

Microbubbles detected in the bloodstream in the absence of larger venous gas emboli (VGE)

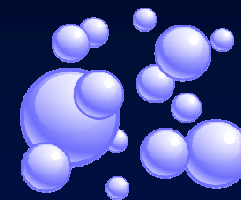


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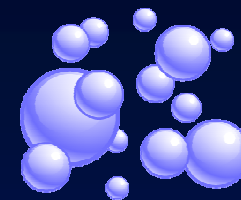
²Creare, Inc., Hanover NH

Funding provided by the ONR



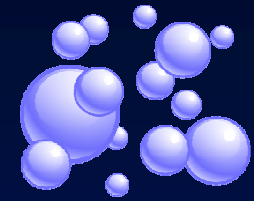
Microbubble Detection-*Background*

- **Following decompression, venous gas emboli (VGE) appear in the bloodstream**
- **VGE are thought to begin as smaller microbubbles**
- **Technology to measure microbubbles has not been available**
- **Dual frequency ultrasound (DFU) can detect microbubbles and we have used DFU previously to detect signals consistent with microbubbles in tissue following decompression**
- **For this study, we hypothesized that DFU would detect microbubbles at vascular sites**



Microbubble Detection-*Questions*

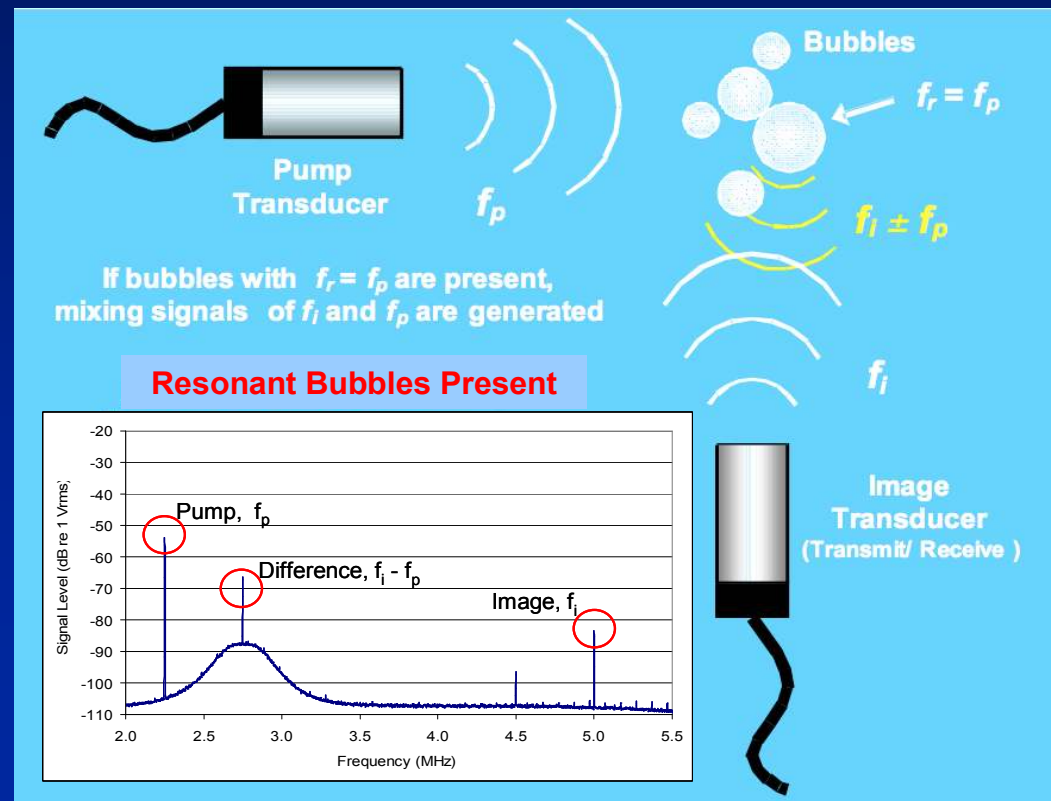
- **Can microbubbles be detected at vascular sites?**
- **Do microbubbles appear following decompression?**
- **Do microbubbles precede the appearance of VGE following decompression?**

