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Estimation of Elasticity by Modeling Blood Flow Using Clinical Ultrasound Data

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Abstract: In the present study, the estimation of elastic modulus of large arteries is used as an index for arterial stiffness. At first, a dynamic model is introduced for pulsatile blood flow in arteries with elastic walls. The model is based on Navier-Stokes equations in fluid mechanics and the theory of elasticity. The system of equations is completed by clinical ultrasound data obtained from Doppler ultrasound images of carotid artery of 40 healthy male volunteers. For this purpose, Doppler ultrasound images are recorded and saved in computer and then center-line blood velocity, arterial wall thickness, and arterial radius measured by offline processing. The results from analytic solution of completed equations show that the mean elastic modulus for the group of healthy volunteers is about 213 kPa. By applying this method, non-invasive clinical evaluation of common carotid artery stiffness by Doppler ultrasound measurement will be possible, without the measurement of local blood pressure.

Key words: Arterial stiffness, elastic modulus, blood flow, carotid artery, Doppler ultrasonography

INTRODUCTION

Cardiovascular disease is responsible for over 50% of all deaths in the western world (Hoskins *et al*., 1998). Researches have shown that stiffening of arteries may be both a cause and a consequence of cardiovascular diseases, such as hypertension. There has been much recent interest in the relationship between arterial stiffness and cardiovascular disease (Mackenzie *et al*., 2002). Arterial stiffness is an important predictor of cardiovascular risk (Cohn *et al*., 2005). It is now apparent that a wide pulse pressure and systolic hypertension are important indicators of morbidity and that systolic hypertension is the predominant risk factor for adverse outcomes in older hypertensive patients. Increased pulse pressure and systolic hypertension represent a later stage in the development of atherosclerosis and are therefore less sensitive than arterial elasticity (Izzo and Shykoff, 2001). Changes in elasticity occur very early in the development of atherosclerosis (Skrabal, 2004).

There are many factors that can be used as indices of arterial stiffness such as compliance, distensibility, Arterial Stiffness Index (ASI), augmentation index and elastic modulus. Various invasive and non-invasive methods have been developed to determine those indices (Mackenzie *et al*., 2002; Mahmud and Feely, 2003). The term Elastic modulus does not have a unique definition. For example Peterson's elastic modulus is pulse pressure divided by the relative arterial diameter change (Liao *et al*., 1999) but according to the theory of elasticity, elastic modulus relates stress to strain by Hooke's law (Fromageau *et al*., 2003; Zamir, 2000). Compliance, distensibility, Arterial Stiffness Index (ASI), augmentation index and Peterson's elastic modulus are based on some simplifying assumption such as steady flow and non-viscous fluid; and also it requires to measure blood pressure. Measuring the blood pressure is a fundamental problem of the methods based on these indices, since there is no direct and non-invasive method to measure blood pressure of central arteries. Thus, measurements of pulse pressure in the periphery, for example in the upper arm, do not always accurately reflect the actual central pulse pressure (Pauca *et al*., 1992).

Lagrée (2000) has suggested an inverse method to estimate the arterial elasticity by simplified Navier-Stokes equations which have been derived by Ling and Atabek (1972). This research has no clinical data and has assumed that measurement of displacement of the artery as a function of time at three distinct locations is applicable (Lagree, 2000). In our previous study, arterial pressure gradient were estimated by measuring the center-line blood velocity using ultrasonic methods according to

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Navier-Stokes equations. Then elastic modulus of an artery could be evaluated according to elasticity and viscoelasticity equations (Khooshkar *et al*., 2005). In this study, effects of Poisson's ratio and axial displacement of artery have been ignored. Khooshkar *et al*. (2005) have also assumed that blood is non-viscous.

In the present study, we have estimated elastic modulus of large arteries that is used as an index for arterial stiffness. At first, a suitable fluid dynamic model is introduced for pulsatile blood flow in arteries based on Navier-Stokes equations and the theory of elasticity. The system of equations is completed by clinical ultrasound data that is extracted from carotid artery.

