Noninvasive Portal Pressure Estimation Model using Finite Element Analysis

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Abstract: Currently, portal pressure is measured by the standard method known as hepatic venous pressure gradient (HVPG). But it is an invasive procedure; therefore, an alternative noninvasive technique to estimate portal pressure is required to monitor portal hypertension. In this work, a 3D portal vein model is developed to study the acoustic interaction with microbubbles in the portal vein. Ultrasound scattering by ultrasound contrast agent (UCA) is modelled and analyzed using finite element analysis in order to estimate portal pressure. It was found from the analysis that the subharmonic component dropped by 1.5 dB as the portal pressure raised from 0 mmHg to 10 mmHg. Over the same pressure range, the fundamental component reduced by only 0.2 dB. The results suggest that the subharmonic component from the nonlinear response of microbubble is strongly affected by the ambient pressure, and the proposed model may be used to estimate portal pressure noninvasively.

1 INTRODUCTION

Portal hypertension (PH) is defined as a condition when the pressure in the portal vein is greater than 6-10 mmHg, or the pressure gradient is greater than 5 mmHg between the portal vein and the hepatic vein or the inferior vena cava (Cokkinos et al., 2009). Portal pressure is usually measured by the hepatic venous pressure gradient (HVPG), which is the difference between wedged and free hepatic vein pressure (Berzigotti et al., 2018).

The objective of the work reported in this paper was to develop a methodology to estimate the portal pressure noninvasively, through the use of Ultrasound signal. Ultrasound contrast agents (UCA) consists of gas-filled bubbles (encapsulated by lipids, proteins, or polymers) with diameters ranging from 0.5 to 10 μm (Sirsi et al., 2009). Microbubble provides a nonlinear response, when driven by the acoustic pressure, and generate signals at integer and fractional multiples (i.e., harmonic components including subharmonic components) of exciting frequency (Tremblay-Darveau et al.,2014). The technique of noninvasively measuring and predicting changes in scattering from UCA as a function of ambient pressure was reported four decades ago (Fairbank et al., 1977). However, the unavailability of stable microbubble has prevented the practical exploitation of this understanding (Fairbank et al., 1977, Hok et al., 1981). The compressibility of microbubble is different from the compressibility of blood. A change in size and acoustic characteristics of the microbubbles results from pressure changes around it (Adam et al., 2005).

There have been studies to estimate ambient pressure using microbubble as a pressure sensor. Techniques based on resonance frequency shift (Fairbank et al., 1977), and amplitude of single bubble echos (Hok et al.,1981) and later dual-frequency excitation technique (Shankar et al., 1986) have been developed, but the resolution of these techniques are not clinically useful. A technique to determine ambient fluid pressure based on the subharmonic response from UCA called subharmonic aided pressure estimation (SHAPE) has been reported (Shi et al.,1999). The reported sensitivity of the technique based on SHAPE is -6.58 mmHg/dB in simulation (Andersen et al.,2009), whereas in vitro studies, it has a range of -13.98 to -4.55 mmHg/dB (Dave et al., 2011, Halldorsdottir et al., 2011). In vivo studies had a range of -4.92 to -1.44 mmHg/dB (Dave et al., 2012, Forsberg et al., 2005). Analytical models such as the Rayleigh Plesset model and its modified forms were developed to study the acoustic response of microbubble in free space (Faez et al., 2012). But analytical techniques have assumed that the microbubble oscillation is spherical, and has not considered non-spherical oscillations, bubble-bubble interaction, and bubble wall interaction.

Portal pressure estimation using the finite element method has not been carried out till recently (Cai et al., 2018). Therefore, the objective of this work is to develop a finite element method to understand the mechanisms of hydrostatic pressure on subharmonic oscillations, and to utilize the subharmonic component to estimate portal pressure noninvasively.