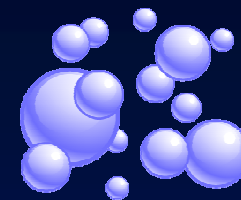


Bubble Detection-*Methods*

Dual Frequency Ultrasound

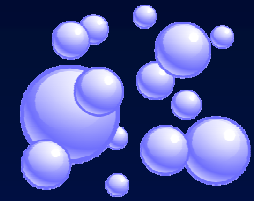
- Based on non-linear behavior of resonating bubbles
- Can detect and size stationary microbubbles in tissue



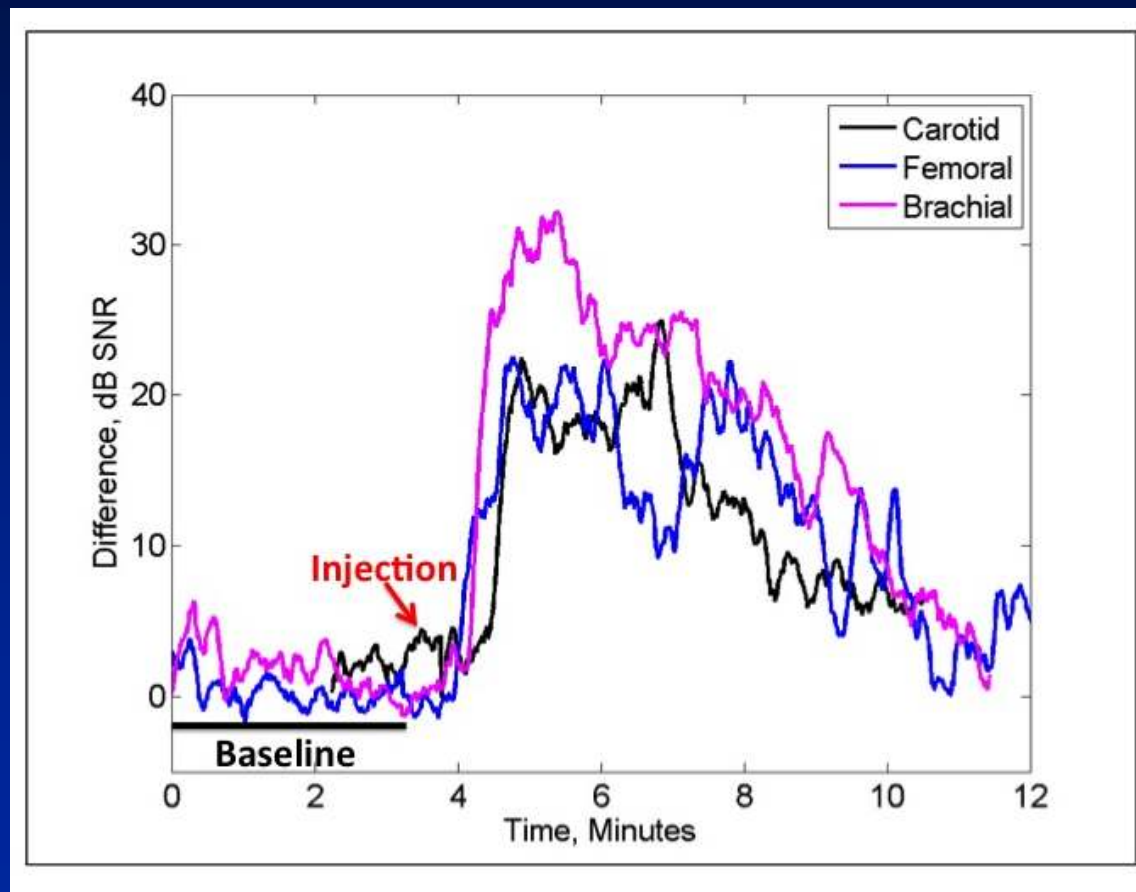


Microbubble Detection-*Anatomic Methods*

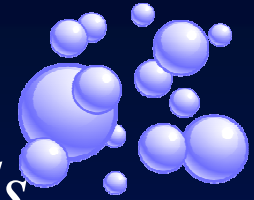
- **Ultrasound contrast agent (Definity™) used as non-linear target**
- **Definity™ was injected intravenously into swine**
- **Measurements were made in real time using DFU over the carotid, brachial and femoral vascular areas**



Microbubble Detection-*Anatomic Results*



