

Detection of Stationary Microbubbles in Tissue Using Dual-Frequency Ultrasound

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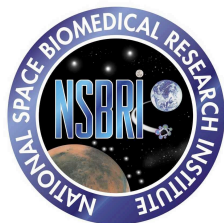


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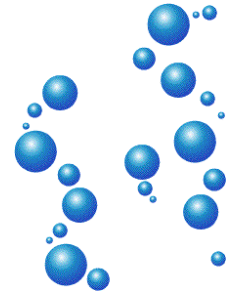
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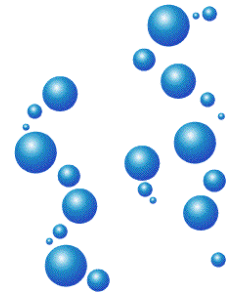
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Introduction

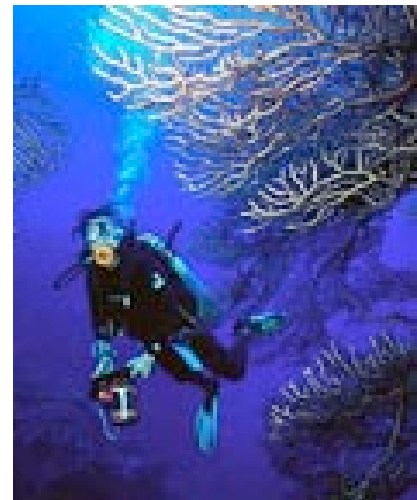
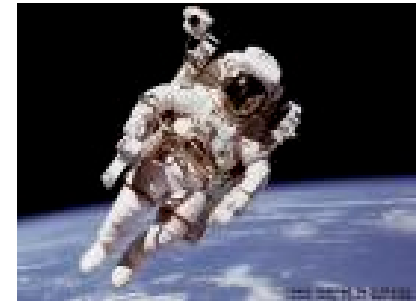


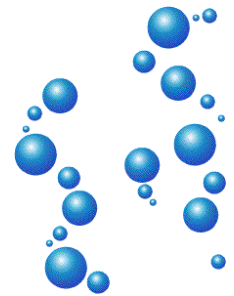
- It is believed that small bubbles normally exist in tissue
 - Bubble formation in tissue during decompression may be the cause of many DCS symptoms
- Current technology has not been able to verify these hypotheses
- Using dual-frequency ultrasound, we have detected stationary microbubbles in tissue

