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# Dependence of Cavitation Bubble Size on Pressure Amplitude at Therapeutic Levels

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**Abstract**

High-intensity, focused ultrasound therapy is a minimally invasive therapy technique that is effective and relatively safe. It can be used in areas including histotripsy, thermal ablation, and administering medication. Inertial cavitation is used to improve these therapy methods. The purpose of this study was to determine the effect of pressure amplitude on cavitation resonance frequency/bubble size at therapeutic field levels. Earlier work has indicated that the resonance size depends on pressure amplitude; however, the investigation only considered pressure amplitudes up to 1 MPa [1]. Our study was conducted by simulating the response of bubbles to linearly propagating sine waves using the Gilmore-Akulichev formulation to solve for the bubble response. The frequency of the sine wave varied from 1 to 5 MHz while the amplitude of the sine wave varied from 0.0001 to 9 MPa. The resonance size for a particular frequency of excitation and amplitude was determined by finding the initial bubble size that resulted in the maximum bubble expansion for an air bubble in water. The simulations demonstrated a downshift in resonance size with increasing pressure amplitude. Therefore, smaller bubbles will have a more dramatic response to ultrasound at therapeutic levels.

**Keywords**

Bubble dynamics, cavitation, therapeutics, high pressure, sound pressure

**Disciplines**

Biomedical | Biomedical Devices and Instrumentation | Electrical and Computer Engineering

**Comments**

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# Dependence of Cavitation Bubble Size on Pressure Amplitude at Therapeutic Levels

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**Abstract** High-intensity, focused ultrasound therapy is a minimally invasive therapy technique that is effective and relatively safe. It can be used in areas including histotripsy, thermal ablation, and administering medication. Inertial cavitation is used to improve these therapy methods. The purpose of this study was to determine the effect of pressure amplitude on cavitation resonance frequency/bubble size at therapeutic field levels. Earlier work has indicated that the resonance size depends on pressure amplitude; however, the investigation only considered pressure amplitudes up to 1 MPa [1]. Our study was conducted by simulating the response of bubbles to linearly propagating sine waves using the Gilmore-Akulichev formulation to solve for the bubble response. The frequency of the sine wave varied from 1 to 5 MHz while the amplitude of the sine wave varied from 0.0001 to 9 MPa. The resonance size for a particular frequency of excitation and amplitude was determined by finding the initial bubble size that resulted in the maximum bubble expansion for an air bubble in water. The simulations demonstrated a downshift in resonance size with increasing pressure amplitude. Therefore, smaller bubbles will have a more dramatic response to ultrasound at therapeutic levels..

**Keywords:** Cavitation, Bubble Resonance Size, Amplitude Dependence
**PACS:** 43.35.Ei, 43.80.Sh

## INTRODUCTION

For years ultrasound has shown remarkable potential as a tool for minimally invasive therapy. Recently, ultrasound thermal ablation of tissue has successfully treated some cancers and uterine fibroids. Ultrasound thermal ablation uses the energy in the ultrasound waves to heat and kill targeted tissue and has been extensively studied [2-14]. In addition to killing tissue, ultrasound therapies are being successfully developed to enhance thrombolysis [15,16], improve drug and gene delivery [17-22], control bleeding and hemorrhaging from severe trauma [13,24], and erode or liquefy tissue by controlled technique [7,25-30]. Many of these developing therapies have been found to depend upon or be significantly enhanced by the cavitation of microbubbles. Therefore, it is critical to understand the interaction of microbubbles with high intensity sound waves. Fully understanding the interaction will better ensure effective ultrasound therapy.

In this paper, the response of a spherically symmetric air bubble in an unbounded water media to ultrasound waves was simulated. The goal was to determine how the bubble responded to pressure amplitudes at therapeutic levels. The hypothesis was that as the pressure amplitude increased the resonant bubble size would decrease where resonance size was defined as the initial bubble size that results in the greatest bubble expansion relative to the initial size. Earlier work has indicated that the resonance size depends on pressure amplitude; however, the investigation only considered pressure amplitudes up to 1 MPa [1].