2 MATERIALS AND METHODS

The acoustic wave propagation in the fluid surrounding the bubble is described by the acoustic medium, the fluid is assumed to be compressible, linear, adiabatic and inviscid, and the equation of motion can be given as (Abaqus Manual, 2014).

$$\frac{1}{k_L}P'' + \frac{\gamma}{\rho_L K_L}P' - \frac{\partial}{\partial x}\left(\frac{1}{\rho_L}\frac{\partial P}{\partial x}\right) = 0 \qquad (1)$$

Where P' and P'' are the first and second derivatives of the pressure with respect to time, x is the spatial position of the fluid particle, ρ_L is the density of the fluid, γ is the volumetric drag and K_L is the bulk modulus of the fluid.

The surface-based fluid-filled cavity can be modelled to couple the deformation of the microbubble shell and the gas pressure. The behavior of the gas is described by an ideal gas equation (Abaqus Manual, 2014).

$$P + P_A = \rho_g R\,(T - T^Z) \qquad (2)$$

Where P is the gauge pressure, P_A is the ambient pressure, R is the gas constant, T^Z is the absolute zero temperature. The gas constant can be determined as follows.

$$R = \frac{\widehat{R}}{MW} \qquad (3)$$

Where $\widehat{R}$ is the universal gas constant, and MW is the molecular weight, the contents of the gas within the microbubble are considered to be air. The hyperelastic material model is used to describe the microbubble shell, and hyperelastic materials are described by a strain energy potential. Arruda-Boyce strain energy potential can be written as (Abaqus Manual, 2014).

$$\begin{aligned} U = \mu\Bigg\{&\frac{1}{2}(I_1 - 3) + \frac{1}{20\lambda_m^2}(I_1^2 - 9) \\ &+ \frac{11}{1050\lambda_m^4}(I_1^3 - 27) \\ &+ \frac{19}{7000\lambda_m^6}(I_1^4 - 81) \\ &+ \frac{519}{673750\lambda_m^8}(I_1^5 - 243)\Bigg\} \\ &+ \frac{1}{D}\left(\frac{J_{el}^2 - 1}{2} - \ln J_{el}\right) \end{aligned} \qquad (4)$$

Where, U is the strain energy per unit of a reference volume, μ, λ_m, and D are the material parameters, I_1 is the first deviatoric strain invariant, J_{el} is the elastic volume ratio. The initial shear modulus μ_0 is related to the material parameter μ with the expression (Abaqus Manual, 2014).

$$\mu_0 = \mu\left(1 + \frac{3}{5\lambda_m^2} + \frac{99}{175\lambda_m^4} + \frac{513}{875\lambda_m^6} + \frac{42039}{67375\lambda_m^8}\right) \qquad (5)$$

The initial bulk modulus K_0 and material parameter D is related by an expression (Abaqus Manual, 2014).

$$K_0 = \frac{2}{D} \qquad (6)$$

A tie type constraint is applied between the microbubble shell and the surrounding fluid to ensure acoustic shell interaction. The coupling between the shell motion and acoustic pressure can be expressed by (Abaqus Manual, 2014).

$$n.\ddot{u} = -n.\left(\frac{1}{\rho_L}\frac{\partial p}{\partial x}\right) \qquad (7)$$

Where $\ddot{u}$ is the fluid particle acceleration. Similarly, vessel wall and fluid are coupled by tie type constraint to ensure coupling of acoustic pressure between the vessel wall and the fluid.

Fig.1 shows the 3D Geometry of the portal vein model, where the microbubble is located at the center.

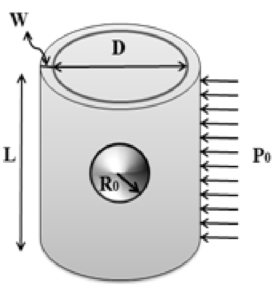


Figure 1: The geometry of the 3-D portal vein model with microbubble placed at the center.

The vessel length L, was set to be 5 mm, the diameter of the vessel D was set to 10 mm, the radius of the microbubble was R_0 = 3 μm and the thickness of the vessel wall was set to W= 0.5 mm. These values were taken so as to be consistent with the normal portal vein dimension.

A plane wave was incident on the vessel boundary with peak pressure amplitude P_0, the local spherical coordinate system was defined at the center of the microbubble, and only the radial motion of the spherical bubble has been considered.