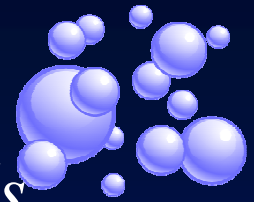
Injected microbubbles produce increased difference signal after injection into the bloodstream



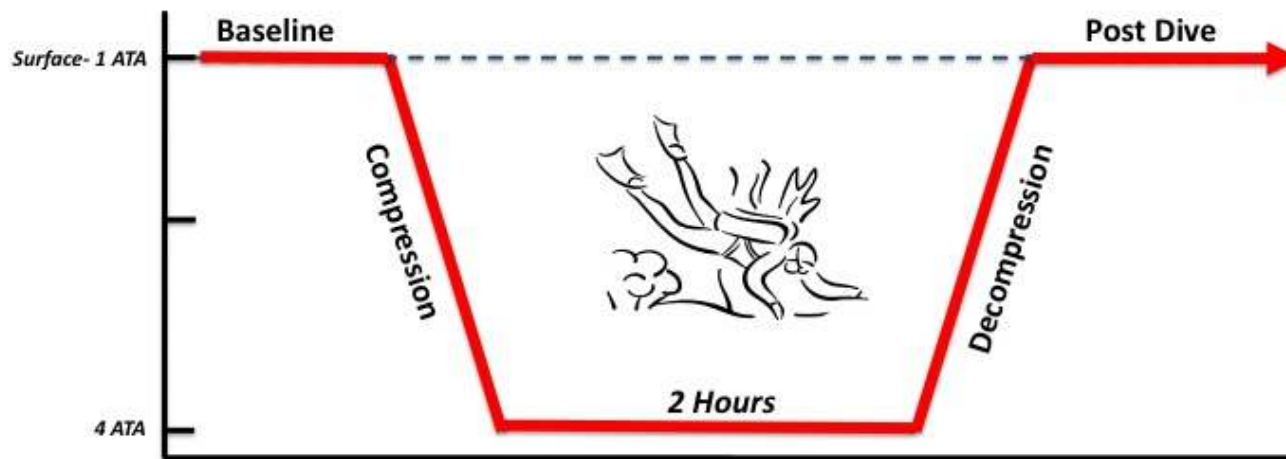
Microbubble Detection-*Decompression Methods*

- **Swine (n=12; 20kg) were compressed to 4.0-4.5 ATA for 2 hours**
- **Compression/Decompression rate = 10psi/min**
- **DFU used to measure microbubbles over 3 vascular bundles (carotid, femoral, brachial) and over 1 tissue site (biceps femoris)**
- **Microbubble signals recorded at baseline and for 1 hour following decompression**

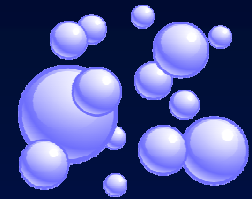
Microbubble Detection-*Decompression Methods*



