Estimation of Arterial Stiffness through Pulse Transit Time Measurement

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Abstract: Early detection of cardiovascular disease (CVD) and its treatment is significantly expected to reduce the mortality rate across the world. While several diagnostic techniques have been developed for early detection of the CVD, recent focus has been on measuring the 'arterial stiffness', which appears to be a major indicator of onset of cardio vascular disease. In this work, authors consider three mathematical models that relate pulse wave velocity (PWV) with arterial stiffness. While one model considers blood to be a non-viscous and incompressible fluid, the other considers it to be a viscous and compressible. Pulse transit time has been measured experimentally for five different individuals of different ages and heights from where PWV has been estimated. Using values of PWV, Young's modulus of elasticity has been derived. Data related to arteries such as radius, wall thickness, density and viscosity of blood have been taken from published literature where these parameters have been measured using techniques such as MRI. Initial results indicate that different models predict different estimates for arterial stiffness that depend on assumptions made.

1 INTRODUCTION

Arterial stiffness is considered to be an indicator of vascular changes that may eventually result in major vascular disease (Fung et al., 2004); (Hasegawa et al., 2004); (Mazumdar et al., 2004). Early detection of a stiffening artery might help in taking preventive medication that will slow down the progress of vascular changes.

Propagation of blood pressure pulse wave is affected by the arterial stiffness and thus pulse wave velocity (PWV) is a good measure of stiffness of artery. Since PWV is related to pulse transit time (PTT), it is possible to derive PWV by measuring PTT experimentally (Fung et al., 2004;Ye et al., 2010). There are two different ways in which PWV can be measured:

1. By dividing the distance between two arterial sites by the difference in time of pressure pulse arrival w.r.t the R wave of EKG signal
2. By measuring the time difference between R wave of ECG signal and characteristics point of PPG signal and dividing the same with length of the artery.

Further, different mathematical models have been proposed from time to time to estimate arterial stiffness by relating PWV with young's modulus of elasticity (Fung et al., 1984); (Olufsen et al., 2000); (Kurtz et al., 2003). These models include that of inviscid (incompressible) flow and viscous flows. In what follows, these models are discussed in some detail and used to estimate young's modulus of elasticity of arteries of a small sample of subjects using experimental data obtained. A comparison is also made of estimates given by different models.

2 MATHEMATICAL MODELS

2.1 Inviscid Flow – Moens-Kortweg Equation

We know that the flow of blood in arteries is pulsative due to the beating of the heart. This beating produces a pressure wave to travel through the blood. Let u and v be the axial and radial components of the fluid velocity. Let ρ be the density of the fluid. The following assumptions have been made in deriving a mathematical model for the above mentioned problem (Mazumdar et al., 2004).

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The flow is pulsatile and axi-symmetric

- The pipe is an elastic circular straight pipe with radius ‘a’.
- The fluid is Newtonian with constant viscosity ‘μ’
- The axial flow velocity is small relative to the pulse wave velocity
- The vessel diameter is of an order of magnitude smaller than the wave length.

Hence, the equation of continuity and the momentum equation take the form:

$$\frac{\partial u}{\partial x}+\frac{1}{r}\frac{\partial}{\partial r}\left(rv\right)=0 \tag{1}$$

$$\rho\frac{\partial u}{\partial t}=-\frac{\partial p}{\partial x} \tag{2}$$

$$\frac{\partial p}{\partial r}=0 \tag{3}$$

The wall displacement η is governed by

$$\eta=\frac{a^2}{hE}p\left(x,t\right) \tag{4}$$

Where E is the wall material elastic modulus and h is the thickness of the wall.

Using the boundary conditions given by

$$v_w\left(x,t\right)=\dot{\eta}\left(x,t\right) \tag{5}$$

Where v_w is the wall velocity, we have that the pressure p satisfies the wave equation

$$\frac{\partial^2 p}{\partial x^2}=\frac{1}{c^2}\frac{\partial^2 p}{\partial t^2} \tag{6}$$

With

$$c=\left(\frac{Eh}{2a\rho}\right)^{1/2} \tag{7}$$

where c is the pulse wave velocity.

2.2 Viscous Flow

In this model, the viscous effects are taken into consideration. The governing equations are:

$$\frac{\partial u}{\partial x}+\frac{1}{r}\frac{\partial}{\partial r}\left(rv\right)=0 \tag{8}$$

$$\rho\frac{\partial u}{\partial t}=-\frac{\partial p}{\partial x}+\mu\left(\frac{\partial^2 u}{\partial r^2}+\frac{1}{r}\frac{\partial u}{\partial r}\right) \tag{9}$$

$$\frac{\partial p}{\partial r}=0 \tag{10}$$

Further, the displacement equations of the elastic tube of wall thickness ‘h’, wall density ‘ρ_w’, wall modulus ‘E’ and Poisson ratio ‘ν’ are taken as

$$\begin{aligned}\rho_w h\frac{\partial^2\eta}{\partial t^2}&=-p-\frac{Eh}{1-\nu^2}\left(\frac{\eta}{a^2}+\frac{\nu}{a}\frac{\partial\xi}{\partial x}\right)\\ \rho_w h\frac{\partial^2\xi}{\partial t^2}&=-\mu\frac{\partial u}{\partial r}-\frac{Eh}{1-\nu^2}\left(\frac{\partial^2\xi}{\partial x^2}+\frac{\nu}{a}\frac{\partial\eta}{\partial x}\right)\end{aligned} \tag{11}$$

Where ζ is the axial displacement and η is the radial displacement of the tube (Mazumdar et al., 2004).