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## SIMULATION PARAMETERS

The response of the bubbles to the acoustic wave was simulated by solving the Gilmore-Akulichev (eq1) formulation for bubble dynamics [30-34]. The calculations assumed that the ultrasound waves were not corrupted by nonlinear propagation distortion and that the bubble remained spherical throughout the simulation.

$$R\left(1-\frac{U}{C}\right)\frac{dU}{dt}+\frac{3}{2}\left(1-\frac{U}{3C}\right)U^2 = \left(1-\frac{U}{C}\right)H+\frac{U}{C}\left(1-\frac{U}{C}\right)R\frac{dH}{dR} \quad (1)$$

Equation 1 represents the response of a single bubble with respect to time. The R corresponds to the initial radius, U is the first derivative with respect to time, C is the speed of sound of the liquid that the bubble is in, and H is the enthalpy of that liquid. Equation 1 is dependent on four basic equations (2-5).

$$P = (C_0^2\rho/P_0 m)(\rho/\rho_0)^m - \left(\frac{C_0^2\rho}{P_0 m}-1\right) \quad (2)$$

$$H = \int_{P_\infty}^{P(R)}\frac{dP}{\rho} \quad (3)$$

$$P(R) = P_g - 2\sigma/R - (4\mu/R)U \quad (4)$$

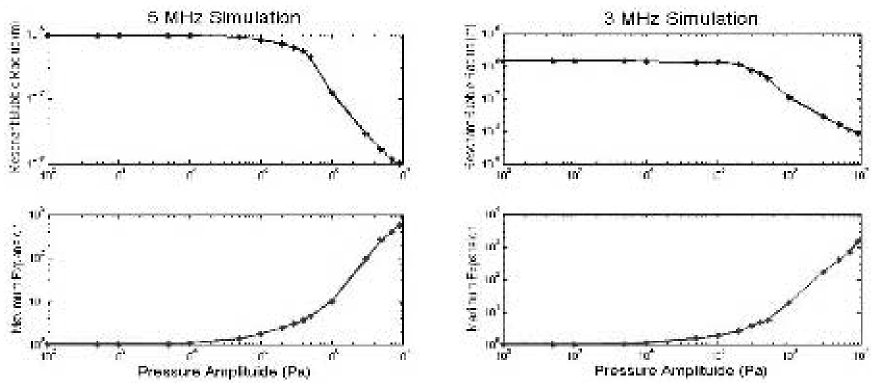
$$C = [C_0^2 + (m-1)H]^{1/2} \quad (5)$$

Equations 2-5 define parameters accounted for while simulating a bubble using the Gilmore-Akulichev formulations. P is the pressure of the fluid around the bubble, the equilibrium liquid density is $\rho_0$, and the time varying density of the fluid is $\rho$. $C_0$ is the infinitesimal speed of sound in the liquid, and $P_0$ is the ambient pressure of the liquid surrounding the bubble and the variable m is seven [34]. The enthalpy of the liquid (H) is described by equation 3, where $P_\infty$ is the pressure of the sound wave and P(R) is the pressure at the bubble wall. P(R) in equation 4, depends on $P_g$, the pressure of the gas inside the bubble, the surface tension σ, and the coefficient of shear viscosity, μ. C in equation 5 is the speed of sound at the bubble wall.

The frequency for each set of simulations was chosen as well as a set of pressure amplitudes. The amplitudes ranged 100 Pascals up to 9 MPa in varying step size depending on areas of interest, and three frequencies were selected; 1, 3, and 5 MHz because of their relevance to therapeutics. The function in MATLAB scanned initial bubble sizes searching for the maximum expansion relative to initial size, prior to inertial collapse. An inertial collapse was defined as when the bubble radius dropped below 1/10$^{th}$ of its initial radius. The simulation ran for a maximum of fifty cycles in the absence of an inertial collapse to insure that any transients present in the stable cavitation cases would not impact the results. After the resonance size was found, it was used to find the maximum expansion of the bubble relative to the initial size.

