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Exploring capillary-tissue fluid exchange: Insights into red cell deformation in narrow vessels and its clinical implications

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Abstract
This work focuses on how blood move between tiny blood vessels (capillaries) and surrounding tissues, especially when the capillary diameter is smaller than that of red blood cells (RBCs). It has shown that in such narrow vessels, there is very little space between the RBC and the vessel wall, allowing plasma to squeeze through. It is shown in this work at how different factors like the shape of deformed RBCs, their speed, and how easily tissues allow fluids to pass (permeability) affect the flow of blood. It has also shown that when tissues are less permeable, blood flow is smoother. Also, faster-moving RBCs encounter less resistance. By comparing its findings with other models, this study demonstrates its value in understanding blood flow dynamics in small vessels. This knowledge could lead to the development of new diagnostic tools for various diseases.

Keywords: Fluid exchange, narrow capillaries, cell deformation, resistance to flow, red blood cells

1. Introduction
Understanding the intricate dynamics of red blood cell (RBC) deformation within narrow capillaries is pivotal for unraveling crucial physiological processes and pathological conditions. The biomechanical approach to studying such phenomena offers a comprehensive framework that integrates principles from both mechanics and biology. By delving into the mechanical behavior of RBCs under the constraints of confined spaces, this approach provides invaluable insights into the mechanisms governing blood flow at the microscale [4, 14, 25, 34]. In this study, we embark on a journey to explore the biomechanics of RBC deformation within narrow capillaries, aiming to shed light on the underlying principles dictating their behavior. With a focus on elucidating the intricate interplay between cellular morphology, fluid dynamics, and tissue biomechanics, our investigation seeks to unravel the complexities of RBC motion in constrained microenvironments [9, 18, 29, 45, 49]. Through a synthesis of theoretical modeling, experimental observations, and clinical correlations, we aim to decipher the biomechanical signatures of RBC deformation and its implications for health and disease [2, 13, 22, 53]. By unraveling the fundamental principles governing RBC behavior in narrow capillaries, we strive to pave the way for the development of innovative diagnostic and therapeutic strategies targeting microcirculatory disorders and related pathologies [6, 17, 26, 37, 46]. Thus, this biomechanical exploration serves as a cornerstone for advancing our understanding of blood flow dynamics at the microvascular level, offering profound insights into the intricate interplay between mechanical forces and biological phenomena within the circulatory system [3, 43, 52].
Blood is made up of tiny red blood cells floating in a liquid called plasma. Imagine it like a bowl of fruit salad, where the red blood cells are the fruits and the plasma is the syrup. Scientists have spent a lot of time studying these red blood cells to understand how they work [5, 7, 10, 16, 25, 27, 47]. Under normal conditions, red blood cells look like tiny, round discs, kind of like miniature pancakes. They're about 8 micrometers wide and only 2 micrometers thick, so you'd need a microscope to see them. Inside these cells, there's a gooey fluid that behaves a bit like thick syrup [8, 19, 28, 36, 39, 48]. The outer part of these cells is made up of a special kind of skin called a membrane. It's like the peel of a fruit, but much thinner. This membrane is really good at keeping its shape and doesn't like changing size easily [11, 20, 21, 51]. It's kind of like trying to stretch or squish a balloon - it resists changes to its surface.

This membrane is made of two layers of molecules, sort of like a sandwich. The molecules in these layers can slide past each other, but they don't like to separate. Also, this membrane isn't very good at bending [1, 31, 40, 41, 50]. It's quite stiff compared to other materials. When the red blood cells move around, this membrane can resist changes caused by forces pushing on them from different directions. It's a bit like how a rubber band resists being stretched or twisted. Scientists have even come up with fancy mathematical models to describe how this membrane behaves when it's pushed or pulled. This study will help to understand how red blood cells keep their shape and move around in our bodies, which is pretty important for keeping us healthy.

