Evaluation of the Histotripsy-Induced Sonochemical Reactions

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ABSTRACT & BACKGROUND

- Current cancer treatments are associated with caustic side effects, significant failure rate, or cannot be implemented for critically ill patients[1]
- Histotripsy is a form of therapeutic ultrasound that lyses cells mechanically via bubble cloud formation (**Fig. 1**)[2]

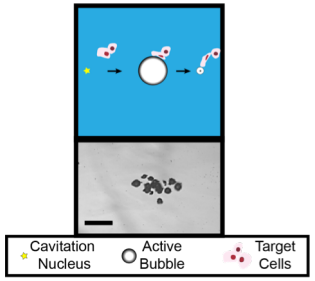

Fig. 1: (Top Panel) Schematic of histotripsy bubble activity inducing lethal strain to nearby cells. (Bottom Panel) High speed image of bubble cloud formation.[3]

Fig. 2: The gaseous contents of the inertially collapsing bubble becomes a warm, dense plasma in which ROS and light emissions (red arrow) are produced.

- The inertial collapse of a bubble can sonochemically generate reactive oxygen species (ROS) capable of inducing cell death[4]; light emissions are also a byproduct of the sonochemical reaction (**Fig. 2**)
- **Assessing and accentuating ROS generation during histotripsy is a promising therapeutic candidate to treat cancer**

HYPOTHESIS/OBJECTIVE

- The **central hypothesis** of this study is that *histotripsy can be utilized to generate in situ sonochemical reactions*.
- The **objective** of this study is to *quantify the degree of ROS formation and light emissions from histotripsy-induced bubble cloud activity in vitro*.

MATERIALS AND METHODS

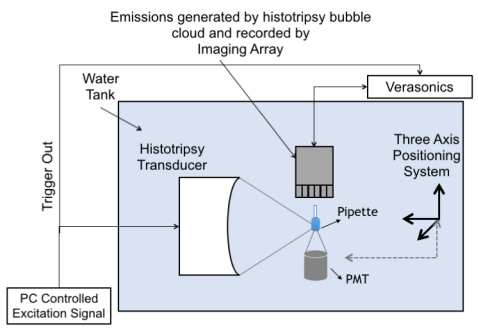

Fig. 3: Diagram of experimental set up

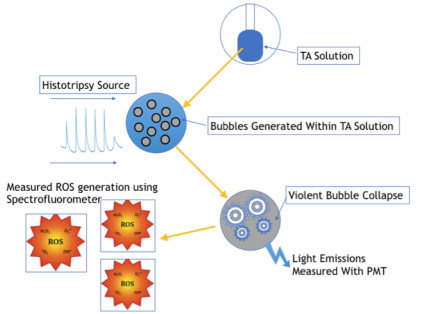

Fig. 4: Overview of potential sonochemical processes during histotripsy insonation

- Conversion of terephthalate acid (TA) to hydroxylxerephtalate acid (HTA) via ROS formation quantified with spectrofluorometric assay[4]
- Light emissions were recorded with a photomultiplier tube (PMT)
- Bubble cloud activity was assessed with passive cavitation imaging (PCI)[5]

RESULTS

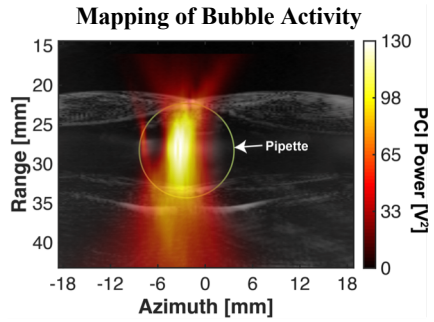

Fig. 5: Strength of bubble cloud activity registered with B-mode image of pipette. The 1-MHz histotripsy pulse (5 cycle pulse duration, peak negative pressure of 24.5 MPa) is propagating left to right in the image.

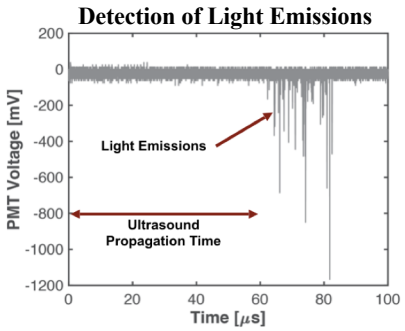

Fig. 6: Light emissions recorded by the PMT during histotripsy-induced bubble cloud activity. The histotripsy pulse had a 1-MHz fundamental frequency, 25-cycle pulse duration, and 29.0 MPa peak negative pressure.

RESULTS (CONT.)

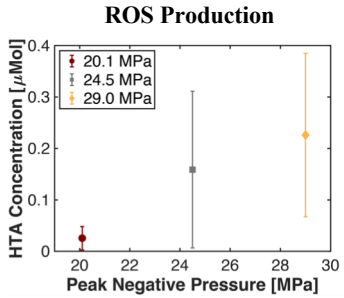

Fig. 7: Dependence of ROS-induced TA to HTA conversion on the histotripsy pulse peak negative pressure. The pulse was 5 cycles in duration and 1-MHz fundamental frequency pulse.

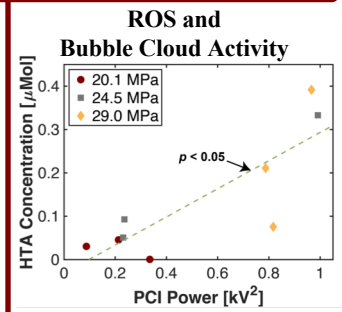

Fig. 8: Correlation of ROS-induced HTA and bubble cloud activity assessed with PCI. The peak negative pressure of the histotripsy pulse is noted in the legend.

FUTURE DIRECTIONS

- The presence of both light emissions and ROS indicate histotripsy induces sonochemical reactions
- The total ROS production was an order of magnitude lower than previous studies[4], but ROS production rate 25-fold greater
- Future study of histotripsy-induced ROS include optimizing insonation parameters and combining histotripsy with sonosensitizers[1]
- Utilizing histotripsy for cell lysis and the generation of toxic ROS levels is an innovative method to treat cancer.

ACKNOWLEDGEMENTS

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BADER LAB

LITERATURE CITATIONS

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[5] Haworth et al., IEEE UFFC, 64(1): 177-191, 2017

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