formulation

Upadhyay and Pandey (Upadhyay *et al.*, 2012) have already considered the blood flow as two phased. One of which is that of red blood cells and other is plasma. The equation of motion is based on this principle. According to this principle, the total momentum of any fluid system is conserved in absence of external force.

$$\frac{dp}{dt} + P - F_{v(viscosity)} = 0 \text{ (External Force)}$$

The blood can be considered as homogeneous mixtures of two phases and we have conceder the fundamental equation of continuity, which is a mathematical expression of principal of conservation of matter.

Equation of Continuity

If mass ratio of cells to plasma is r then clearly: $$r = \frac{X\rho_c}{(1-X)\rho_p} \quad (1)$$

Where ρ_c and ρ_p are densities of blood cells and plasma respectivily. Usually this mass ratio is not a constant. Even then this may be supposed to constant in present context. The both phase of blood, i.e. blood cells and plasma move with the common velocity. According to Campbell and Pitcher (Campbell and Pitcher, 1957), Upadhyay and Pandey have already discussed about two phase model. It has been transformed in to biofluid mechanical set up. For this purpose, blood has been assumed to be constituted by plasma and blood cells which is realistic so for (Upadhyay *et al.*, 2012). The principles of conservation of mass in pulmonary circulatory system, equation of continuity for two phases are following as –

$$\frac{\partial(X\rho_c)}{\partial t} + (X\rho_c V^i)_{,i} = 0 \quad (2)$$

$$\frac{\partial(1-X)\rho_p}{\partial t} + \quad 1 - X \ \rho_c V^i)_{,j} = 0 \quad (3)$$

Where V is the common velocity of two phase blood cells and plasma. If we define the uniform density of blood ρ_m as follows:

$$\frac{1+r}{\rho_m} = \frac{r}{\rho_c} + \frac{1}{\rho_p} \quad (4)$$

Then equation (3.2) and (3.3) can be combined together as: $\frac{\partial \rho_m}{\partial t} + (\rho_m V^i)_{,j} = 0$ (5)

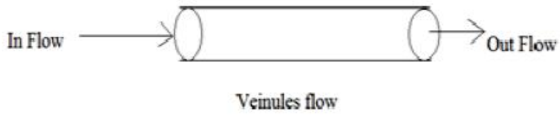


Fig. 3. Pulmonary venules blood flow

Equation of motion for blood-flow

The hydro dynamical pressure between the two phases of blood can be supposed to be uniform because the both phases i.e. blood cells and plasma is always in equilibrium state in blood. Taking viscosity coefficient of blood cells to be $\eta_c$and apply the principle of conservation of momentum in pulmonary circulatory system, we get the equation of motion for the phase of blood cells as follows:

$$X_{\rho_c}\frac{\partial V^i}{\partial t} + X_{\rho_c}V^j \ V^i,j = -X_p,j\,g^{ij} + X\eta_c\ g^{jk}V^i,k\ ,j \quad (6)$$

Similarly, taking the viscosity coefficients of plasma to be equation of motion for plasma will be as fallows-

$$(1-X)_{\rho_c}\frac{\partial V^i}{\partial t} + \{(1-X)_{\rho_c}V^j\}V^i,j = -\ 1-X\ _p,j\,g^{ij} + (1-X)\eta_c\ g^{jk}V^i,k\ ,j \quad (7)$$

Now adding equation (3.6) and (3.7) and using this relation (3.4), the equation of motion for blood flow with the both phases will be as fallows-

$$\rho_m\frac{\partial V^i}{\partial t} + \rho_m V^i\ V^i,j = -P,j + \eta_m\ g^{jk}V^i,k\ ,j \quad (8)$$

Where $\eta_m = X\eta_c + \ 1-X\ \eta_p$are the viscosity coefficients of blood as a mixture of two phase. Hence a yield stress is produced. Though this yield stress is very small, even then the viscosity of blood is increased nearly ten times.

The Herschel- Bulkley law holds good on the two phase blood flow through venules and whose constitutive equation is as fallows- $T' = \eta_m e^n + T_p\ \ T' \geq T_p$ .where, $T_p$is the yield stress.

When strain rate $e = 0\ (T' < T_p)$a core region is formed which flows just like a plug. Let the radius of the plug be r_p. The stress action on the surface of plug will be T_p. Equating the forces acting on the plug, we get, Whose generalizes from will be as follows-

$$T^{ij} = -Pg^{ij} + T_e^{ij} \quad (9)$$

Where $T^{ij} = \eta_m(e^{ij})^n$ while $e^{ij} = (g^{jk}V^i_{,k} + g^{ik}V^j_{,k})$, and there symbols have their usual meanings. Now we have consider the basic equation for Herschel-Bulkley flow as follows.