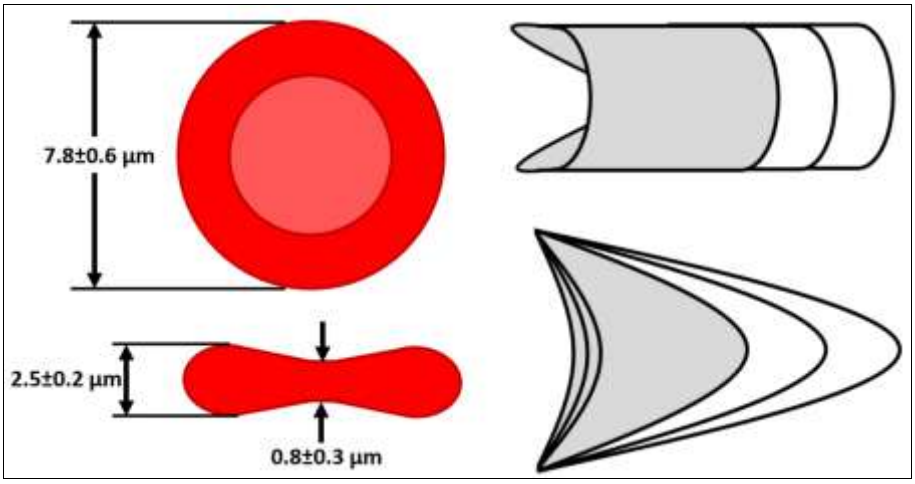

Fig 1: Deformation of Red Cells

Blood flows like a transportation system in your body. It carries important stuff like nutrients and removes waste, kind of like how trucks deliver groceries and pick up trash. In healthy blood vessels, the flow is smooth, like water flowing down a river. But sometimes, things can go wrong, and this can lead to problems like heart disease. In really tiny blood vessels called capillaries, which are thinner than a single strand of hair, blood flow is super important. Imagine trying to squeeze through a tight alley [30, 35, 44]. It's a bit like that for your blood cells. As your blood cells travel through these tiny capillaries, they change shape to fit through. It's like squeezing a big balloon through a narrow gap. It squishes and stretches to get through. This change in shape is caused by pressure from the surrounding plasma, which is like the fluid that surrounds the cells. This pressure makes the cells kind of squishy, so they can fit through the narrow capillaries. And there's another important thing happening: a thin forms between blood cell and wall of capillary [23, 32, 38]. This layer helps with stuff like moving nutrients and oxygen between the blood and the tissues, and it also affects how easily the blood flows. These processes are really important for keeping your body working well and making sure everything gets where it needs to go.

2. Defining the problem statement

This model represents red blood cell like an axisymmetric structure having incompressible fluid. It considers a scenario where red blood cells flow in a single file, and interactions between cells are disregarded. In this context, 'H' denotes thickness of porous matrix, 'u' represents velocity of cell at a certain point, and 'h' stands for the fluid film thickness. Additionally, 'a' signifies the focal length of the initially assumed parabolic shape, while $(\alpha\pm\beta)'(p'-p_0)$ represents further deformation resulting from increased pressure within wedge formed between the parabolic shape and capillary [15, 24]. Flow region is divided into two distinct regions, and governing equations are separately formulated for each region, as outlined below.

Within the capillary region, equation is as follows.

$$\left(-\frac{\partial p'}{\partial x'}\right)+\mu\frac{\partial^2 u'}{\partial y'^2}=0 \quad (1)$$

The equation of continuity describes how the flow of fluid is conserved within a given system.

$$\frac{\partial u'}{\partial x'}+\frac{\partial v'}{\partial y'}=0 \quad (2)$$

In the porous region, the velocity components within the matrix can be described using Darcy's law.

$$\underset{u'}{\rightarrow}=(K/\mu\frac{\overrightarrow{\partial P}}{\partial x'}) \quad (3)$$

$$\underset{v'}{\rightarrow}=(-K/\mu\frac{\overrightarrow{\partial P}}{\partial y'}) \quad (4)$$

The equation that governs the distribution of pressure within the porous matrix is given by.

$$\frac{\partial^2 \bar{p}'}{\partial x'^2} + \frac{\partial^2 \bar{p}'}{\partial y'^2} = 0 \quad (5)$$

To solve the aforementioned equations, the following matching and boundary conditions are introduced.

