Implications of acoustic emissions acquisition window on microbubble-mediated treatment monitoring via three-dimensional passive cavitation imaging

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Background, Motivation and Objective

Three-dimensional (3D) passive cavitation imaging (PCI) is a promising approach for online monitoring and control of microbubble (MB)-mediated focused ultrasound (FUS) therapy [1,2]. Previous studies correlating PCI data with bioeffect distributions following FUS + MBs have acquired channel data over a small fraction of the total FUS on-time (*e.g.*, 0.01-6% at the start of each pulse [3-5]) due to hardware limitations. Here we investigate how the acoustic emissions acquisition window impacts the ability of 3D PCI data to predict the volume of tissue damage following MB-mediated nonthermal brain ablation.

Statement of Contribution/Methods

Experiments were performed on craniotomized rabbits (3-4 kg) using a clinical-scale prototype FUS brain system [2]. Pulsed FUS (612 kHz, 10 ms pulses every 1 s for 120 s) was electronically steered over a 2 x 2 square grid (6 mm side length) starting concurrently with MB infusion (0.2 ml/kg Definity^{TM}, 90 s) via 3D PCI-based exposure calibration [2]. Exposures were carried out at 0/50/100/150% of the pressure required to detect subharmonic activity *in vivo* ($\boldsymbol{p}_{sub}$), and acoustic emissions were acquired over the entire duration of FUS on-time. Tissue damage volumes assessed via 3T MRI and histology (48 hr post-FUS) were compared with 3D PCI data generated retrospectively from different acoustic emissions acquisition windows (*i.e.*, variable onset/duration).

Results/Discussion

T_2*-weighted MRI displayed signal hypointensities induced by exposures at $\boldsymbol{p} \geq 100\%\ \boldsymbol{p}_{sub}$ [Fig.1A], which were associated with regions of red blood cell extravasations and tissue necrosis on H&E sections. 3D PCI data generated by processing fully-sampled acoustic emissions correlated linearly with the MRI- and H&E-assessed tissue damage volumes [Fig.1B]. Under-sampling of the acoustic emissions data (*i.e.*, acquisition window duration < FUS on-time) introduced regions of false positive/negative signal in the 3D PCI data [Fig.1A,C]. Our results underscore the importance of maximizing the proportion of FUS on-time over which acoustic emissions are acquired when performing PCI for guiding MB-mediated FUS therapy.

[1] O'Reilly *et al*, *IEEE TBME* 2014 [2] Jones *et al*, *Theranostics* 2018 [3] Arvanitis *et al*, *PMB* 2013 [4] Wu *et al*, *Sci Rep* 2018 [5] Yang *et al*, *Sci Rep* 2019

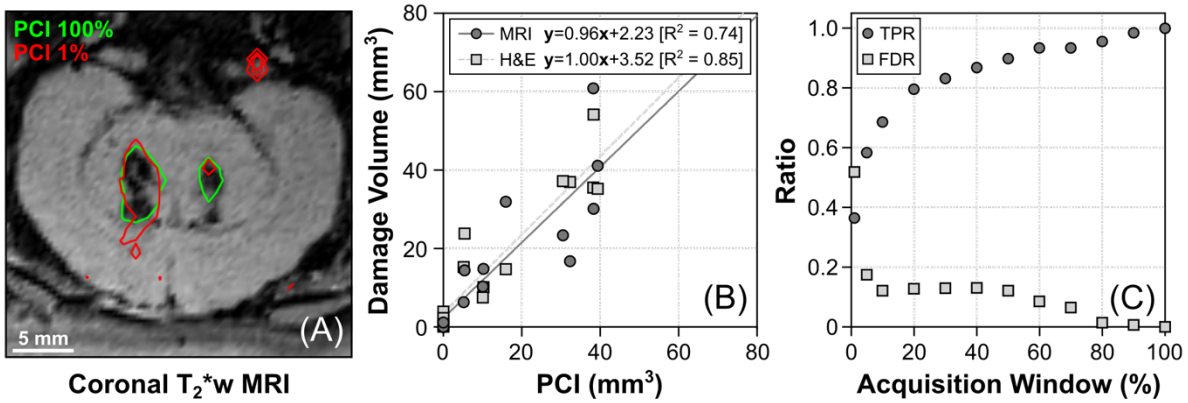

Fig 1. (A) Coronal T_2*w MRI with 3D PCI data overlaid (maximum intensity projection over entire brain). Contours of 3D PCI data reconstructed with 1% (red) and 100% (green) of the FUS on-time are plotted (1% = 0.1 ms at start of each pulse). (B) Correlation of MRI (T_2*w hypointense) and histology (H&E necrotic region) tissue damage volumes with 3D PCI data (acquisition window = 100% total FUS on-time). (C) True positive rate (TPR) and false detection rate (FDR) as a function of the acquisition window duration (gold standard = 100% window). Data in (B,C) are from 15 targets over 5 animals.