DCS: Potential Benefits of *in-vivo* Stationary Bubble Detection



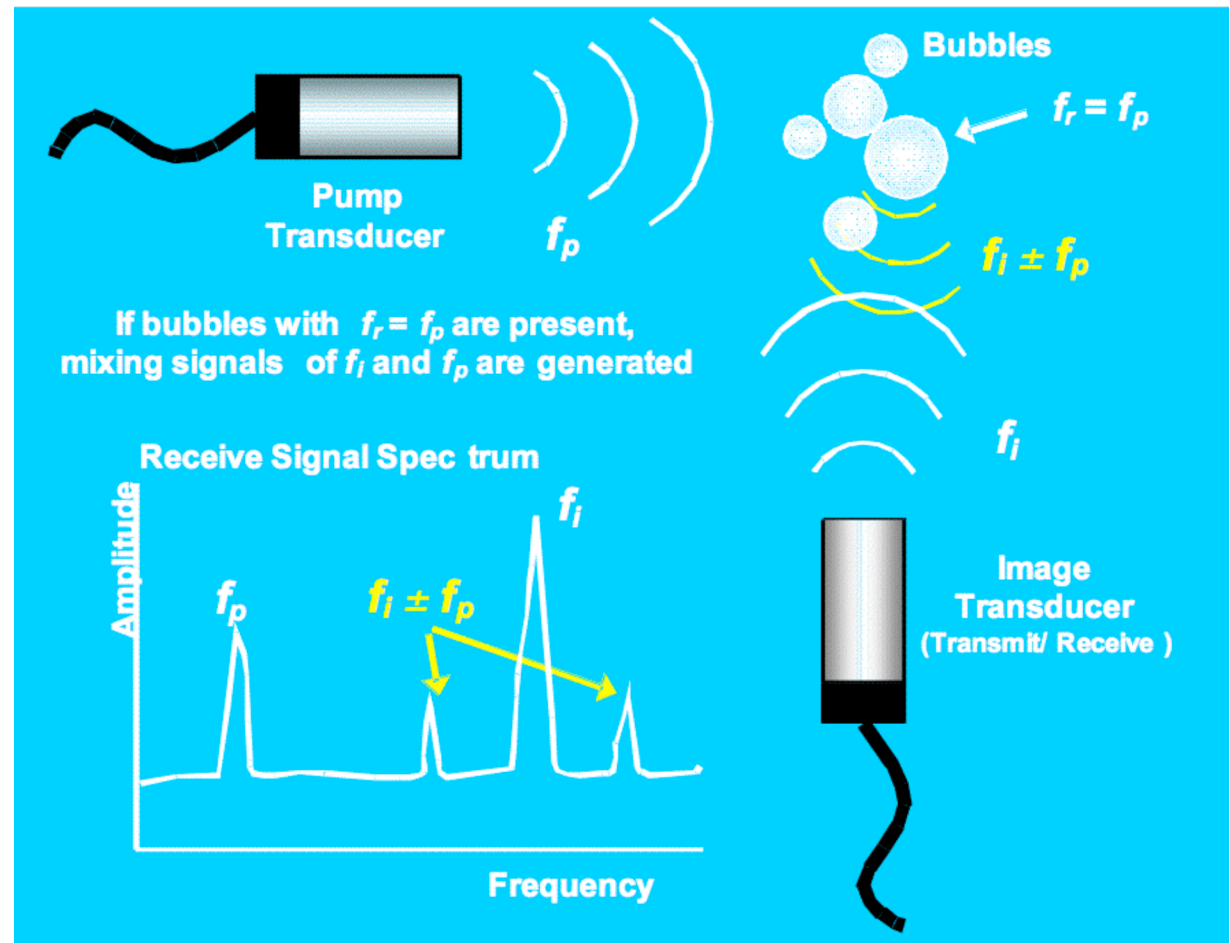
- The detection and sizing of microbubbles during and following decompression could yield:
 - new insights on the progression of DCS
 - provide a metric for the effectiveness of DCS risk mitigation strategies
 - provide real-time assessment of personal DCS risk



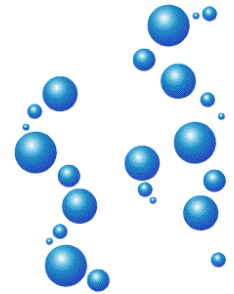


Dual-Frequency Ultrasound

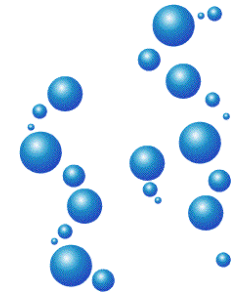
- Bubbles driven by two frequencies
- 'Pump' frequency drives bubbles at resonance
- Resonant bubbles emit the sum and difference of the two driving frequencies