The numerical solution was obtained by the finite element software ABAQUS® (Dassault Systems SIMULIA, version 6.14). The material parameter values used in this work are shown in Table.1 and correspond to those reported in the literature (Bei et al., 2010, Hoff et al., 2001).

Table 1: Material Parameters.

Medium	Parameters	Values
lood	Density Bulk Modulus Speed of sound	1000 kg/m^3 2250 MPa 1500 m/s
Shell	Thickness Density Initial Shear Modulus Initial Bulk Modulus Speed of sound	4 nm 1100 kg/m^3 50 MPa 2816 MPa 1600 m/s
Vessel wall	Speed of sound Density	1580 m/s 1100 kg/m^3
Gas	Density Universal Gas constant Molecular Weight Initial gas pressure	1.225 kg/m^3 8.314510 J mol^{-1} K^{-1} 0.0289 101325 Pa

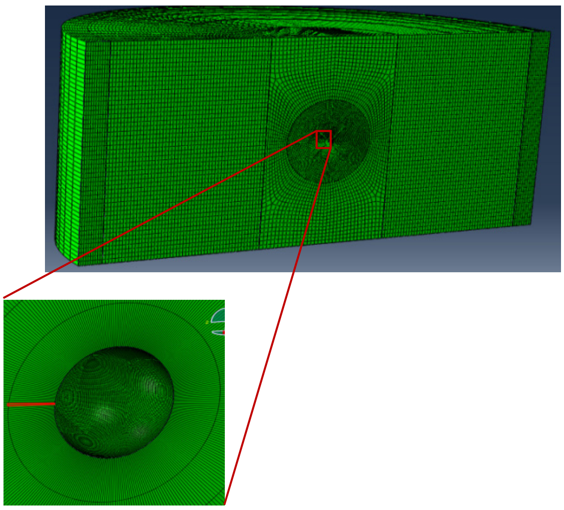


Figure 2: Mesh of the portal vein model with microbubble at the center.

The mesh of the portal vein model is shown in Fig.2

- The element type “AC3D8R” was used for fluid and vessel wall, with only acoustic pressure degree of freedom.
- Microbubble's encapsulation discretized by the element type “S4R”.
- The fluid and vessel wall were discretized by 766153 acoustic elements.
- The microbubble's encapsulation was discretized by 60000 shell elements.

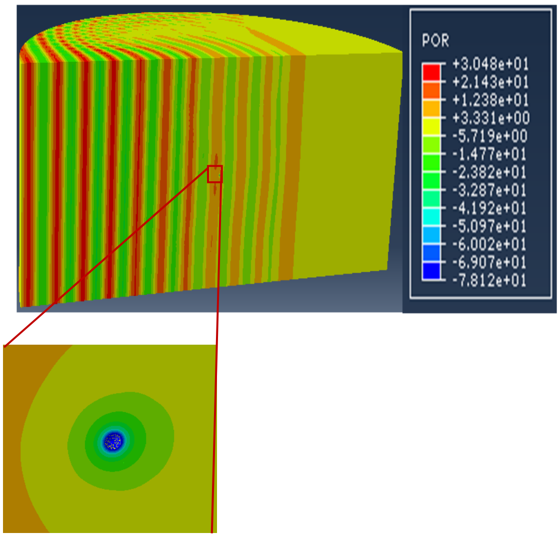
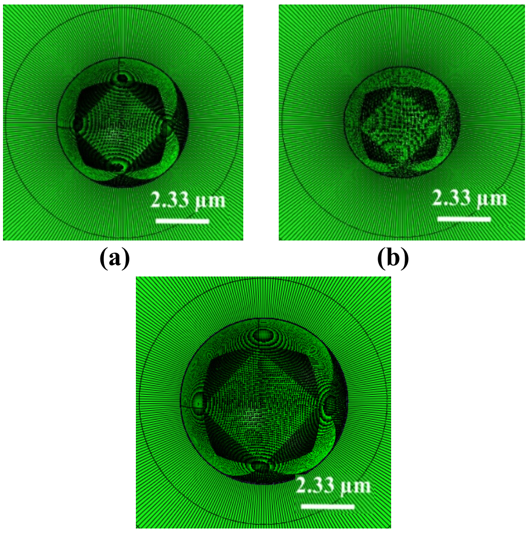


Figure 3: Acoustic pressure profile from portal vein with microbubble at the center and magnified view of microbubble response.