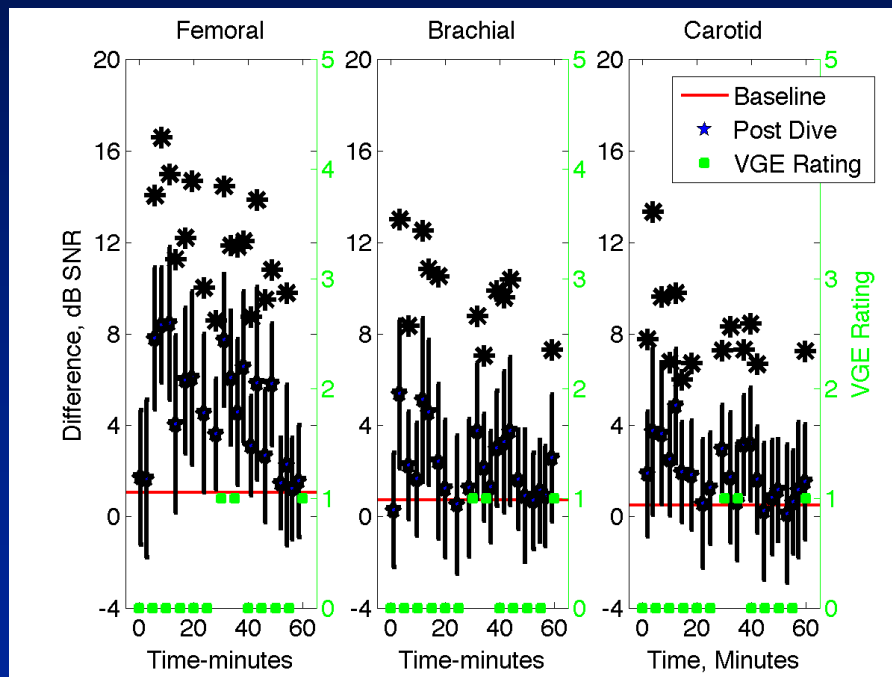
Dive Profile



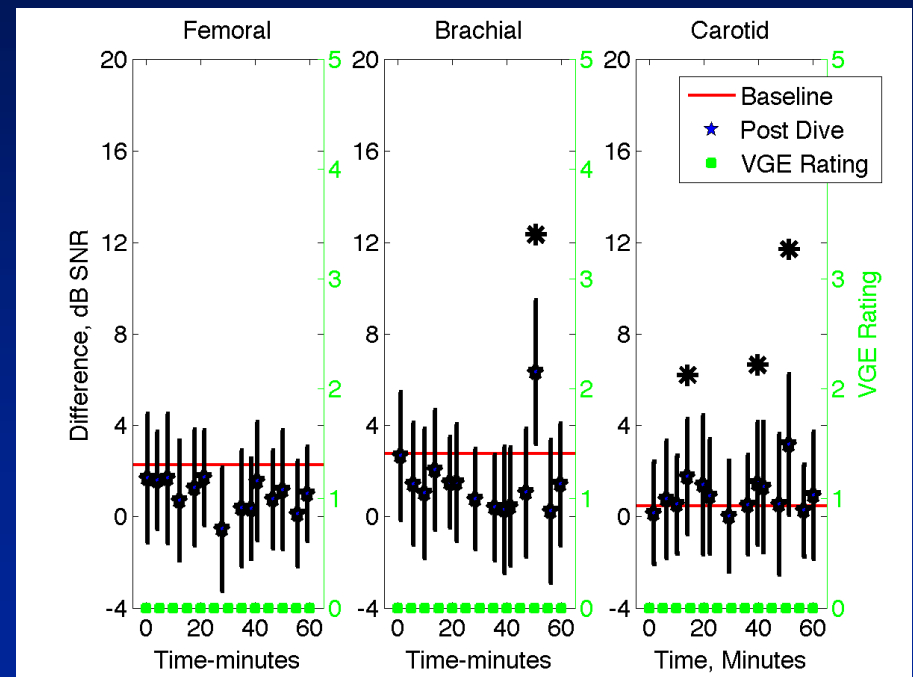
Microbubble Detection-*Decompression Results*