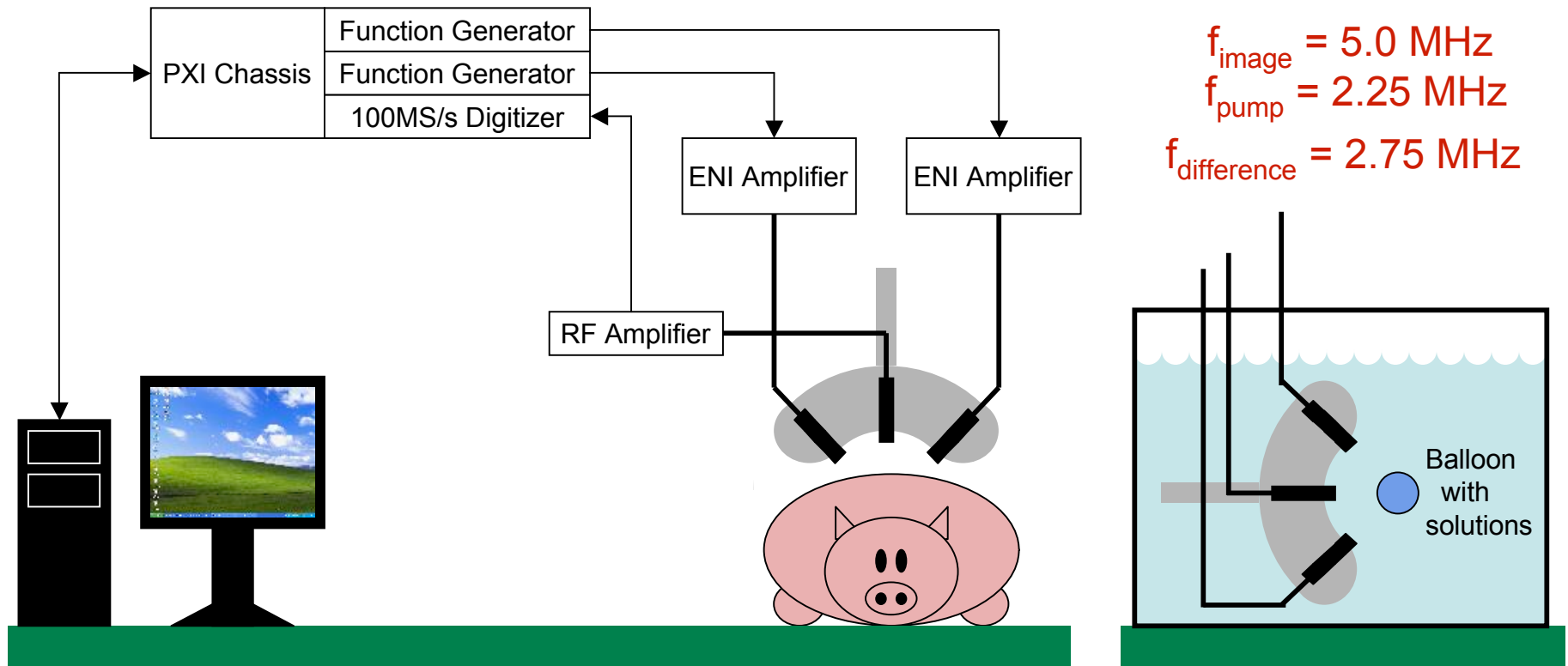
Bubble Models and Experimental Procedure



- Ultrasound Contrast Agent (USCA) Bubbles
 - Definity® (Bristol-Meyers Squib Medical Imaging)
 - Shell-encapsulated bubble
 - 1-3 μm mean diameter
- Solid Polymer Microspheres (SPM)
 - Polylactic acid particle standard (Postnova Analytics)
 - Non-resonant solid sphere
 - 2 μm mean diameter
- USCA and SPM were mixed in solutions ranging from 1×10^5 to 1×10^9 particles/mL
- Solutions were injected into the thigh of an anesthetized swine
- Injection sites were imaged using dual-frequency ultrasound prior to and following injection
- Resonant frequency of a 2 μm free bubble is $\approx 3\text{MHz}$