$$u' = u_0 \qquad at \qquad u' = h'$$

$$u' = \left[(-\sigma)\left(\frac{\partial u'}{\partial x'}\right)\right] \qquad at \qquad y' = 0$$

$$u' = \left[(-\mathrm{K}/\mu \frac{\overrightarrow{\partial P}}{\partial x'}) \right] \qquad at \qquad y' = 0$$

$$v' = 0 \qquad at \qquad y' = h'$$

$$v' = \left[(-\mathrm{K}/\mu \frac{\overrightarrow{\partial P\prime}}{\partial y'}) \right] \qquad at \qquad y' = 0$$

$$\left(\frac{\overrightarrow{\partial P\prime}}{\partial x'}\right) = 0 \qquad at \qquad x' = 0$$

$$\underset{p'}{\rightarrow} = 0 \qquad at \qquad x' = 1$$

$$\left(\frac{\overrightarrow{\partial P\prime}}{\partial y'}\right) = 0 \qquad at \qquad y' = 0$$

$$\underset{p'}{\rightarrow} = p_0 \qquad at \qquad x' = 0 \quad (6)$$

1. The slip parameter σ' is like a measure of how easily things can slide past each other. So, when μ is high, it means things can slide past each other easily, and when it's low, things don't slide as easily.
2. The reference pressure P_0 is like a starting point. It's the pressure we use as a reference when talking about changes in pressure.
3. The radial compliances (α and β) are like measures of how much the capillary and cell can stretch or change shape sideways. When we talk about them together ($\alpha + \beta$), we're considering them as a combined effect.
4. The effective length of the capillary (2l) is just how long the capillary is, but it's doubled for some reason, because we're looking at both ends of it.
5. Initial gap at point where parabola touches is like a small space between the parabola shape and the capillary wall. We are saying it's so tiny compared to the thickness (H) of the porous layer that we can ignore it. It's like saying a crack in the sidewalk is so small that it doesn't really matter.

2.1 The equations are solved using a non-dimensional scheme introduced as follows

$$x = x'/H'; \; y = y'/H';$$

$$p = p'/P_0; \; u = u'/u_0;$$

$$Re = \rho u_0 H/\mu; \; v = v'/u_0;$$

$$(\alpha+\beta) = (\alpha+\beta)'/(H'^3/\rho u_0^2);$$

$$p = p'/P_0; \sigma = \sigma'/H';$$

$$\varepsilon = H'/4a'; h = \eta(p\text{-}1) + \varepsilon x^2 \quad (7)$$

To solve the aforementioned equations, the following boundary conditions and matching conditions are applied.

$$u = 1 \qquad at \qquad y = h$$

$$u = \left[(-\sigma)\left(\frac{\partial w}{\partial y}\right)\right] \quad at \quad y = 0$$

$$v = 0 \quad at \quad y = h$$

$$v - \left[(-\mathrm{Kp}/\mu Uo\, H \frac{\overrightarrow{\partial P}}{\partial y})\right] \quad at \quad y - 0$$

$$\left(\frac{\overrightarrow{\partial P}}{\partial x}\right) = 0 \quad at \quad x = 0$$

$$\underset{P}{\rightarrow} = 0 \quad at \quad x = 1$$

$$\left(\frac{\overrightarrow{\partial P}}{\partial y}\right) = 0 \quad at \quad y = -1$$

$$p = 1 \quad at \quad x = 1 \qquad (8)$$

3. Problem Solution

The blood is moving and it is considered that the amount of blood going in equals the amount coming out (equation of continuity), and we've set up the rules for how the blood behaves at the edges (boundary and matching conditions), we can work out exactly how fast the blood is moving at different points in the capillary by solving the equations.

$$u = \frac{P_0 H}{U_0 \mu}\frac{\partial p}{\partial x}(y^2 - \frac{(\mathrm{y\text{-}\sigma})}{(\mathrm{h\text{-}\sigma})}h^2) + \frac{\mathrm{y\text{-}\sigma}}{\mathrm{h\text{-}\sigma}} \qquad (9)$$

By solving above equation, we have

$$\bar{p} = \sum_{n=0}^{\infty} 2\mathrm{En}\cosh\{\alpha_n(\mathrm{H+y})\}\cos(\alpha_n x) \qquad (10)$$