4.5 ATA Dive; $VGE \leq 1$

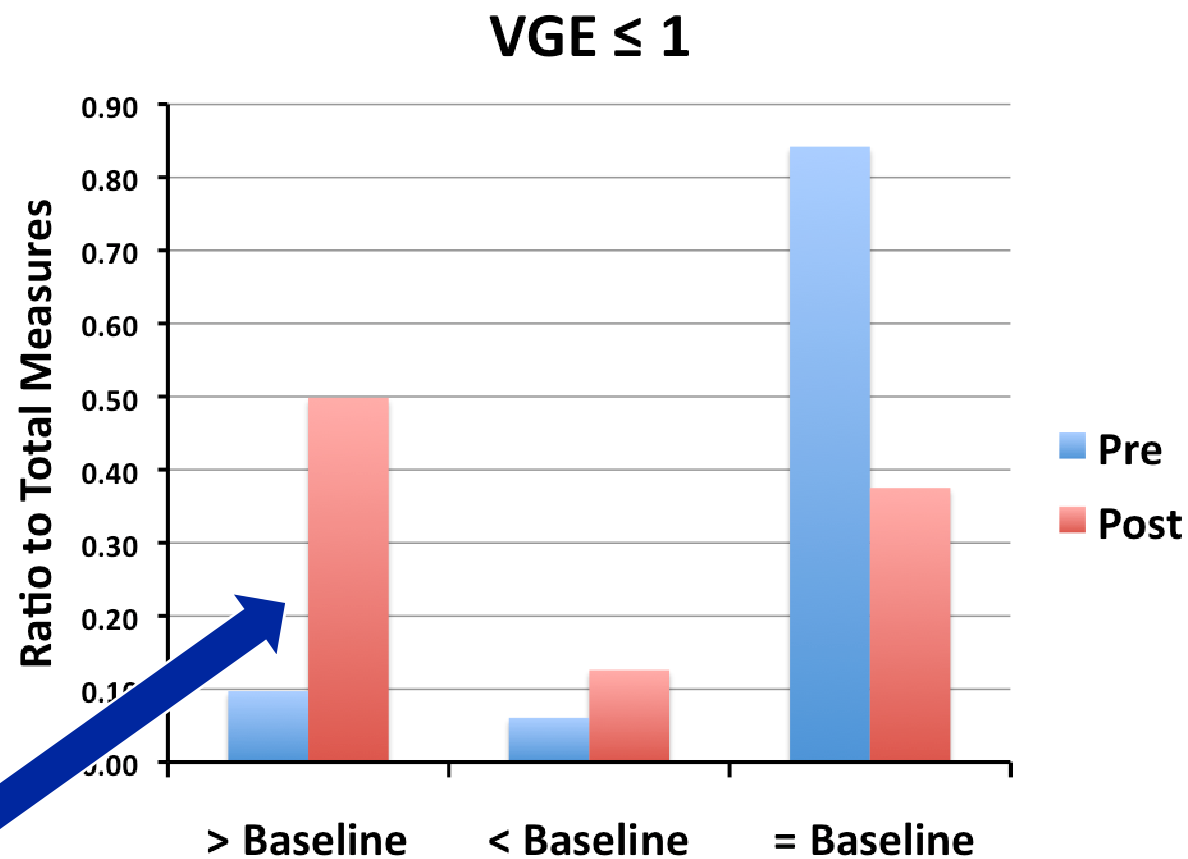
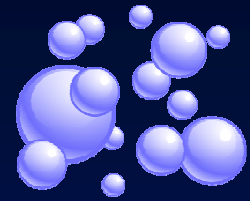