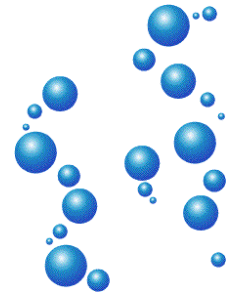


Experimental Setup

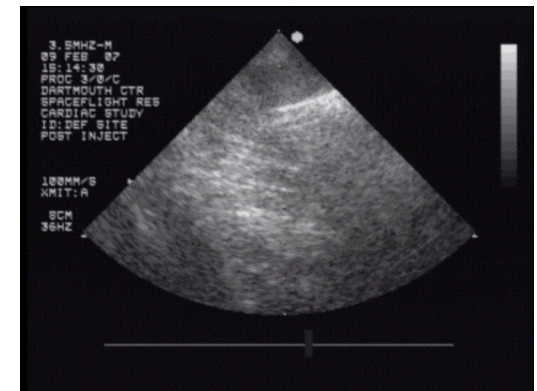
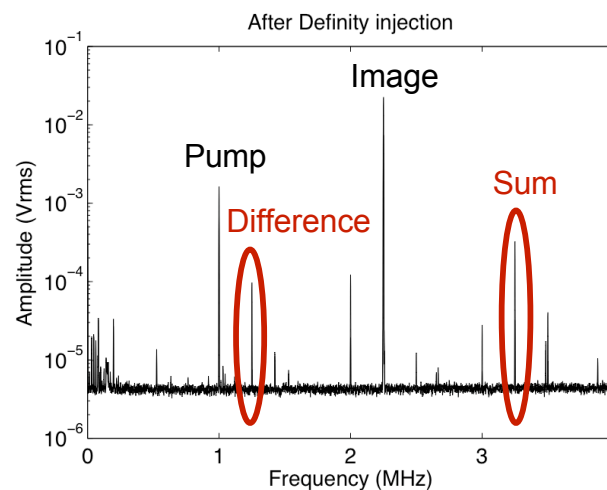
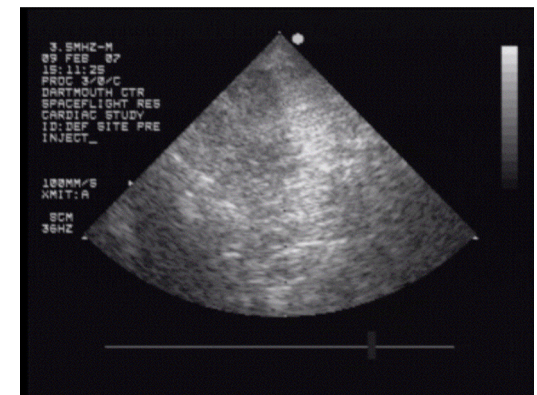
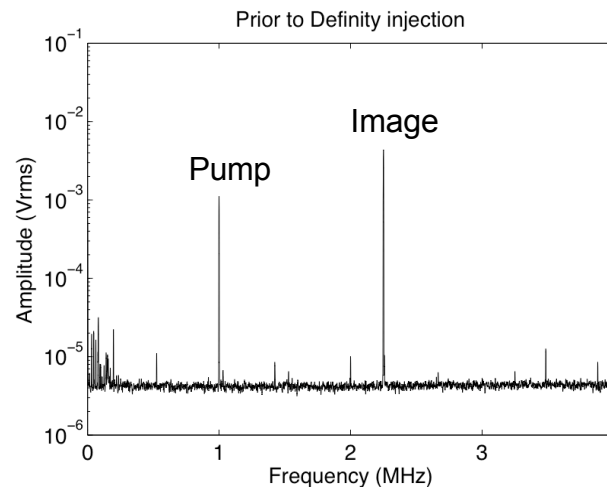


- Each solution of USCA and SPM was
 - Imaged *in vivo* in the thigh (muscle tissue) of an anesthetized swine
 - Imaged *in vitro* in a balloon in a water tank

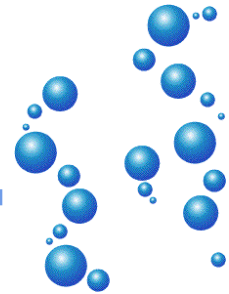
Validation



- No mixing signals were detected prior to injection of USCA
- Significant mixing signals were detected following injection
- 2-D ultrasound cannot distinguish bubbles from other reflectors