Boundary conditions are:

$$\left(\frac{\partial\xi}{\partial t}\right)_{r=a}=u,\left(\frac{\partial\eta}{\partial t}\right)_{r=a}=v \tag{12}$$

Assuming that

$$\begin{aligned}u(x,r,t)&=u_0(r)e^{i(kx-wt)}\\ v(x,r,t)&=v_0(r)e^{i(kx-wt)}\\ p(x,t)&=p_0e^{i(kx-wt)}\\ \xi(x,t)&=\xi_0e^{i(kx-wt)}\\ \eta(x,t)&=\eta_0e^{i(kx-wt)}\end{aligned} \tag{13}$$

Where,

$$\omega=\frac{2\pi}{60}*Heartrate$$

$\lambda=\frac{2\pi}{k}$ (Wave length) and $c=\frac{\omega}{k}$ (wave speed).

Solving equations (8)-(11) and using the boundary conditions given by (12), we have that the elastic modulus E is given by

$$\left(\left(1-2\nu\right)\bar{X}-2\rho\right)\left(\left(\frac{\nu}{a\beta}-\frac{J_0\left(a\beta\right)}{J_1\left(a\beta\right)}\right)\bar{X}+\frac{\rho}{a}\right)+\left(2-\nu\right)\left(\frac{1}{a\beta}-\frac{J_0\left(a\beta\right)\nu}{J_1\left(a\beta\right)}\right)\bar{X}^2=0 \tag{14}$$

Where

$$\bar{X}=\frac{k^2Eh}{\omega^2(1-\nu^2)a} \tag{15}$$

$$\beta = \frac{i\omega\rho}{\mu} \tag{16}$$

3 EXPERIMENTS

Experiments have been performed on a small sample of five different human subjects of different ages and heights. Experimental measurement of ECG and PPG has been carried out and time difference between R-wave peak and characteristic point of PPG signals calculated to determine PTT.

The following picture illustrates the recorded ECG/PPG signals on one subject for the calculation of PTT.

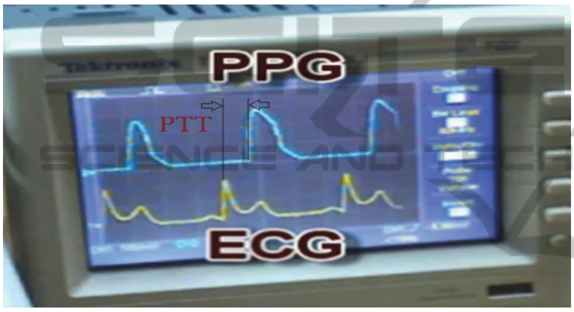

Figure 1: Measurement of PTT from PPG and ECG.

Two mathematical models described above have been used to estimate the Young's Modulus E of the arteries.

Since both models require value of PWV, PTT needs to be calculated using which PWV is estimated by equation below (Avril et al., 2008).

$$PWV = \frac{d}{PTT} \tag{17}$$

Where d is the arterial length between the heart and fingertip, which is correlated with height of a person through (Ye et al., 2010):

$$d = 0.6 \times height \tag{18}$$

4 RESULTS

Table 1 below lists the measurements made on five different individuals of different heights and age.

The estimated value of Young's Modulus using Model 1, assuming physiological parameters of artery given in (Avril et al., 2008), is given in Table 2 below.

Table 1: Physiological parameters.

Parameter	Sub-1	Sub-2	Sub-3	Sub-4	Sub-5
Age	27 years	49 years	25 years	29 years	39 years
Height	174 cms	152.4 cms	175 cms	173 cms	170 cms
PTT	244ms	205 ms	205 ms	275 ms	260 ms
PWV	4.28 m/s	4.46 m/s	5.12 m/s	3.77 m/s	3.92 m/s

Table 2: Parameters for Model I.

Parameter	Sub- 1	Sub- 2	Sub-3	Sub-4	Sub-5
Radius of radial artery	2.5 mm	2.5 mm	2.5 mm	2.5 mm	2.5 mm
Wall thickness of radial artery	0.25 mm	0.25 mm	0.25 mm	0.25 mm	0.25 mm
Young's Modulus	563.8K Pa	612.3 KPa	556.2K Pa	302.1 KPa	326.2K Pa

The estimated value of Young's Modulus using Model 2 and assuming physiological parameters of artery given in (Hasegawa et al., 2004; Mazumdar et al., 2004; Avril et al., 2008) is given in Table 3 below.

Table 3: Parameters for Model II.