Sham Dive; $VGE = 0$



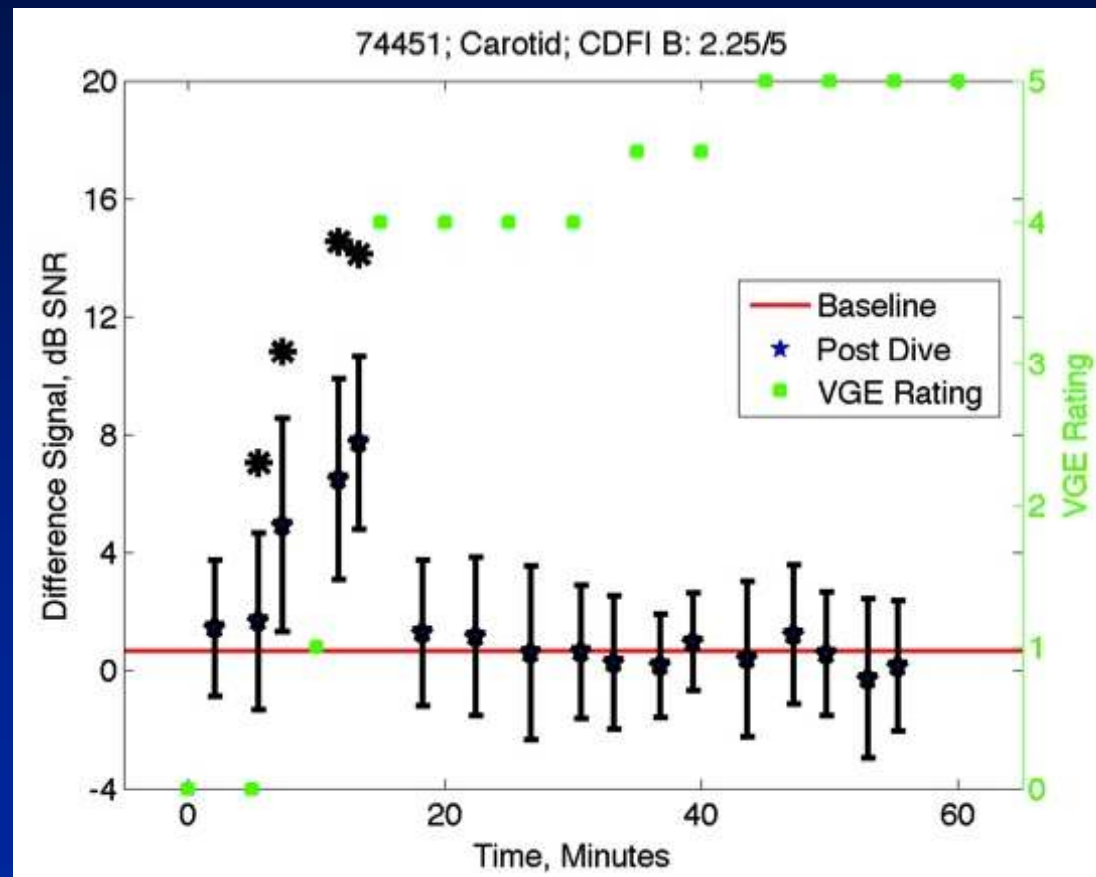
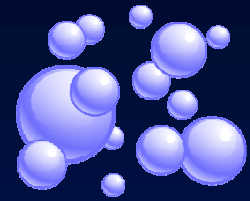
Microbubbles detected at vascular sites following decompression (left)—not seen with sham dive (right)