3 RESULTS AND DISCUSSION

Fig. 3 shows the response of microbubble in the portal vein, where the microbubble radius R_0 of 3 µm, and the acoustic pressure amplitude P_0, and transmitting frequency f, of the continuous wave ultrasound are 0.02 MPa and 2 MHz, respectively.

Fig.4 Shows the microbubble expansion and compression phase when the ultrasound wave interacts with the microbubble. Ultrasound wave takes approximately 3.67µs ($t = \frac{d}{c} = \frac{5.5*10^{-3}m}{1500\ m/s}$) to reach the microbubble surface. It compresses the microbubble during the positive half cycle and expands it during the negative half cycle. This can be noticed in Fig.5a. The volumetric compression and expansion phase are symmetric with lower acoustic pressure amplitude. When the applied ultrasound pressure is less than 0.3 MPa, the subharmonic amplitude is weak. As a result, the subharmonic component is absent as shown in Fig 5c. The time and frequency resolution of the numerical solutions plotted in Fig 5 and 6 are 0.04 µs and 0.7 kHz, respectively.



(c)

Figure 4: Snapshots of radial oscillations of the microbubble, (a) initial bubble size at 3 µs, (b) bubble compression at 3.8333 µs and (c) bubble expansion at 4.125 µs.

Fig. 6 shows the response of microbubble in the portal vein, where the microbubble radius R_0 of 3 µm, and the acoustic pressure amplitude P_0, and transmitting frequency f, of the continuous wave ultrasound are 0.5 MPa and 4 MHz, respectively. The threshold ultrasound pressure is minimum, if the the excitaion frequency (2*2 MHz) is twice the resonance frequency, here the resonance frequency of portal vein model is around 2 MHz. It can be noticed that the volumetric compression and expansion phase are not symmetric.

Damping of radial oscillation and acoustic response are produced due to the ambient pressure raise of 10 mmHg. As a result, the ambient pressure dependent radial oscillations and the acoustic responses are produced, with an ambient pressure increase of 0 and 10 mmHg, it can be observed in Fig. 6a and 6b. It has been reported that when the applied ultrasound pressure in the range 0.3-0.6 MPa, the subharmonic response is maximum (Shi et al.,1999). Since the applied ultrasound pressure in our study was 0.5 MPa, the expected subharmonic component is developed that can be observed in Fig. 6c.

It is also observed that the subharmonic scattering is sensitive to the ambient fluid pressure changes, and decreases with an increase in fluid pressure. Subharmonic component reduction linearly with an ambient fluid pressure raise has been reported (Shi et al.,1999, Andersen et al., 2009, Andersen et al., 2010). In the present model, the subharmonic amplitude dropped by 1.5 dB as the portal pressure is raised from 0 mmHg to 10 mmHg. Over the same pressure range, the fundamental component reduced only by 0.2 dB. Further development of the model is required to include the effects such as, bubble-bubble interaction and population behaviour, to validate with realistic experimental conditions.