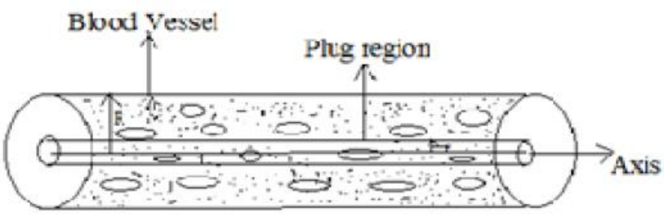


Fig. Herschal-Bulkley blood flow

Equation of Continuity- $\frac{1}{\sqrt{g}}\left(\sqrt{g}V^i\right)_{,i} = 0$ (10)

Equation of Motion- $\rho_m\frac{\partial V^i}{\partial t} + \rho_m V^j V^i,j = -T^{ij}e,j$ (11)

Where, all the symbols have their usual meaning.

Analysis

Since, we have supposed the blood vessels are cylindrical; the above governing equations have to be transformed into cylindrical co-ordinates. As we know earlier: $X^1 = r, X^2 = \theta,\ X^3 = z.$

Matrix of metric tensor in cylindrical co-ordinates is as follows- $g^{ij} = \begin{matrix} 1 & 0 & 0 \\ 0 & r^2 & 0 \\ 0 & 0 & 1 \end{matrix}$

While matrix of conjugate metric tensor is as follows- $g_{ij} = \begin{matrix} 1 & 0 & 0 \\ 0 & \frac{1}{r^2} & 0 \\ 0 & 0 & 1 \end{matrix}$

Where the Christoffel's symbols of 2^{nd} kind as follows-

${1 \atop 2\quad 2} = -r,\quad {1 \atop 2\quad 2} = {1 \atop 2\quad 2} = \frac{1}{r}$ Remaining others is zero.

Relation between contra variant and physical components of velocity of blood flow will be as follows- $\overline{g^{11}v^1} = v_r \Rightarrow v_r = v^1$, $\overline{g^{22}v^2} = v_\theta \Rightarrow v_\theta = rv^2$, $\overline{g^{33}v^3} = v_z \Rightarrow v_z = v^3$, again the physical components of $p_{,j}g^{ij}$ are $\overline{g_{ij}}p_{,j}g^{ij}$ and Now, equation (3.9) and (3.10) are transformed into cylindrical from so as to solve as power law to get –

Equation of continuity: $\frac{\partial V}{\partial Z} = o$

The equation of motion- r-component: $-\frac{\partial p}{\partial z} = 0$, $\theta -$ component: $0 = 0$, z-component: $0 = -\frac{\partial p}{\partial z} + \frac{\eta_m}{r}\ r\ \frac{\partial V_z}{\partial r}\ ^n$, Here, this fact has been taken in view that the blood flow the axially symmetric in arteries concerned, i.e. $V_\theta = 0$ and $V_r, V_z and p = p\ z\ and$

$$0 = -\frac{\partial p}{\partial z} + \frac{\eta_m}{r}\ r\ \frac{\partial V_z}{\partial r}\ ^n \tag{12}$$

Since, pressure gradient$-\frac{dp}{dz} = P$

$r\ \frac{dV}{dZ}\ ^n = -\frac{Pr^2}{2\eta_m} + A$, we apply boundary condition at $r = 0. V = V_0$ than $A = 0$.

$\Rightarrow -\frac{dv}{dr} = \frac{Pr}{2\eta_m}\ ^{\frac{1}{n}}$ Replace from $r - r_p$,

$$-\frac{dv}{dr} = \frac{\frac{1}{2}pr - \frac{1}{2}p_r}{\eta_m}\ ^{\frac{1}{n}} \Rightarrow \frac{dv}{dr} = -\ \frac{P}{2\eta_m}\ ^{\frac{1}{n}} (r - r_p)^{\frac{1}{n}} \tag{13}$$

Now integrating above equation (3.2) under the no slip boundary condition $V = 0$ at $r = R$ so we get -

$$v = \frac{P}{2\eta_m}\ ^{\frac{1}{n}} \frac{n}{n+1}\quad R - r_p\ ^{\frac{1}{n}+1} - \ r - r_p\ ^{\frac{1}{n}+1} \tag{14}$$

This is the formula for velocity of blood flow in venules. Putting $r = r_p$ to get the velocity v_p of plug flow as follows:

$$v_P = \frac{n}{n+1}\ \frac{P}{2\eta_m}\ ^{\frac{1}{n}}\ R - r_p\ ^{\frac{1}{n}+1} \tag{15}$$

Where, the value of r_p is taken form (2.7).