Microbubble Detection-*Decompression Results*



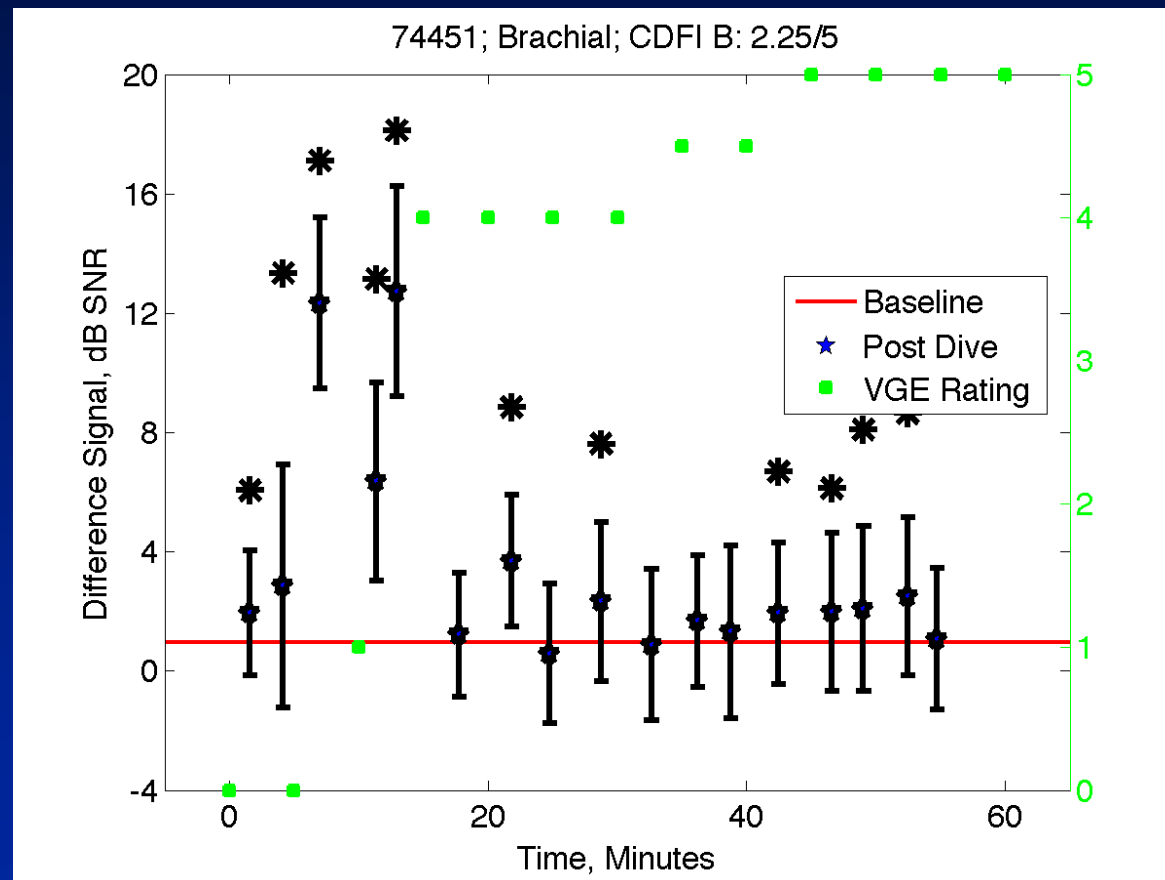
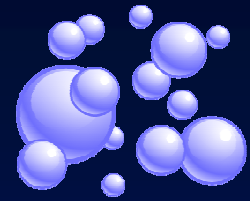
Substantial increase in sites with microbubble signals after decompression when no VGE present ($p < 0.01$; pre vs. post)

Microbubble Detection-*Decompression Results*



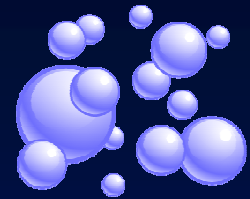
The disappearance of microbubbles with the onset of VGE over the carotid vascular bundle (*, $p < 0.01$)