Methods: A Newtonian, incompressible fluid is assumed and the viscosity is constant. The flow is assumed to be laminar and axisymmetric. Under these conditions, Navier-Stokes equations and the equation of continuity simplify to (Zamir, 2000):

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

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

$$\frac{\partial u}{\partial x}+\frac{\partial v}{\partial r}+\frac{v}{r}=0 \tag{3}$$

In an elastic tube, pressure changes cause local movements of the fluid and tube wall, which then propagate down stream in the form of a wave. Axial and radial blood velocities depend on locations x, r and time t and the radial velocity v is not zero.

Flow distributions within the artery are oscillatory, both in space and time. It may assume that at any point in time, the pressure and flow distributions are sinusoidal in x and at any fixed position they are sinusoidal in t. The analysis is considerably easier if the oscillations are considered as complex exponential rather than sine or cosine functions (Zamir, 2000):

$$p(x,r,t)=P(r)e^{i\omega\left(t-x/c\right)} \tag{4}$$

$$u(x,r,t)=U(r)e^{i\omega\left(t-x/c\right)} \tag{5}$$

$$v(x,r,t)=V(r)e^{i\omega\left(t-x/c\right)} \tag{6}$$

Because the arterial wall is in motion, zero velocities at the arterial wall are no longer valid as the boundary conditions. As a reasonable approximation, the boundary condition is applied at a fixed radius *a*, which is taken to be the neutral position of the arterial wall; so, the required boundary conditions are zero velocities at this radius (a) and finite velocity at the center of artery (Zamir, 2000). Because the radial displacement of the arterial wall is assumed sinusoidal, so the mean arterial radius is used as neutral radius.

Forces acting on an element of the arterial wall result from four mechanical stress, each having the dimensions of force per unit area: axial tension (S_{xx}) within the arterial wall, radial tension (S_{rr}) pulling element of the arterial wall toward the arterial axis arising from angular tension ($S_{\theta\theta}$) in the arterial wall, shear stress (τ_w) exerted by the blood on the inner surface of artery, pressure (p_w) exerted radially by the blood on the inner surface of artery.

The net force in each of the three coordinate directions must equal the acceleration of the element in that direction times its mass; thus, providing an equation of motion in each direction ((Zamir, 2000).

On the other hand, the stress-strain relations for an elastic body are given by (Hooke's law) (Zamir, 2000):

$$e_{xx}=\frac{1}{E}\left[S_{xx}-\sigma\left(S_{rr}+S_{\theta\theta}\right)\right] \tag{7}$$

$$e_{rr}=\frac{1}{E}\left[S_{rr}-\sigma\left(S_{\theta\theta}+S_{xx}\right)\right] \tag{8}$$

$$e_{\theta\theta}=\frac{1}{E}\left[S_{\theta\theta}-\sigma\left(S_{rr}+S_{xx}\right)\right] \tag{9}$$

Final forms of Equation have been obtained by matching Equation of pulsatile flow and arterial wall with clinical ultrasound data (Rahgozar *et al*. 2006; Zamir, 2000).

Noninvasive investigation by processing the sequential frames of color Doppler images were performed on 40 healthy male volunteers; with no history of cardiovascular and/or cerebrovascular disease, hypertension, diabetes and no-smoking (Vértes, 2003); aged 59±12 year. This study was approved by the Ethics Committees of Imam Khomeini Hospital and Tehran Medical Sciences University (Iran). The ultrasonic examination of right common carotid artery was performed after at least 30 min of rest in the supine position when the heart rate and blood pressure had reached a steady state.

