A miniature PVDF receiver for acoustic monitoring of microbubble-mediated ultrasound brain therapy

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Background, Motivation and Objective

Microbubble (MB)-mediated focused ultrasound (FUS) is a non-invasive method for transiently increasing the permeability of the blood-brain barrier (BBB) that enables targeted agent delivery to the brain. Online monitoring of spectral characteristics of the MB acoustic emissions permits assessment of the degree of increased BBB permeability and detection of tissue damage. A high frequency receiver with broad bandwidth, high signal-to-noise ratio (SNR) and low-cost is needed for high spatial temporal resolution in cavitation monitoring, allowing directly assessing MB activities and controlling BBB modulation in preclinical FUS interventions.

Statement of Contribution/Methods

Broadband polyvinylidene fluoride (PVDF) receivers were constructed (film thickness = 110um, active area = 1.2mm^2, n = 6). Silver epoxy was used as acoustic backing to increase bandwidth. A 20dB preamplifier was used to improve the SNR. The receiver sensitivity with amplifier correction was characterized and compared to that of a fiber optic and a previously constructed hydrophone (O'Reilly *et al., IEEE Trans. Biomed. Eng.,* 2011), at discrete frequencies (range = 0.5-5.5MHz) using two calibrated imaging transducers. The receivers were tested on the benchtop with MBs (Definity™, 1:200 v/v in saline) flowing through thin-walled tube phantoms (inner diameter = 2 mm). The MBs were exposed using a spherically-focused transducer (diameter = X mm, radius of curvature = X mm, frequency = 580kHz, pulse length = 10ms, pulse repetition frequency = 1Hz, duration = 60s) using a previously developed acoustic emissions-based feedback controller (O'Reilly *et al.*, *Radiology* 2012).

Results/Discussion

All six receivers showed comparable sensitivity to that of a commercial fiber optic hydrophone in the 1 to 5 MHz low megahertz region (100-200 mV/MPa). During the benchtop experiments, each receiver detected MB emissions up to the fourth harmonic and ultraharmonic. The capability of detecting a wide range of emission characteristics shows potential for sonication calibration using ultraharmonics and BBB modulation using harmonics. The performance and reproducibility of this receiver make it suitable for acoustical monitoring of MB cavitation events Future work will involve the development of a multi-element receiver array to guide BBB modulation in preclinical settings.

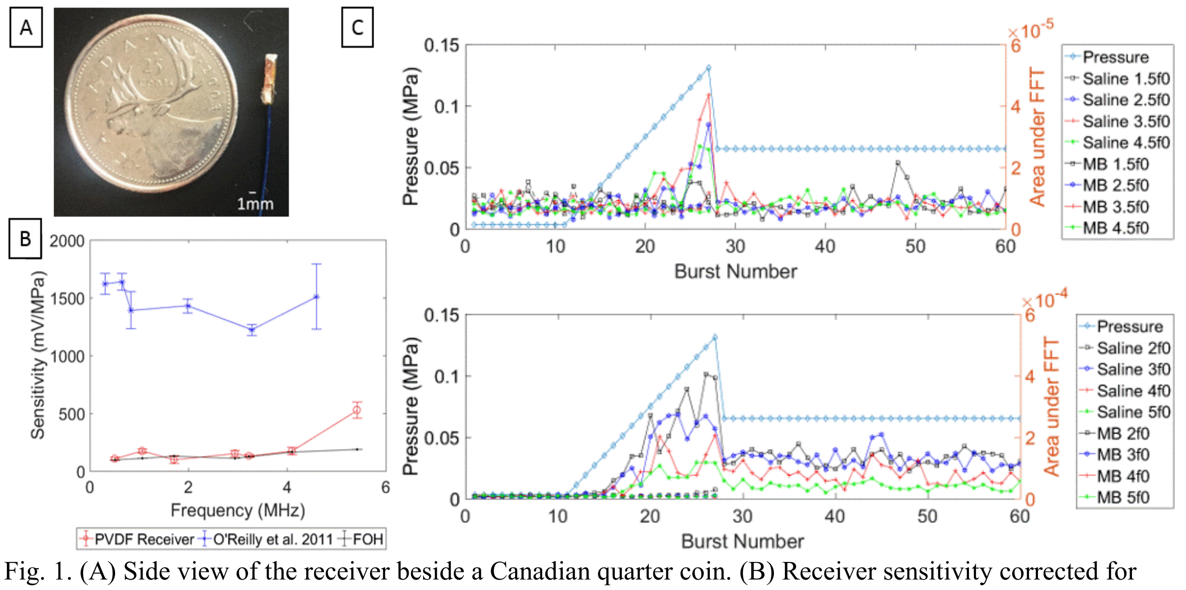

Fig. 1. (A) Side view of the receiver beside a Canadian quarter coin. (B) Receiver sensitivity corrected for preamplifier comparing to that of a receiver with 15 times more active area and a fiber optic hydrophone (FOH). Error bars indicate one standard deviation. (C) Spectral content acquired by the receiver during 60 bursts in the benchtop experiment. Pressure was dropped to 50% of the peak as the 2nd ultraharmonic reached 3.5 times baseline averaged over the first 10 bursts. Sonication to saline was plotted until pressure drop as a negative control. Top graph shows the 1st to 4th ultraharmonics ± 100Hz signal content in each burst. Bottom graph shows the 2nd to 5th harmonics ± 100Hz signal content in each burst. f0 = fundamental frequency.