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**The Subharmonic Behavior and Thresholds of High Frequency Ultrasound Contrast Agents**[1]

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Ultrasound contrast agents are encapsulated micro-bubbles used for diagnostic and therapeutic biomedical ultrasound. The agents oscillate nonlinearly about their equilibrium radii upon sufficient acoustic forcing and produce unique acoustic signatures that allow them to be distinguished from scattering from the surrounding tissue. The subharmonic response occurs below the fundamental and is associated with an acoustic pressure threshold. Subharmonic imaging using ultrasound contrast agents has been established for clinical applications at standard diagnostic frequencies typically below 20 MHz. However, for emerging applications of high frequency applications (above 20 MHz) subharmonic imaging is an area of on-going research. The effects of attenuation from tissue are more significant and the characterization of agents is not as well understood. Due to specificity and control production, polymer agents are useful for high frequency applications. In this study, we highlight novel measurement techniques to measure and characterize the mechanical properties of the shell of polymer contrast agents. The definition of the subharmonic threshold is investigated with respect to mono-frequency and chirp forcing waveforms which have been used to achieve optimal subharmonic content in the backscattered signal. Time frequency analysis using the Empirical Mode Decomposition (EMD) and the Hilbert-Huang transform facilitates a more sensitive and robust methodology for characterization of subharmonic content with respect to non-stationary forcing. A new definition of the subharmonic threshold is proposed with respect to the energy content of the associated adaptive basis decomposition. Additional studies with respect to targeted agent behavior and cardiovascular disease are discussed.

[1]NIH, ONR