Abstract: In these experiments we explored the use of low intensity ultrasound to improve the efficacy of convection enhanced drug delivery in glioblastoma therapy. We studied the effect and mechanisms of acoustic streaming, microbubble oscillation, nucleation and cavitation. Results show that ultrasound improves the spatial distribution of tracer in agarose brain mimicking phantoms. The addition of stabilized microbubbles reduces the spatial distribution of tracer.

I. The Problem: To improve drug delivery
Surgical treatment of brain tumors invariably results in tumor regrowth even when antitumor drugs are introduced. Direct injection of pharmaceuticals into brain tissue/tumor site shows limited penetration into the tissue.

II. Methodology: Studied ultrasound-assisted drug delivery
A 30 gauge needle with ultrasound transducer assembly was used to infuse 0.25wt% Evans Blue Dye in PBS at a flow rate of 0.5uL per min into 0.6wt% agarose brain mimicking phantoms. Infusions were conducted with and without 45mW/cm² ultrasound, and with and without the addition of 5x10⁵ microbubbles per uL of tracer. Additionally we studied the effect of ultrasound at these intensities to cause streaming of tracer, and measured streaming velocities.

Brain Phantom Infusion Results
The diameter of the four groups was measured after 30 minutes of infusion under the four parameters.

- Control: Y=6mm
- US: Y=6.3 mm
- MicroB: Y=4.8 mm
- US+MicroB: Y=5.7 mm

Ultrasound improved the distribution of tracer in the phantoms both with and without microbubbles.

Streaming Investigation Results
Dye streaming was more rapid (140% increase) with applied ultrasound. In addition there were unexpected paths traced by the dye during the infusions with the ultrasound because of eddies developed in the fluid.

Conclusions: The increased transport velocity of the dye with ultrasound was quantitatively shown in a homogeneous fluid. How this mechanism may be used to improve the transport of pharmaceutical in brain tissue will be further investigated in poroelastic medium.