ULTRASOUND CONTRAST MICROBUBBLES: SIMULATIONS AND IN VITRO EXPERIMENTS

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Introduction

Functional images with combined information of blood flow and motion are applicable within a wide range of basal science and physiology.

In a long term perspective the goal of our ultrasound contrast research is to find a new model driven approach for estimation of myocardial perfusion. An aim is to develop nonlinear simulation of the contrast bubble and ultrasound wave interaction as well as wave propagation and to design an in vitro model including a perfusion phantom for ultrasound contrast measurements. We plan to use the simulation and in vitro model to evaluate and optimize the wash-in technique after bubble destruction.

Methods and Results

Modelling of plane wave propagation was carried out in successive forward steps applying the operators of nonlinear distortion, attenuation and speed dispersion. The operator of nonlinear distortion is based on the time domain relation developed by Remenieras, [1] and the operator of attenuation and speed dispersion is based on spectral decomposition and modification methods developed by He, [2].

Modelling of the signal field in a nonlinear medium was carried out under the assumptions that the ultrasound intensity is weak because of safety reasons related to high mechanical index (MI) and ultrasound contrast agents, and to increase contrast bubble survival in acoustic beam. Only nonlinearity effects originating from nonlinear terms in tissue elasticity that relates the pressure and the material compression (expansion) are taken into account. We further assume the medium is a nonlinear homogeneous liquid with power law frequency function of attenuation and sound speed dispersion.

Using a method developed by Jurkonis, [3] based on the spatial impulse response of an aperture (SIRA) as well as spectral decomposition and modification methods we calculated the pulse field of acoustic pressure in nonlinear media. An algorithm of Spatial Superposition of Attenuated Waves method was adopted for field simulation in nonlinear medium. The acoustic pressure waveform in a field point is calculated by adding contributions from elementary waves and is modified in steps accounting for nonlinear propagation, attenuation and speed dispersion.

Simulations of the contrast microbubble response to the incident pressure pulse were based on the Rayleigh-Plesset equation of motion for the surrounding liquid with the addition of a radiation damping factor [4]. The pressure at the bubble surface was calculated for bubbles encapsulated in a very thin viscoelastic shell, assuming an exponential stress-strain relationship [5]. The acoustic bubble response was calculated at a normalized distance.

The shell material parameters used in the simulations are based on the properties of the contrast agent Sonazoid (Amersham Health).

Interaction with nonlinearly distorted pulses was studied in water for series of nonlinearly distorted pulses and was measured by a needle hydrophone in an experimental setup. Simulations of the interaction between contrast bubbles and the sampled ultrasound pressure pulse were performed to yield bubble echoes that correspond to in vitro measures.

The simulations of nonlinear pressure pulses correspond well to the in vitro hydrophone measurements and shows that the attenuation will reduce the effects of pulse distortion due to nonlinear wave propagation. As a consequence, the nonlinear distorted pulse will have a reduced energy content compared to the non distorted pulse as more energy have been shifted to higher frequencies and therefore suffered from a stronger attenuation. The result of bubble response simulations is presented in Figure 3. The simulations are performed with distorted pulses and with theoretically generated non-

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distorted pulse that interacted with the bubble model. The increase of the second harmonic frequency amplitude for the nonlinear distorted pulse is about 3 dB. The difference of the second harmonic amplitudes of the backscattered pulses will increase with higher acoustic pressures but is not detectable at pressure levels below 200 kPa.

Conclusion

The presented results of the pulse wave model in a nonlinear, attenuating and speed-dispersive media look reliable enough for comparative estimation of particular effects. Assumptions taken make simulation quite simple and suitable for model based processing of echographic signals obtained with contrast agents. Quantitative theoretical analysis as well as in-vitro experiments in soft tissue mimicking medium show that the absorption strongly reduces the nonlinear distortion originated in tissue, as the higher frequency components are more absorbed than the fundamental ones. Also theoretical simulations show that contrast bubbles interaction with excitation pulses is the main cause of nonlinear distortions, and a 2-3 dB increase of second harmonic amplitude depends on nonlinear distortions of incident pulse.

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