Microbubble Oscillations Induced by Focused Ultrasound: Key Parameters Influencing Cavitation Dose

In ultrasound-mediated blood–brain barrier (BBB) opening procedures, intravenously injected microbubbles (MBs)—gas-filled agents encapsulated by lipid or protein shells—play a central role. Originally developed as ultrasound contrast agents, MBs have demonstrated considerable potential for modulating BBB permeability. Upon exposure to focused ultrasound within cerebral vasculature, MBs undergo oscillations that transiently disrupt the tight junctions of endothelial cells, facilitating the temporary passage of macromolecules exceeding 400 Da. This bioeffect can be harnessed to improve the delivery and therapeutic efficacy of drugs targeting, among others, neurodegenerative disorders such as Alzheimer’s disease.

This study investigates the influence of various parameters on the acoustic emissions of microbubbles (MBs; SonoVue, Bracco), including MB concentration (0.0008%, 0.004%, 0.016%, 0.08%, 0.4% [V/V]), peak negative pressure (61.5 ± 8, 121 ± 15.5, 252.5 ± 33, 600 ± 80, 1300 ± 165, and 2600 ± 340 kPa), and ultrasound pulse duration (100, 200, and 1000 μs). Experiments were conducted in a flow setup equipped with a focused transducer (H101, Sonic Concepts, f_0 = 1.05 MHz) and a passive acoustic receiver.

Three cavitation metrics were derived from the recorded acoustic signals: stable cavitation dose from harmonics (SCD_{har}), from ultraharmonics (SCD_{ultra}), and inertial cavitation dose (ICD) based on broadband emissions.

The results indicate that SCD_{har} generally increases with pressure, reaching a maximum at 600 kPa before declining at higher pressures. SCD_{ultra} peaked at MB concentrations of 0.004% and 0.016%, while ICD remained relatively uniform across concentrations, with no substantial variations. A pronounced ICD response was observed at pressures ≥ 600 kPa, with the highest values recorded at the maximum MB concentration (0.4%).

Currently, no standardized methodology exists for quantifying cavitation dose, making it a subject of ongoing research. The presented findings highlight key trends in MB behavior under varying experimental conditions. The selected parameter ranges provide a broad perspective on MB acoustic responses within this experimental setup.