Image-guidance for Therapeutic Ultrasound: Passive Cavitation Imaging for Drug Delivery and Tissue Ablation

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Clinical Trials of Cavitation-Based Therapeutic Ultrasound

Enhanced Chemotherapy

Dimcevski et al. 2016
J Control Release

Blood Brain Barrier Disruption

Lipsman et al. 2018
Nature Comm

Mechanical Tumor Ablation

Vidal Jove et al. 2019
Int Symp Ther US
Microbubbles and Cavitation

Exogenous Microbubbles

Wilson and Burns (2010) Radiology

Endogenous Microbubbles

Maxwell J Acoust Soc Am 2011

Change in Pressure

time

Power Spectra [dB]

Fund

Freq [MHz]
Stable and Inertial Cavitation

Surface Modes

Raymond et al. 2016 PMB
‘Traditional’ Cavitation Detection

- Function Generator
- Power Amplifier
- Matching Box
- Therapy Transducer
- Cavitation Detector
- Oscilloscope
- Pre-Amplifier
- Pulser-Receiver

Power Spectra [dB]
Freq [MHz]

- Fund
- Sub
- BB
Standard Contrast-enhanced Ultrasound imaging
Combining Cavitation Detection & CEUS

Focused PCD

Unfocused PCD

Sensitive

Insensitive
Passive Cavitation Imaging

\[ B(\mathbf{r}) = \int_{t_0}^{t_f} \sum_{l=1}^{L} X_l(f) \cdot e^{i 2\pi f \text{ Lateral} [\text{mm}]} \]
Passive Cavitation Imaging

- Image formation can be done in real-time (GPU)

Artifact!
Advanced Algorithms

Adaptive Beamforming

Spatial Filtering

Nonlinear Beamforming

Aberration Correction

Coviello et al. 2015
J Acoust Soc Am

Salido et al. 2019
Int Soc Therap Ultrasound

Abadi et al. 2018
J Acoust Soc Am

Jones et al. 2016
Phys Med Biol
Cavitation Mapping for Drug Delivery
Drug Delivery: Setup

- Intra-arterial infusion of fluorophore-labeled echogenic liposomes
- Porcine Femoral Artery w/ bare metal stent

Haworth et al. (2016) Ultrasound Med Biol
Identifying and mapping cavitation can assist in predicting delivery to vascular tissue

Haworth et al. (2016) Ultrasound Med Biol
Cavitation Mapping for Histotripsy (Mechanical Ablation)
PCI: Histotripsy Liquefication

Bader et al. (2018) IEEE Med Imaging
PCI: Histotripsy Liquefaction

Stained Phantom

B-mode Imaging Overlay

PCI Overlay

True Positive Rate

False Positive Rate

PCI AUROC: 0.93
Bmode AUROC: 0.82

Bader et al. (2018) IEEE Med Imaging
Final thoughts

• Sources of cavitation can be mapped in a quantitative manner
• The image is diffraction limited
  – Poor axial resolution for a clinical diagnostic array
  – Alternate transducer geometries or beamforming algorithms improve image quality
• The ability of PCI to guide a therapy depends on how central cavitation activity is to inducing bioeffects
Acknowledgements

http://med.uc.edu/ultrasound