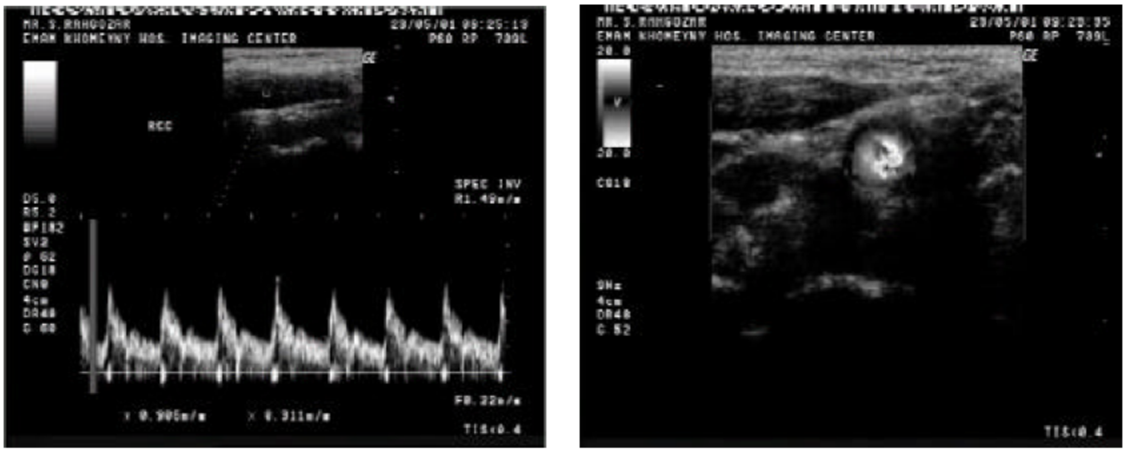

Fig. 1: Clinical data is obtained by ultrasonic device (GE logic 500MD)

All subjects underwent color Doppler ultrasonography. A complete examination including common, external and internal carotids were measured on every subject. The ultrasonic examination of RCCA at a point approximately 2 cm proximal to the bifurcation was done (Mokhtari-Dizaji *et al*., 2005) (Fig. 1). This point was selected near enough to the bifurcation, for its physiologic importance, and far enough to maintain the validity of axisymmetric geometry.

High-resolution B-mode ultrasound and color Doppler images from the right common carotid artery were obtained with a 7.5 MHZ linear array transducer attached to the ultrasound machine (GE-logic-500 MD version 4, USA,±0.1 mm and±.1 cm/s). A data acquisition system consisting of personal computer and multimedia board (Video-blaster Snazzi*1, VCD Master HQ, Singapore) was used for monitoring and grabbing the center-line blood velocity, arterial wall thickness, and the radius of Right Common Carotid Artery (RCCA) (30 frame/s). For each ultrasound examination, matching longitudinal views of the common carotid artery were located and the frames, representing a minimum of two cardiac cycles, were grabbed. Each recorded sequence was saved, frame by frame, on the scanner's hard disk. Pixel-based methodologies allow motion estimation by studying the displacement among the frames at the pixel level. During recording of images, center-line blood velocity, arterial wall thickness and arterial radius were measured by calipers of GE logic 500MD to obtain the scales of images for off-line processing. After saving images, recorded sequence of carotid artery was reviewed by Virtual Dub 1.5.9 software (Copyright © 1998-2003 by Avery Lee) and then images were taken from each frame by Capture Express 1.3.0.1 software (© 1989-1999 Adobe Systems Incorporated) to measure center-line blood velocity, arterial wall thickness and arterial radius. The measurements were made at a constant temperature room (26°C).

Equation 10-16 make a set of seven equations and seven unknown parameters (A, B, C, D, E, c, z), that will be solved by analytic method (Rahgozae *et al*., 2006). Where ç, h and U(0) are obtained by ultrasound.

