ESTIMATION OF MICROBUBBLE SURVIVAL TIME FOR SONOPORATION TEMPORAL DOSIMETRY BY SIGNAL PROCESSING

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The microbubbles (MBs) are ultrasound (US) contrast agents, which are used to improve the visibility in diagnosis by contrast imaging techniques. Moreover, in the therapeutic applications of sonoporation, it causes a significant reduction of acoustic cavitation threshold. In the cell sonoporation phenomenon, the microbubble (MB) cavitation results due to the interaction of MBs with US. At low acoustic pressure, MB stable cavity (MB-SC) exists and MB acts as a linear system exhibiting linear and periodic oscillations in response to the ultrasonic excitation. In this state, scattered US is generated comprising the harmonic, subharmonic and ultra harmonic spectral contents of the fundamental frequency [1]. However, at higher acoustic pressures, the MBs oscillate and continuously grow in size until the drastically implosion. In this transitional state, the cavitation is called as MB inertial cavitation (MB-IC). This phenomenon leads to introduce the broadband noise in the scattered spectrum, which can be used for the quantification of MB-IC extent. The explosion of MB exhibits various physical effects such as sudden temperature increase, microjets, shock waves, etc. In order to form sonoporation an effective and controllable drug delivery system in the temporal and spatial domain, one of the prime necessities is the development of an adequate and precise MB-IC dosimetry system [2, 3].

The objective of this work is to apply the signal processing approach for the estimation of optimal value of MB exposure time in order to achieve the maximum sonoporation efficiency with high cell viability. During the experiment, sonoporation cuvette of 1 cm path-length is used. It was filled either by 1 ml of MB suspension (+MB) or 1 ml of the phosphate-buffered saline-background group (MB-). The US waves were excited by an ultrasonic transducer having center frequency of 1 MHz and bandwidth up to 1.2 MHz (– 6 dB). The other parameters were: pulse repetition frequency of 1 kHz, 10 % duty cycle, 100 to 700 kPa peak-negative-pressure (PNP) and overall exposure duration of 6 s. The receiving transducer to detect the scattered US signals was positioned 90º to the transmitter.

Firstly, the denoising of received US signals was performed by applying the discrete wavelet transform (DWT) with the Daubechies mother wavelet [4]. Later on, the time-frequency analysis of amplitudes of magnitude spectrums in each case (with or without MBs) at different pressures (100-700 kPa) was performed for better visualization. In order, to estimate the optimal frequency, the differential root-mean-square (RMS) amplitudes (the difference between the RMS amplitudes obtained with MBs and without MBs) and differential inertial cavitation dose (ICD) are compared for different frequency ranges from 1.5-1.8 up to 9.5-9.8 MHz. After selecting the optimal frequency range (1.5-1.8 MHz in this case), the MB survival time and rate of MB survival time were estimated at different pressure conditions, which are the proposed metrics for the optimal MB exposure duration and cavitation control respectively.

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