Where $\alpha_n = (2\mathrm{n}+1)\pi/21)$

$$\mathrm{En} = \frac{1}{\alpha_n}\operatorname{sech}(\alpha_n H)\cos(\mathrm{n}\pi) \qquad (11)$$

$$P = [Z_n(P_0 A_1 x^2 + \mathrm{A}_2 x^4 + \mathrm{A}_3 x^2)] -$$

$$[Z_n({\alpha_n}^2/2)(P_0 x^4(A_1/6) + \mathrm{x}^6(2\mathrm{A}_2/5)$$

$$+\mathrm{x}^4(A_3/6))] + 1 - [Z_n(P_0 A_1 + \mathrm{A}_2 + \mathrm{A}_3)] +$$

$$[Z_n({\alpha_n}^2/2)(P_0(A_1/6) + (2\mathrm{A}_2/5) + (A_3/6))] \qquad (12)$$

We determine the Flow Resistance as.

$$R^* = (1/\mathrm{Q})[\mathrm{Zn}(P_0 A_1 x^2 + \mathrm{A}_2 x^4 + \mathrm{A}_3 x^2)] -$$

$$[\mathrm{Zn}({\alpha_n}^2/2)(P_0 x^4(A_1/6) + \mathrm{x}^6(2\mathrm{A}_2/5) + \mathrm{x}^4(A_3/6))] \qquad (13)$$

$$\text{Where}\mathrm{Zn} = [(3\mathrm{K}/2\mathrm{H}^2\sigma)\sum_{n=0}^{\infty}\mathrm{En}{\alpha_n}^3\sinh\alpha_n(\mathrm{H+y})] \qquad (14)$$

$$A_1 = ((-3\sigma/2\eta^2) + (1/8\sigma) - (3/4\eta)),$$

$$A_2 = (-(3\varepsilon'\sigma/12\eta^3) + (\varepsilon'/48\sigma\eta) - (3\varepsilon'/24\eta^2))$$

$$A_3 = (-(\sigma/2\eta^3) + (1/8\sigma\eta) - (3/8\eta^2))$$

$$\eta = (H^2 P_0(\alpha+\beta)/\rho {U_0}^2) \qquad (15)$$

4. Results and discussion

To understand how different factors affect blood flow resistance in narrow capillaries, we have created computer programs. These programs helped to assess the quantitative impact of parameters like cell shape and velocity. Then we have used the data generated by these simulations to evaluate how blood flow resistance behaves under normal conditions. This process ensures that the computational models accurately reflect real world physiological scenarios. In Figure 2, the plotted data demonstrates the relationship between the resistance to flow and variations in a specific parameter. As this parameter increases, there is a corresponding decrease in the resistance to flow. This phenomenon arises due to alterations in pressure gradients within the wedge-shaped region, leading to deformations in both erythrocyte and the capillary wall near narrowest part of interstitial space. These deformations directly impact the resistance to flow. Elevated pressure levels induce more pronounced cell deformations, consequently reducing the resistance to flow [33, 42]. In Figure 3, the graph depicts the changes in resistance to flow relative to variations in the parameter H. As the values of H increase, resistance to flow in gap decreases. Our observations align closely with previously reported findings [12].