RESULTS AND DISCUSSION

Examination: Hematocrit v/s blood pressure in during Lung Cancer patient.

Patient name: Mr. Ratiram

Age: 64 years old

Diagnosis: Lung cancer (Pulmonary disease)

Table 1. For Hemoglobin v/s blood Pressur in Clinical data

Date	HB(Hemoglobin) in (gram/dl)	Hematocrit in ($\mathbf{3} \times \boldsymbol{HB}$) (kg/m^3)	Blood Pressure (BP) in (mmhg)	Venules Pressure Drop in Pascal-second $\frac{2}{3}\frac{\frac{S+D}{2}+D}{3} - \frac{\frac{S+D}{2}+D}{3}$
17/06/2016	8.0	0.02265	120/80	-2662.64
18/06/2016	11.3	0.03207	110/70	-2366.79141
21/06/2016	7.2	0.02038	130/90	-2958.48993
24/06/2016	7.0	0.01982	140/80	-2810.56563

The flow two phase blood flows in venules is-

$$Q = \int_o^{r_p} 2\pi r v_p + \int_{r_p}^{R} 2\pi r v dr$$

$$= \int_0^{r_p} 2\pi r \frac{n}{n+1} \left(\frac{P}{2\eta_m}\right)^{\frac{1}{n}} (R - r_p)^{\frac{1}{n}+1} dr + \int_0^{r_p} 2\pi r \frac{n}{n+1} \left(\frac{P}{2\eta_m}\right)^{\frac{1}{n}} \left[(R - r_p)^{\frac{1}{n}+1} - (R - r_p)^{\frac{1}{n}+1} \right] dr$$

Using equations (3.2) and (3.4), we get

$$Q = \frac{\pi n}{(n+1)} \left(\frac{P}{2\eta_m}\right)^{\frac{1}{n}} R^{\frac{1}{n}+3} \left[\frac{r_p^2}{r^2}\left(1 - \frac{r_p^2}{R}\right)^{\frac{1}{n}+1} + \left(1 + \frac{r_p}{R}\right)^{\frac{1}{n}+1}\left(1 - \frac{r_p}{R}\right)^{\frac{1}{n}+2} - \frac{2\left(1-\frac{r_p}{R}\right)^{\frac{1}{n}+2}}{\frac{1}{n}+2} + \frac{2\left(1-\frac{r_p}{R}\right)^{\frac{1}{n}+3}}{\left(\frac{1}{n}+2\right)\left(\frac{1}{n}+3\right)} \right] \quad (16)$$

Now, we have, $Q = 425 \frac{\text{ml}}{\text{min}}$, $Q = 0.00708333\ m^3/\text{second}$ and $R = 1$, $r_p = \frac{1}{3}$,

According to Gustafson, Daniel R. (1980), $\eta_p = 0.0013$ pascal second and according to Glenn Elert (2010), $\eta_m = 0.0271$ pascal second and $H = 0.01982$, Pressure drop $P_f - P_i = 2810.56563$ Pascal second, Pulmonary venules average length = 0.15 cm or $0.15 \times 10^{-9} m^3$ (According to J.T. Ottesen, M.S. Olufsen, and J.K. Larsen, 2006)

By using relation $\eta_m = \eta_c X + \eta_p (1 - X)$ Where, $X = \frac{H}{100}$, and we get η_c

$\eta_m = \eta_c X + \eta_p (1 - X)$, $\Rightarrow \eta_c = 136.364694$ Pascal second

Again using above relation and change in to the hematocrit-

$\eta_m = \eta_c X + \eta_p (1 - X)$ $\Rightarrow \eta_m = 136.364694H + 0.0012998$

Now substituting the values of r_p and R in Equation (4.1)-

$$Q = \frac{\pi n}{(n+1)} \left(\frac{P}{2\eta_m}\right)^{\frac{1}{n}} R^{\frac{1}{n}+3} \left[\frac{r_p^2}{r^2}\left(1 - \frac{r_p^2}{R}\right)^{\frac{1}{n}+1} + \left(1 + \frac{r_p}{R}\right)^{\frac{1}{n}+1}\left(1 - \frac{r_p}{R}\right)^{\frac{1}{n}+2} - \frac{2\left(1-\frac{r_p}{R}\right)^{\frac{1}{n}+2}}{\frac{1}{n}+2} + \frac{2\left(1-\frac{r_p}{R}\right)^{\frac{1}{n}+3}}{\left(\frac{1}{n}+2\right)\left(\frac{1}{n}+3\right)} \right]$$

