Ultrasound-mediated Scavenging of Dissolved Oxygen

Image-Guided Ultrasound Therapeutics Laboratories

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MOTIVATION & OBJECTIVE

- Excess dissolved gases in blood can affect tissue health. Reactive oxygen species produced during reoxygenation following an ischemic event can significantly increase infarct volume (Murry 1996, Zorov 2014).
- Current treatments employ systemic adminstration of a therapy, which can have deleterious off-target effects.
- *The objective of this study is to demonstrate gas scavenging using acoustic droplet vaporization (ADV).*

BACKGROUND

ADV is the ultrasound-mediated conversion of a liquid perfluorocarbon droplet emulsion into gas microbubbles (Figure 1). The conversion only occurs when the ultrasound pressure amplitude exceeds a threshold value.

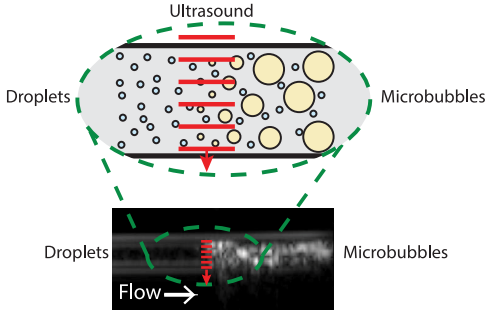

Figure 1: (Top) Schematic of the ultrasound-mediated droplet to microbubble conversion. (Bottom) B-mode ultrasound image demonstrating the formation of microbubbles.

HYPOTHESIZED MECHANISM

ADV results in a 125-fold increase in the perfluorocarbon volume. This creates a microbubble undersaturated with dissolved gases. The concentration differential results in gases moving from the surrounding fluid into the microbubble, thereby scavenging the gas (Figure 2).

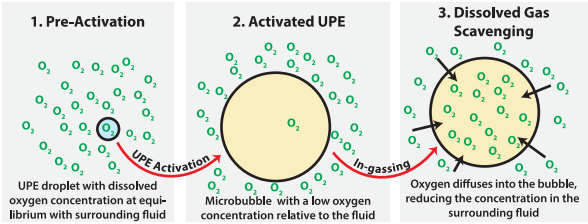

Figure 2: Schematic of ADV and scavenging of dissolved oxygen (O_2).

METHODS

- To create size-isolated droplets, the emulsion was differentially centrifuged (Feshitan 2009).
- Droplets were flowed through a vessel phantom that includes dissolved oxygen (DO) sensors (Figure 3).
- Droplets were insonified with 2 MHz ultrasound at 0 MPa (no ultrasound), 1 MPa (sub-threshold), 3 MPa (super-threshold), and 5 MPa (super-threshold).
- The dissolved oxygen was measured upstream and downstream of the ultrasound insonation location.
- The effluent was measured to determine the droplet size distribution and conversion fraction (Figures 3 and 4).

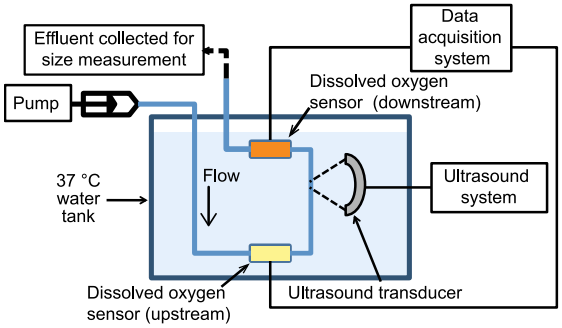

Figure 3: Experimental setup. The fluid required approximately 20 s to travel from the ultrasound insonation location to the downstream dissolved oxygen sensor. The upstream and downstream DO measurements were recorded simultaneously throughout the experiment.

RESULTS

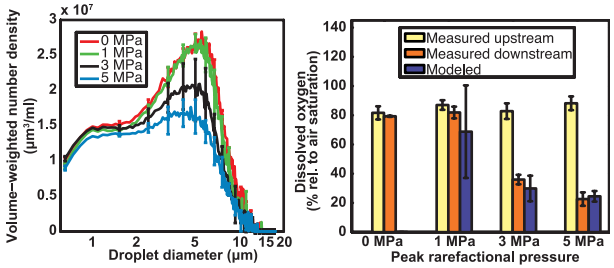

Figure 4: Volume-weighted number-density size-distributions for droplets in saline that were not size-isolated (left) and corresponding changes in dissolved oxygen (right). A sub-threshold insonation at 1 MPa did not convert an appreciable number of droplets. At 3 MPa and 5 MPa, fewer droplets were measured, indicating that droplets were converted into microbubbles. Even at the highest ultrasound insonation pressure amplitude, less than 5% of droplets smaller than 2 μm were converted into microbubbles. Significant ultrasound-mediated decreases in dissolved oxygen only occurred at pressure amplitudes above the ADV threshold (1.7 MPa).

RESULTS CONTINUED

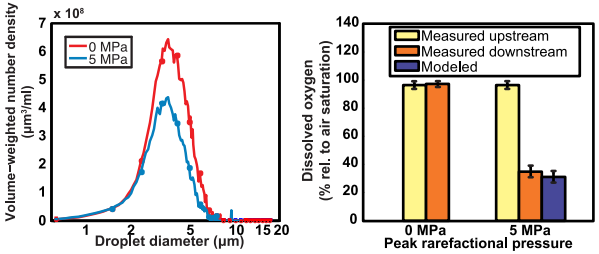

Figure 5: Volume-weighted number-density size-distributions for size-isolated droplets in saline (left) and corresponding changes in DO (right). Differential centrifugation increased the fraction of droplets between 2 μm and 5 μm from 29% to 93%. A model based on the hypothesized mechanism and droplet conversion fraction agreed with the experimental measurements.

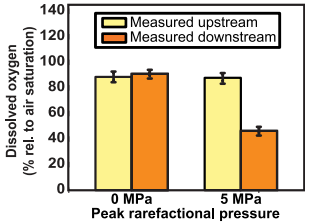

Figure 6: Experimentally measured dissolved oxygen scavenging in porcine whole blood with droplets that were not size isolated (Figure 4, left). The droplet number density was approximately matched to experiments in saline.

DISCUSSION & IMPACT

- Ultrasound-mediated conversion of perfluorocarbon droplets into gas microbubbles scavenged dissolved oxygen.
- Oxygen scavenging was observed in saline and whole blood.
- A numerical model based on concentration gradients accurately predicted the amount of gas scavenged, implying the mechanism of scavenging is the diffusion of dissolved gases from the fluid and into the microbubbles.
- Differential centrifugation isolated droplets between approximately 2 μm and 5 μm.
- Next steps include measuring gas scavenging kinetics and the efficacy for reducing reactive oxygen species production.

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