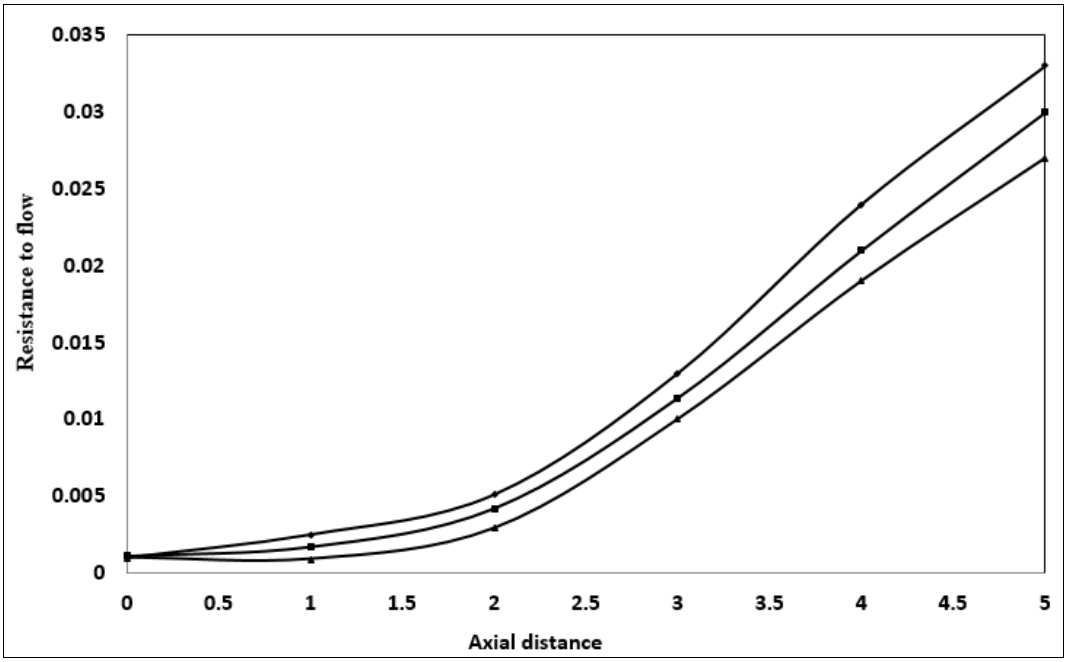

Fig 2: Resistance to flow for different shapes of cell

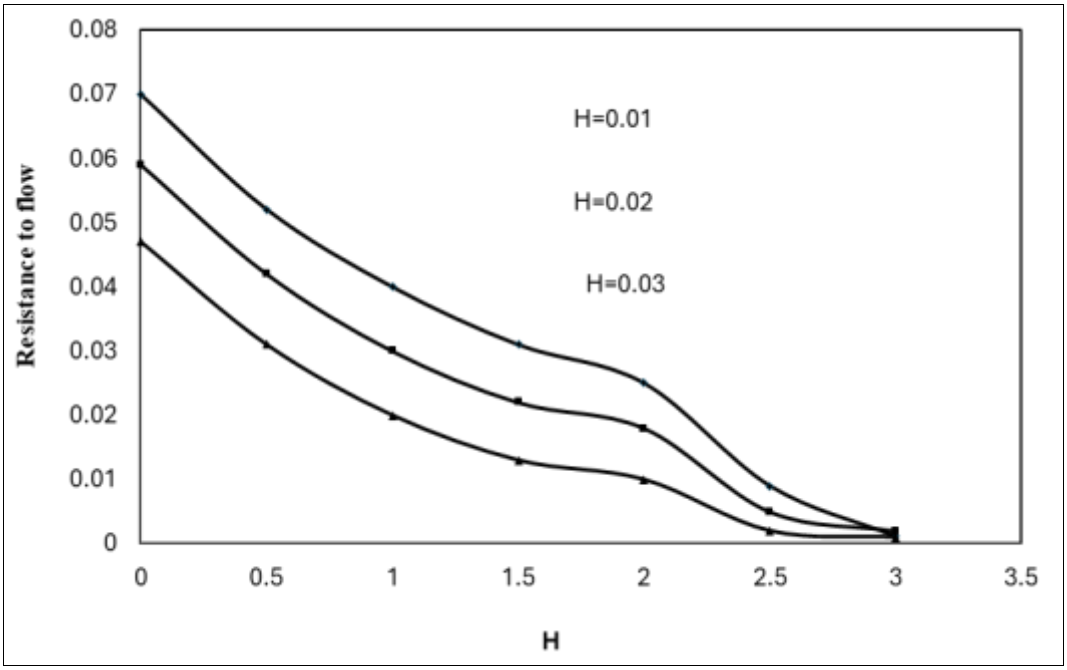

Fig 3: Resistance to flow for different H

5. Conclusion

This study employs a computational model to investigate the dynamics of capillary-tissue fluid exchange when diameter of capillary is smaller than that of a red blood cell. This investigation explores resistance to flow under diverse conditions,

encompassing variations in the shapes of deformed red blood cells, cell velocities, and permeability. The findings reveal a direct correlation between decreased permeability and reduced resistance to flow, suggesting a resemblance to impermeable surfaces in tissue behavior. Additionally, the analysis demonstrates that resistance to flow within the gap diminishes as cell velocity increases. Through a comparative analysis with existing models, the study underscores the significance of the proposed model, both theoretically and computationally. Notably, this model accurately predicts fundamental characteristics of physiological fluid dynamics, offering valuable insights for researchers in biomedical science and medical professionals.

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