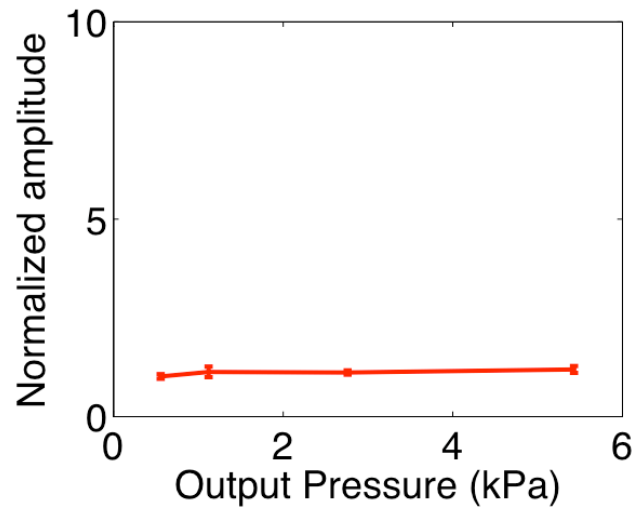


Power Measurements

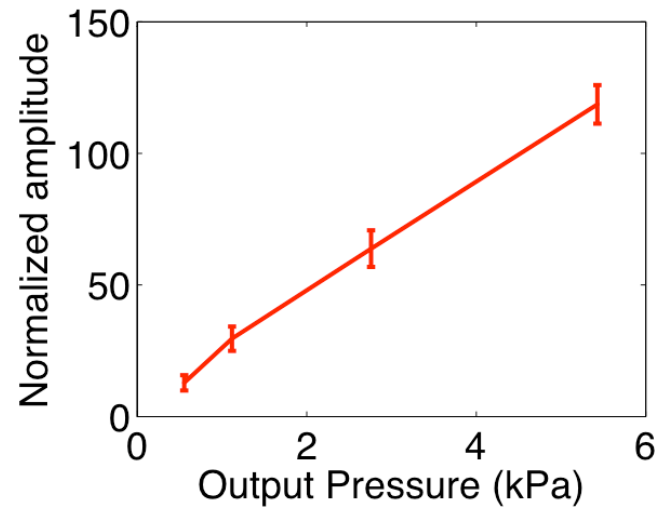


IN-VITRO

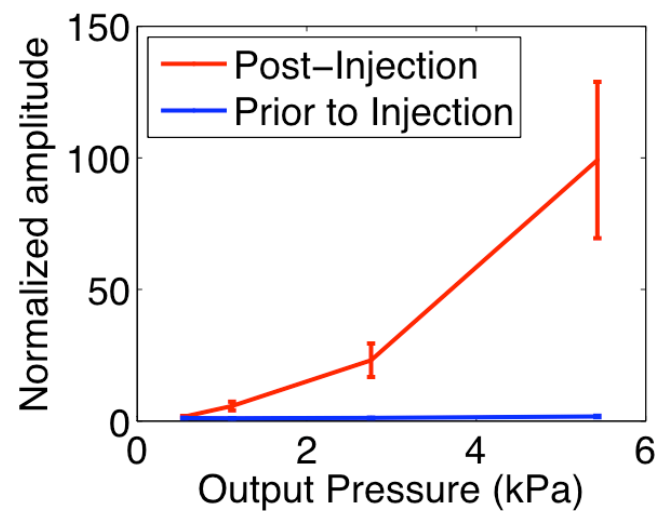
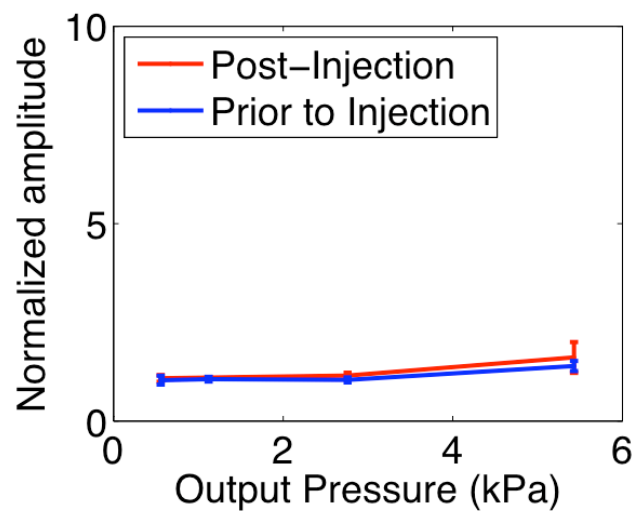
SOLID POLYMER
MICROSPHERES