$$A = \frac{c}{aJ_0(\Lambda)}\left[\frac{2 + z(2\sigma - 1)}{g + \sigma z(g-1)}\right]D \tag{10}$$

$$B = \frac{\rho c^2}{a}\left[\frac{z(g - 2\sigma)}{g + \sigma z(g-1)}\right]D \tag{11}$$

$$C = \frac{ic}{\omega a}\left[\frac{z(1-g) - 2}{g + \sigma z(g-1)}\right]D \tag{12}$$

$$\eta(x,t) = De^{i\omega\left(t - x/c\right)} \tag{13}$$

$$\left[(g-1)(\sigma^2-1)\right]z^2 + \left[\frac{\rho_w h}{\rho a}(g-1) + \left(2\sigma - \frac{1}{2}\right)g - 2\right]z + \frac{2\rho_w h}{\rho a} + g = 0 \tag{14}$$

$$z = \frac{Eh}{(1-\sigma^2)\rho a c^2} \tag{15}$$

$$U(0) = A + \frac{B}{\rho c} \tag{16}$$

Where U (0) express the maximum velocity of blood in the center-line of artery with acceptable approximation. On the other hand, with regard to clinical measurements, arterial radius changes (η) are known; thus, according to Eq. 13, the maximum change of radius can be determined. In these Equation Ω, Λ and g are defined as:

$$\Omega = \sqrt{\frac{\rho\omega}{\mu}}\alpha \tag{17}$$

$$\Lambda = \left(\frac{i-1}{\sqrt{2}}\right)\Omega \tag{18}$$

$$g = \frac{2J_1(\Lambda)}{\Lambda J_0(\Lambda)} \tag{19}$$

Performing a test on a subject and analyzing the obtained information requires the following default data:

$\rho = 1060$ kg .m^{-3}	Density of blood (Duck, 1990)
$\rho_w = 1060$ kg .m^{-3}	Density of arterial wall (Duck, 1990)
$\mu = 0.003465$ pas	Viscosity of blood (Belardinelli and Cavalcanti, 1992)
$\sigma = 0.45$	Poisson's ratio (Giannakoulas *et al.*, 2005)

RESULTS

It is assumed that the frequency of oscillation is 72 beat per minute for healthy volunteers. Results for 40 healthy men volunteers are shown in Table 1. Results from the individual volunteers were averaged and shown as mean±Standard Deviation (SD) with 95% confidence interval [CI (95%)]. The neutral radius is average of maximum and minimum radius of artery throughout two cardiac cycles. Table 1 summarized the estimated values of the right common carotid artery through processing B-mode and color Doppler images.

All of the observations were made by the same investigator at the same standard conditions. A scatter plot of individual values for the elastic modulus as a function of age is presented in Fig. 2. Using Pearson correlation analysis, correlation coefficient between the elastic modulus and the age was 0.5 (correlation is significant at the 0.01 level).

Table 1: Characteristics of right common carotid artery [Mean±Standard Deviation (SD) with CI (95%)] in 40 healthy men volunteers

Parameters	Mean±SD	Confidence Interval [95%]
a: Neutral radius of artery (mm)	4.05±0.60	3.86-4.25
h: Arterial wall thickness (mm)	1.32±0.32	1.22-1.43
D: Maximum change of arterial radius (mm)	0.39±0.15	0.17-0.22
U(0): Maximum velocity of blood in center-line of artery (cm/s)	59.01±10.91	55.52 -62.50
E: Elastic modulus (Pa)[a]	213221±107507	178838-247603

[a] Resulting of solving seven equations, Eqs. [10-16]

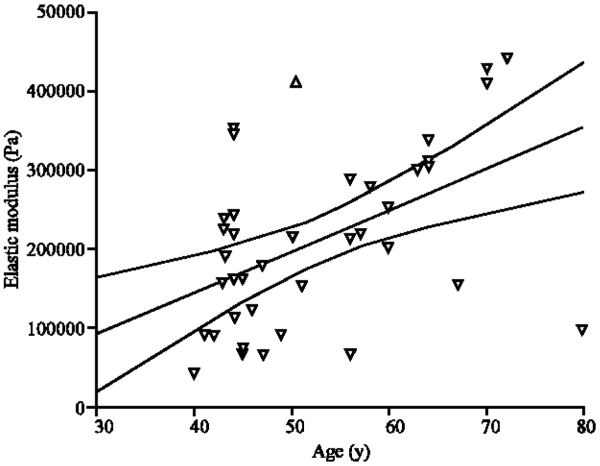

Fig. 2: A scatter plot of individual values for the elastic modulus as a function of age

