Reduction in Dissolved Oxygen Resulting from Acoustic Droplet Vaporization

Karla P. Mercado\textsuperscript{1}, Kirthi Radhakrishnan\textsuperscript{1*}, Christy K. Holland\textsuperscript{1,2}, Kevin J. Haworth\textsuperscript{1,2}

1: University of Cincinnati, College of Medicine, Department of Internal Medicine, Division of Cardiovascular Health and Disease
2: University of Cincinnati, College of Engineering and Applied Science, Biomedical Engineering Program

* Now with Philips Electronics North America
Acoustic Droplet Vaporization (ADV)

- Imaging\(^1\) and Aberration Correction\(^2\)
- Embolootherapy\(^3\)
- Drug delivery\(^4\)
- Thermal ablation\(^5\)

\(^1\)(Rapoport et al. 2007 JNCI, Sheeran 2013 UMB, Sheeran 2015 UMB)
\(^2\)(Kripfgans et al. 2002 IEEE UFFC, Haworth 2008 UMB)
\(^3\)(Kripfgans 2005 IEEE UFFC, Zhang 2011 Acad. Radiol.)
\(^4\)(Fabiilli 2010 UMB, Rapaport 2011 JCR, Moncion 2016 Acta Biomater.)
ADV Ingassing\textsuperscript{1,2,3}

1. Pre-ADV

2. Post-ADV

3. Dissolved Gas Scavenging

- Concentration gradient
- Solubility Difference

\[ DO_{l,f} = \frac{d_{i} V_{d, i}^{+} + k_{O_{2},d} + k_{O_{2},l} }{V_{i,i}^{+} k_{O_{2},l} (1 + \frac{k_{O_{2},d} V_{b,f} R T}{\kappa_{O_{2},d} V_{i} + k_{O_{2},d} / V_{i}})} \times DO_{l,i} \]

Droplet formation

- 0.25 mL PFP
- 0.75 mL 4% (w/v) BSA in saline

High-speed Shaking

Volume-weighted number density/10^6 (μm^3/mL)

Diameter (μm)
**Droplet formation**

### Large Droplet Removal

- **Initial droplet solution**
- **Step 1**: Centrifuge
- **Step 2**: Separate pellet and supernatant
- **Small droplets**
- **Large droplets**
- **Supernatant**
- **Pellet**

### Small Droplet Removal

- **Supernatant**
- **Step 3**: Centrifuge (supernatant centrifugation)
- **Step 4**: Discard supernatant, resuspend pellet in PBS
- **Step 5**: Centrifuge (pellet centrifugation)

*Repeat Steps 4 and 5 according to the number of pellet centrifugation steps*

---

**Graph**:

- **Original**
- **1 μm – 3 μm**
- **2 μm – 5 μm**

**X-axis**: Diameter (μm)

**Y-axis**: Volume-weighted number density/10^6 (μm^3/mL)
Experimental Setup

- Syringe pump
- RF Amplifier
- Verasonics Vantage
- Imaging array
- EVA tubing
- Dissolved oxygen sensor (upstream)
- Dissolved oxygen sensor (downstream)
- Flow
- Function generator
- Data acquisition system
- PVC tubing

Effluent collected for size measurements

37°C
Oxygen scavenging at 2 MHz

- Number Density: $4 \times 10^8$ droplets/mL
- PFP Volume Fraction: 0.22%
Predicted Effect of Droplet Dilution

Predicted Dissolved Oxygen (% re air saturation)

Phase-transitioned PFP Liquid to Diluent (% v/v)

Predicted Dissolved Oxygen (% re air saturation)

Phase-transitioned PFP Liquid to Diluent (% v/v)
Measured Effect of Droplet Dilution

- Droplets size isolated to 1-6 μm
- 5 MHz, 4.25 MPa peak neg. pressure
Acoustic Shadowing

Fraction of surviving droplets (%)

Diameter (µm)

0 1 2 3 4 5 6 7 8

100
80
60
40
20
0

Non-size isolated droplets

Droplets size isolated to 1-3 µm

Droplets size isolated to 2-5 µm

Size isolated Droplets (1-3 µm)

Non-size isolated droplets

(cm)

-1 0 1

(cm)

-1 0 1
Conclusions

- Acoustic droplet vaporization induces dissolved gas scavenging

- Magnitude of scavenging depends on volume fraction of perflurocarbon phase transitioned (~0.02%, v/v)

- Emulsion composition, including concentration and size distribution, plays a significant role
Acknowledgements

Biomedical Ultrasonics & Cavitation Laboratory
Haili Su, MD, PhD
Arunkumar Palaniappan, PhD
Austin Wanek
Vincent Huang
Drew Dresmann
Niusha Jahanpanah
Joseph Brune
Stacy Loushin
Kyle Stewart
Sarah Li
Devin Ryan
Lindsay Snider

Research Support Provided By:
NIH-NHLBI (K25 HL133452)
NIH-NCATS (KL2 TR000078)
AHA (16SDG27250231)
University of Cincinnati

Other Collaborators
Andrew Redington, MD
Karin Przyklenk PhD
John Lorenz, PhD
T. Douglas Mast, PhD
David McPherson, MD
Kenneth Bader, PhD
Vishnu Reddi, PhD
Quan He, PhD
Shaoling Huang, PhD
Melvin Klegerman, PhD
Himanshu Shekhar, PhD
Shenwen Huang
Robert Kleven
Kyle Rich

ultrasound.uc.edu
Extra Slides
Ultrasound Parameters

- 2 MHz
- 10 cycles
- PRF: 100 Hz
- Peak Neg Pressure
  - 2.5 MPa
  - 7.3 MPa
  - 12.2 MPa

- 5 MHz
- 10 cycles
- 500 Hz
- Peak Neg Pressure
  - 4.25 MPa
Estimation of ADV Gas Scavenging

- **Equal Partial Pressures**

\[ \frac{R T n_{O_2,b,f}}{V_{b,f}} = \frac{k_{O_2,d} \cdot n_{O_2,d,f}}{V_{d,f}} = \frac{k_{O_2,l} \cdot n_{O_2,l,f}}{V_{l}} \]

- **Conservation of Mass**

\[ \frac{P_{O_2,d,i} V_{d,i}}{k_{O_2,d}} + \frac{P_{O_2,l,i} V_{l}}{k_{O_2,l}} = n_{O_2,b,f} + n_{O_2,d,f} + n_{O_2,l,f} \]

- **Droplet Expansion**: \( V_{b,f} = (V_{d,i} - V_{d,f}) \cdot E \)

\[ DO_{l,f} = \frac{P_{O_2,d,i} \cdot V_{d,i} \cdot k_{O_2,d} + P_{O_2,l,i} \cdot V_{l,i} \cdot k_{O_2,l}}{P_{O_2,l,i} \cdot V_{l,i} \cdot k_{O_2,l} \cdot \left(1 + \frac{k_{O_2,d} V_{b,f}}{R T V_{l}} + \frac{k_{O_2,d} V_{d,f}}{k_{O_2,l} V_{l}} \right)} \times DO_{l,i} \]
Size isolated vs non-size isolated

Distribution A
Supernatant Centrifugation Speed: 230 × g
Pellet Centrifugation Speed: 230 × g
Number of Pellet Centrifugations: 4

Distribution B
Supernatant Centrifugation Speed: 100 × g
Pellet Centrifugation Speed: 100 × g
Number of Pellet Centrifugations: 5