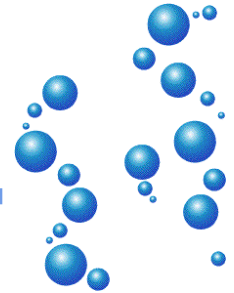
ULTRASOUND CONTRAST
AGENT BUBBLES



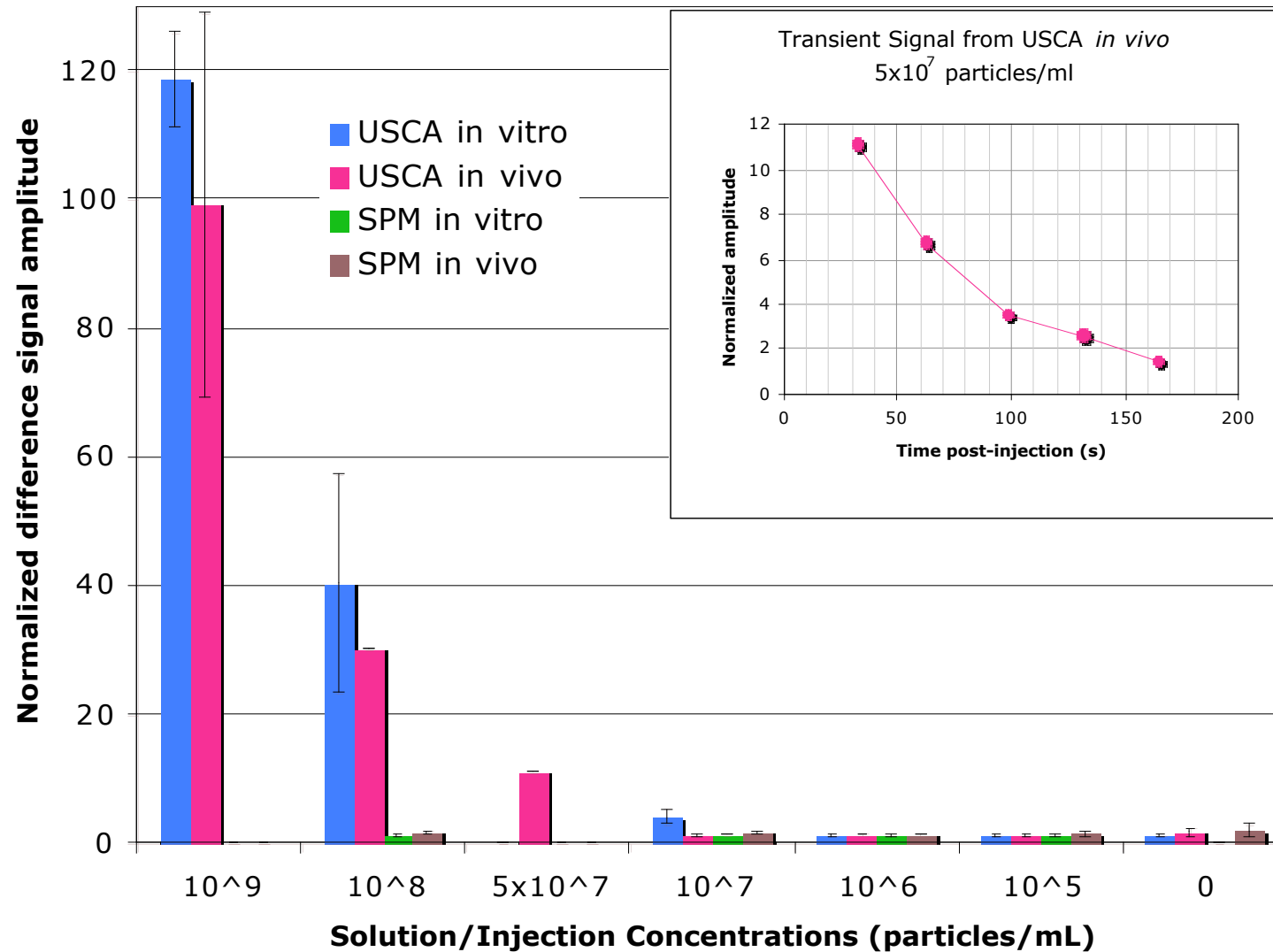
IN-VIVO

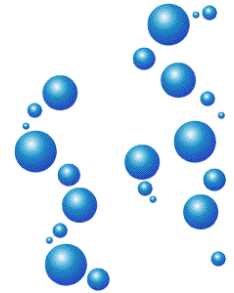


Sensitivity



Signals from USCA and SPM





Conclusions

- This is the first demonstration that stationary microbubbles can be detected non-invasively in tissue.
- Concentrations of USCA bubbles as low as 5×10^7 particles/mL were detected *in vivo*. (0.06% free gas phase by vol.)
- Research is underway using this technique to detect
 - existing microbubbles in tissue
 - decompression-induced bubble formation in tissue
- This technology could provide a better understanding of bubble formation during activity and decompression