DISCUSSION

Estimation of the elastic modulus as an index of arterial stiffness can be an independent predictor of cardiovascular risk (Cohn *et al.*, 2005). In health sciences, non-invasive methods are preferred to invasive ones. In this research, a non-invasive method is introduced to estimate the elastic modulus by modeling blood flow in arteries according to Navier-Stokes equations and modeling arterial wall according to elasticity equations and matching these two set of equations with achieved equations from clinical ultrasound data. Axisymmetric geometry besides simplifying the model is also consistent with physiologic condition that has been used in many researches (Fung, 1984). Clinical information is obtained by color Doppler ultrasound which is valid accurate and standard method (Schulte-Altedorneburg *et al.*, 2001). Researches based on modeling blood flow and arterial wall are so less than other studies.

The obtained elastic modulus in our research is similar to the value reported in the literature (214 kPa) (Karner *et al.*, 1999; Calvo and Gabaldón, 2003). In our previous study by omitting Poisson's ratio and axial displacement and also estimating the wave speed from the non-viscous equation, the elastic modulus was estimated about 137-186 kPa (Khooshkar *et al.*, 2005).

This research presents a new approach to estimate arterial stiffness alleviating the need for blood pressure measurements. Estimation of the Arterial Stiffness Index (ASI), compliance, distensibility, and Peterson's elastic modulus necessitate measurements of blood pressure, which in turn necessitates invasive techniques (Berbich *et al.*, 2001). Also several methods have been introduced to estimate arterial stiffness based on changes in the brachial blood pressure, but due to the error that result from substituting the brachial blood pressure for central arteries, such as carotid (Mackenzie *et al*., 2002), it will be very important to present arterial stiffness based on the mechanical models without any emphasis on brachial blood pressure.

We have not ignored Poisson's ratio and axial displacement in this study. To estimate the wave speed, we have not used Moen-Korteweg formula which is for non-viscous fluid; instead, we have used general equations for viscous fluid. It is not necessary to know blood velocity and arterial radius each time, only the maximum domain needs that; so, it does not need that the velocity measurements be in phase with radius measurements.

It is concluded that by applying this method, non-invasive and clinical evaluation of arterial stiffness by Doppler ultrasound measurement of the common carotid artery will be possible, without any further measurement of local blood pressure. Authors of this paper suggest this dynamics model for evaluations of the effects of age and various diseases, such as atherosclerosis, on arterial stiffness.

NOMENCLATURE

u	Axial velocity
ν	Radial velocity
x	Axial variable
r	Radial variable
t	Time
ρ	Density of blood
μ	Viscosity of blood
P	Pressure
$P(r)$	Maximum domain of pressure
$U(r)$	Maximum domain of axial velocity
$V(r)$	Maximum domain of radial velocity
ω	Frequency of oscillation
c	Wave speed
α	Neutral radius
Ω	Parameter introduced in Eq.17
Λ	Parameter introduced in Eq. 18
J_0	Bessel function of order 0
J_1	Bessel function of order 1
A, B	Arbitrary constants
C, D	Arbitrary constants
E	Elastic modulus
σ	Poisson's ratio
z	Parameter defined by Eq.15
g	Parameter defined by Eq.19
ρ_{ω}	Density of arterial wall
η	Radial displacement
P_{ω}	Blood pressure on arterial wall
h	Arterial wall thickness
i	$\sqrt{-1}$
e_{xx}	Axial strain
e_{rr}	Radial strain
$e_{\theta\theta}$	Angular strain
τ_{ω}	Shear stress on arterial wall
S_{xx}	Axial tension
S_{rr}	Radial tension
$S_{\theta\theta}$	Angular tension

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