Parameter	Sub-1	Sub-2	Sub-3	Sub-4	Sub-5
Poison's ratio	0.5	0.5	0.5	0.5	0.5
Density of blood	1050 kg/m3	1050 kg/m3	1060 kg/m^3	1060 kg/m^3	1060 kg/m^3
Radius of radial artery	2.5 mm	2.5 mm	2.5 mm	2.5 mm	2.5 mm
Wall thickness of radial artery	0.25 mm	0.25 mm	0.25 mm	0.25 mm	0.25 mm
Viscosity of blood	0.004 PaS	0.004 PaS	0.004 PaS	0.004 PaS	0.004 PaS
Young's Modulus	4.8964 MPa	5.3169 MPa	7.01229 MPa	3.8082 MPa	4.1138 MPa

A comparison of Young's modulus obtained by both the models for all five subjects is given in Table 4 below.

Table 4: A Comparision of young's modulus derived using Model I and Model II.

Subject / Model Used	Model I	Model II
Subject 1	388.12 KPa	4.8934 MPa
Subject 2	421.794 KPa	5.3181 MPa
Subject 3	556.17 KPa	7.01229 MPa
Subject 4	302.04 KPa	3.8082 MPa
Subject 5	326.28K	4.1138 MPa

5 DISCUSSION

Table 4 provides the value of Young's modulus for five different subjects of different ages and heights. It is clear from the Table there is a wide variation in the modulus values predicted by the two models with almost 2-3 orders of difference in magnitude. This may possibly be because of the assumptions made while deriving the models, that is, while one model assumes the blood to be an inviscid fluid, the other assumes it to be a viscous one. However, the measured values of blood pressure for each of the subjects showed a strong correlation with PTT, that is smaller the PTT, higher the blood pressure.

Further, the arterial data considered in this paper have been taken from the literature and no distinction has been made between the five subjects. That is, same data related to arterial radius, wall thickness, etc. have been used for all the subjects. This may have again given rise to errors in values for arterial stiffness.

Additionally, but more importantly, there appears to be still no agreement on true values of arterial stiffness even using the same model as other researchers have reported widely varying values for the Young's modulus that may even differ by about 300% (Avril et al., 2008).

6 A MORE REALISTIC MODEL

In view of limitations of above-mentioned models, the authors have started working on another model that attempts to model blood more realistically. This model considers blood to be a non-Newtonian fluid due to the presence of plasma, red blood cells etc. This model is known as power law model (Nadeem et al., 2011); (Basu et al., 2013). The constitutive equation for this model is given by

$$\tau = \kappa\left(-\frac{\partial u}{\partial r}\right)^n \tag{19}$$

Using the expression for the stress tensor given by equation (19) and using the assumptions mentioned in the beginning of the paper, the continuity and momentum equations, take the form

$$\frac{\partial u}{\partial x} + \frac{1}{r}\frac{\partial}{\partial r}\left(rv\right) = 0 \tag{20}$$

$$\rho\frac{\partial u}{\partial t} = -\frac{\partial p}{\partial x} - \kappa\left(\frac{\partial}{\partial r}\left(-\frac{\partial u}{\partial r}\right)^n + \frac{1}{r}\left(-\frac{\partial u}{\partial r}\right)^n\right) \tag{21}$$

$$\frac{\partial p}{\partial r} = 0 \tag{22}$$

As in the case of the viscous fluid model, the displacement equations of the wall are taken as follows:

$$\rho_w h\frac{\partial^2 \eta}{\partial t^2} = -\frac{Eh}{1-\nu^2}\left(\frac{\eta}{a^2} + \frac{\nu}{a}\frac{\partial \xi}{\partial x}\right) \tag{23}$$

$$\rho_w h\frac{\partial^2 \xi}{\partial t^2} = -\kappa\left(-\frac{\partial u}{\partial r}\right)^n - \frac{Eh}{1-\nu^2}\left(\frac{\partial^2 \xi}{\partial x^2} + \frac{\nu}{a}\frac{\partial \eta}{\partial x}\right) \tag{24}$$

Using the boundary conditions given in equation (12) together with the forms for velocity, pressure and the displacement components given by equation (13), we solve equations (20) - (24) for the velocity and the displacement components.

As the equations given by equation (20) – (24) are nonlinear in nature, approximate analytical methods are to be adopted to find an approximate analytical solution to the problem. In a future study, it is proposed to use OHAM (Optimal Homotopy Asymptotic Method) to find an approximate solution to the problem.

7 CONCLUSIONS

In this work, an attempt has been made to understand the mathematical models for blood flow and arterial stiffness as well as derive practical values for Young's modulus of elasticity that is an indicator of stiffness. There appears to be a wide variation which needs to be understood through further experimentation.

It should however be mentioned that results reported in this study are based on an extremely small set of data (with no controls) and many assumptions have also been made. It is proposed to extend this work by considering more realistic models such as the power law model mentioned above, a much larger sample size, standardizing the experiments and using more accurate data for arterial dimensions while computing the arterial stiffness in our future studies.

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