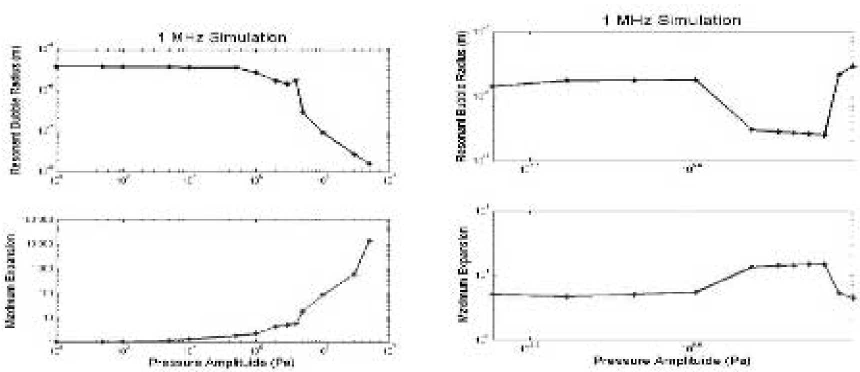
# RESULTS

The results for the simulation are shown below. For the 3 and 5 MHz cases, there is a consistent decrease in resonance size with increasing pressure amplitude. There is also a corresponding increase in maximum expansion relative to initial size. For the 1 MHz case, there is also a decrease in resonance size with increasing pressure amplitude, but there is a discontinuity at 0.49-0.50 MPa which needs to be investigated further.




(a) (b)

**FIGURE 1:** The simulation results for 5 MHz 1(a) and 3MHz 1(b) illustrate the dramatic decrease in resonance size with increasing pressure. The top graph represents a decrease in bubble size as the pressure increases and the bottom graph corresponds to the maximum expansion relative to initial size.

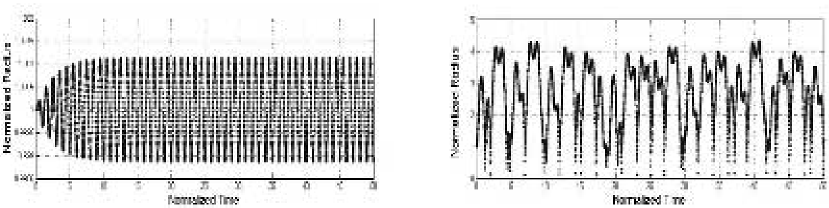



(a) (b)

**FIGURE 2:** The simulations driven at 1MHz generally displayed a linear downshift except in the region of the discontinuity. Graph 2(b) magnifies the discontinuity. The top graphs represent a decrease in bubble size as the pressure increases and the bottom graphs correspond to the maximum expansion relative to initial size.

## CONCLUSIONS

Simulation results show pressure amplitudes of 1MPa through 9MPa correspond to a drastic downshift in resonance size. The discontinuity shown in Fig. 2(b) is probably an artifact of the minimization routine used in the simulated search for the resonance bubble size perhaps resulting from a transition from stable to inertial cavitation. Fig. 3(a) shows the oscillation of a bubble during stable cavitation driven at low pressure amplitudes. During higher amplitude excitation, as seen in Fig. 3(b), the bubble is undergoing inertial cavitation. This hypothesis needs to be further explored in the future. In all cases, the growth of bubble expansion normalized to initial size is dramatic and may mean an increase the effectiveness or efficiency of cavitation at therapeutic treatment levels.




(a) (b)

**FIGURE 3:** Figure 3(a) demonstrates a bubble oscillating at low pressure levels (10KPa) displaying stable cavitation and a bubble oscillating at high pressure levels (1MPa) displaying inertial cavitation is shown in 3(b).

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