Characterizing the effect of agitation post - activation of lipid shelled microbubbles used for focused ultrasound
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Introduction

Blood - Brain Barrier (BBB)
- Selective and protective barrier from potentially harmful substances
- 98% of small molecules do not penetrate the BBB¹
- Limits passage of therapeutic agents for neurodegenerative diseases including Alzheimer’s Disease (AD)

Focused Ultrasound Blood Brain Barrier Opening (FUS - BBB0)
- Used to enhance drug delivery, disrupt blood-brain barrier in a safe, reversible, and targeted manner²
- FUS promotes mechanical stresses termed acoustic cavitation within the cerebral vasculature upon introduction of lipid - shelled microbubbles through IV injection³.

Parameters that influence Microbubble(MB) stability
- Parameters affecting the microbubble stability include composition of the lipid shell, gas core, and radial size⁴
- Agitation of the lipid shell that the MB is composed of is a method to create stable microbubbles through homogenization⁵

Objective
Understand the impact of agitation post-activation for the reuse of microbubbles.

Hypothesis
Microbubbles need to be agitated for stable formation through understanding concentration and MB diameter.

Materials and Methods

Activating Lipid - Shelled Microbubbles
1. Lipids were retrieved from the 4°C refrigerator.
2. Alternating sequence of vacuum and introduction of perfluorobutane was conducted (20 seconds each while retaining 40 seconds of gas at the end).
3. The Vialmix (R) was used to agitate and induce microbubble formation for 45 seconds.

Microbubble Sizing
1. 10 µL pipette was used to put isoton II (diluent) into 4 cuvettes
2. Using one vial of isoton II to clean unblock and flush
3. Inserting 2µL into one vial and then starting the program to size.
4. Select distribution of MB between 1 to 10 µm
5. Repeating this three times for each vial of microbubbles

Experiment
1. n=4 MB vials were activated and
2. n=2 were agitated for 45 seconds (agitation)
3. n = 2 were left alone and only used when sizing (non - agitation)
4. All vials were sized on Day(s) 0, 3, 4, 5, and 7
5. Concentration and MB mean diameter was recorded.

Discussion and Conclusion

Microbubbles need to be in a certain range in order to be effective. It needs to be small enough to enter the BBB and large enough to expand the BBB and allow drugs to enter when combined with FUS. (Fig. 1)

Agitation of MB seems to be not as important as both produced result similar to each other in the end(Fig. 6-7)

Average diameter and concentration in both cases of agitation and non agitation decreases throughout (Fig. 6 -7).

Ongoing & Future Work
- Seeing or finding a greater difference between agitation and non agitated MB
- Perform in vitro experiment to absorb cavitation of MB under FUS

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References


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