And we get equation- $Q = \pi \left(\frac{2P}{6\eta_m}\right)^{\frac{1}{n}} \frac{2}{27} \frac{26n^3+33n^2+9n}{6n^3+11n^2+6n+1}$ Or, $\frac{27\times Q}{2\pi} = \left(\frac{P}{3\eta_m}\right)^{\frac{1}{n}} \frac{26n^3+33n^2+9n}{6n^3+11n^2+6n+1}$

And limit from the pressure from Z_f to Z_i then - $\int_{P_f}^{P_i} dP = -\int_{Z_f}^{Z_i} \left(\frac{27\times Q}{2\pi A}\right)^n . 3\eta_m dz$

$P_f - P_i = \left(\frac{27\times Q}{2\pi A}\right)^n . 3\eta_m . (Z_f - Z_i)$ Or, $\frac{27\times Q}{2\pi A} = \left(\frac{P_f - P_i}{(Z_f - Z_i) 3\eta_m}\right)^{1/n}$, $\frac{27\times Q}{2\pi} = \frac{26n^3+33n^2+9n}{6n^3+11n^2+6n+1} \left(\frac{P_f - P_i}{(Z_f - Z_i) 3\eta_m}\right)^{1/n}$

Substituting the value of Q, η_m, $P_f - P_i$ *and* $Z_f - Z_i$ and solve by numerical methods $\frac{27\times 0.0070833}{6.28} = \frac{26n^3+33n^2+9n}{6n^3+11n^2+6n+1} \left(\frac{2810.56563}{0.15\times 10^{-9}\times 0.0813}\right)^{1/n}$ $\Rightarrow 0.03045669 = \frac{26n^3+33n^2+9n}{6n^3+11n^2+6n+1} (69140610000000)^{1/n}$ and we get $n = -6.52$

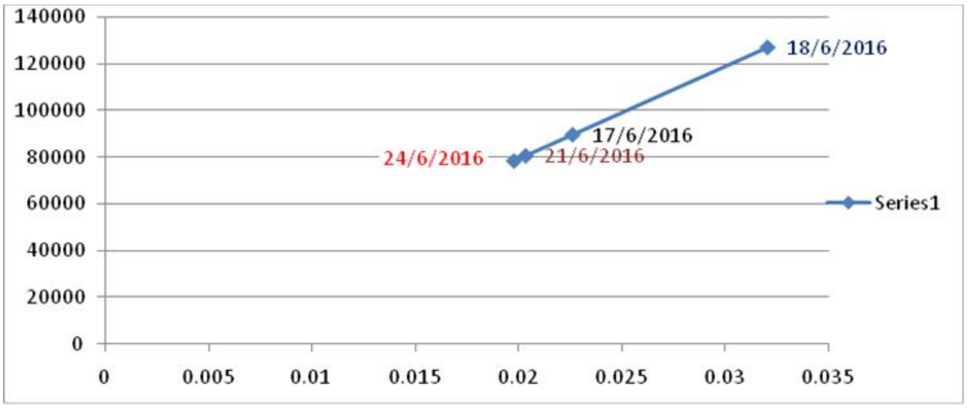
Now again using equation $P_f - P_i = \left(\frac{27\times Q}{2\pi A}\right)^n . 3\eta_m . (Z_f - Z_i)$ $\Rightarrow \Delta P = \left(\frac{27\times Q}{2\pi A}\right)^n . 3\eta_m . (Z_f - Z_i)$

$\Delta P = 3957842.060422H + 37.7253303$

Table 2. For Hematocrit v/s blood Pressure drop in Clinical data

Date	17/6/2016	18/6/2016	21/6/2016	24/6/2016
H (Hematocrit) In kg/m^3	0.02265	0.03207	0.02038	0.01982
BPD (Blood Pressure drop) In Pascal-second	89682.847999	126965.720209	80698.5465218	78482.8479989

Biophysical Interpretation (Graphical presentation of Clinical Data)



Observation

A mathematically investigation of the graph from 17/6/2016 to 18/6/2016 shows increasing sence. Whereas from 18/6/2016 via 21/6/2016 to 24/6/2016 shows decreasing sence.

Conclusion

When blood pressure drop is increased then we cannot suggest for operation but when blood pressure drop is decreased we suggest for successful operation. Between 17/6/2015 to 24/6/2016 successful operation is suggested otherwise not.

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