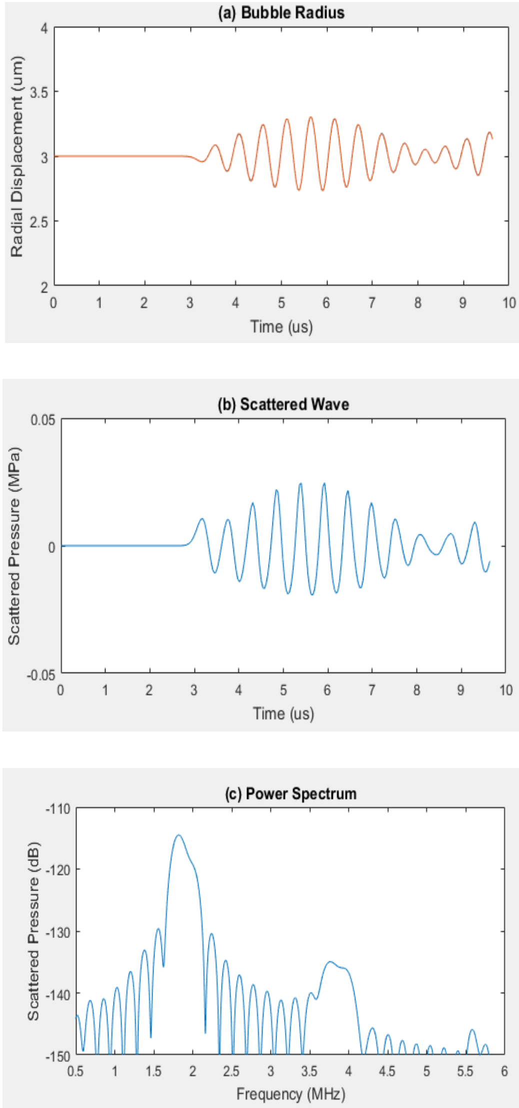


Figure 5: Acoustic response of the microbubble placed at the center of the portal vein, (a) radial oscillation of the microbubble, (b) scattered wave and (c) Power spectrum of acoustic response.

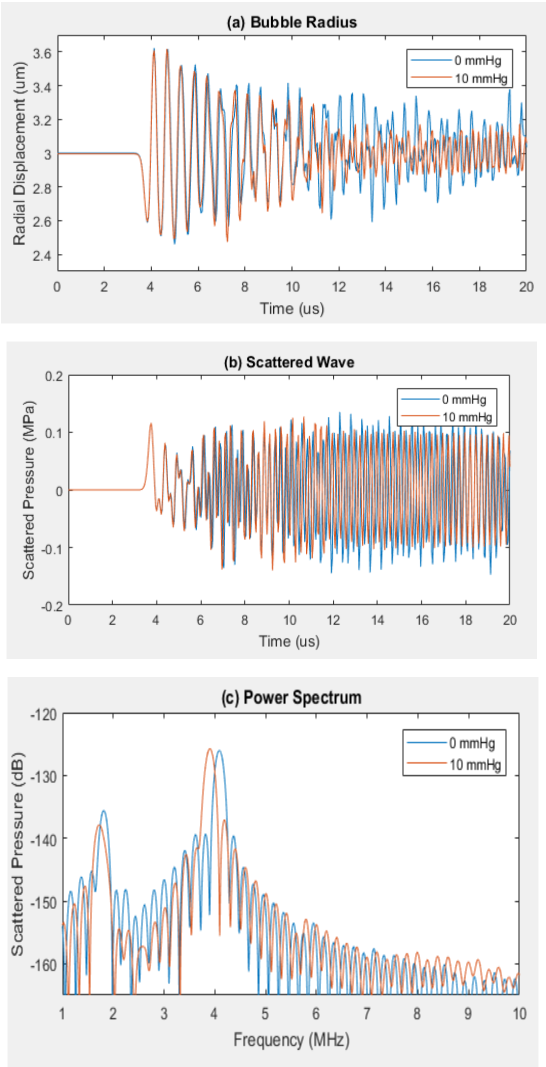


Figure 6: Acoustic response of the portal vein with microbubble placed at the centre, due to an ambient pressure raise of 0 mmHg (blue curves) and 10 mmHg (orange curves), (a) radial oscillation of the microbubble, (b) scattered wave and (c) Power spectrum of acoustic response.

4 CONCLUSIONS

The finite element model has been developed that can allow to study the relationship between the subharmonic response from microbubble and ambient pressure, which may be used to estimate the portal pressure non-invasively. It can be observed from the results that as the portal pressure is changed, the change at the subharmonic component is more compared to that at the fundamental component.

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