Microbubble Detection-*Decompression Results*

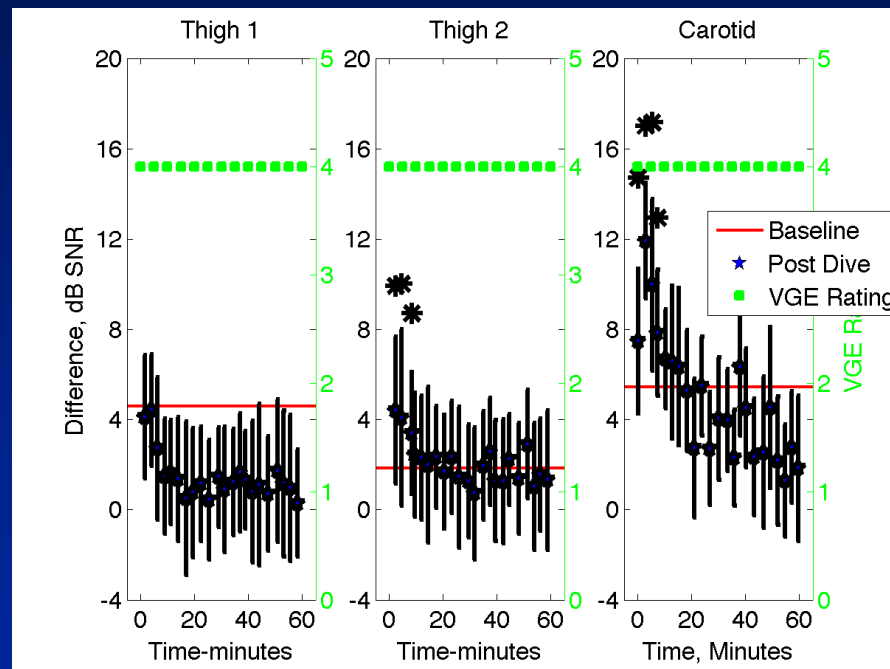


The disappearance of microbubbles with the onset of VGE over the brachial vascular bundle (*, $p < 0.01$)

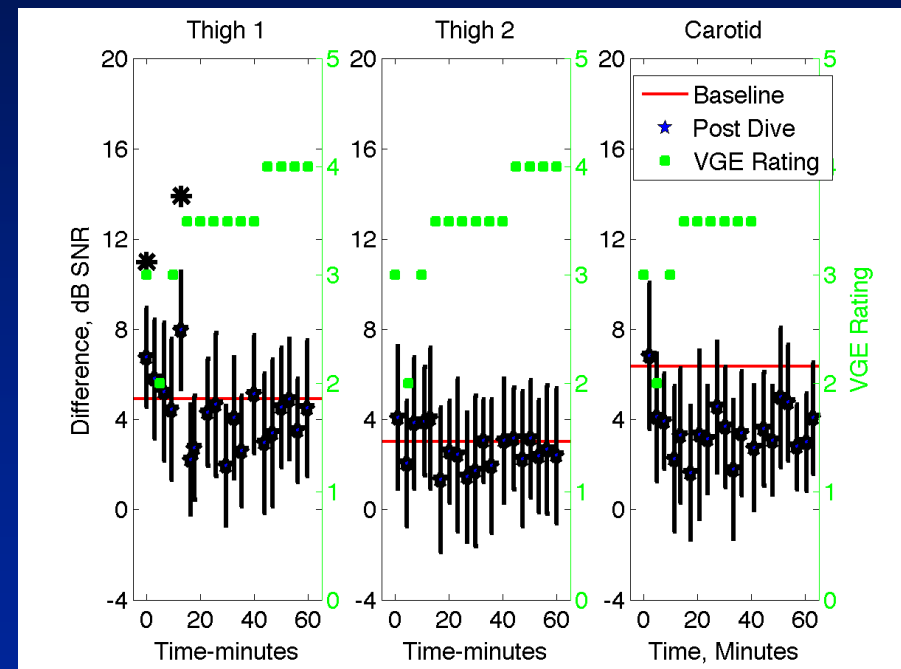
Microbubble Detection-*Decompression Results*



4.0 ATA Dive; VGE = 4

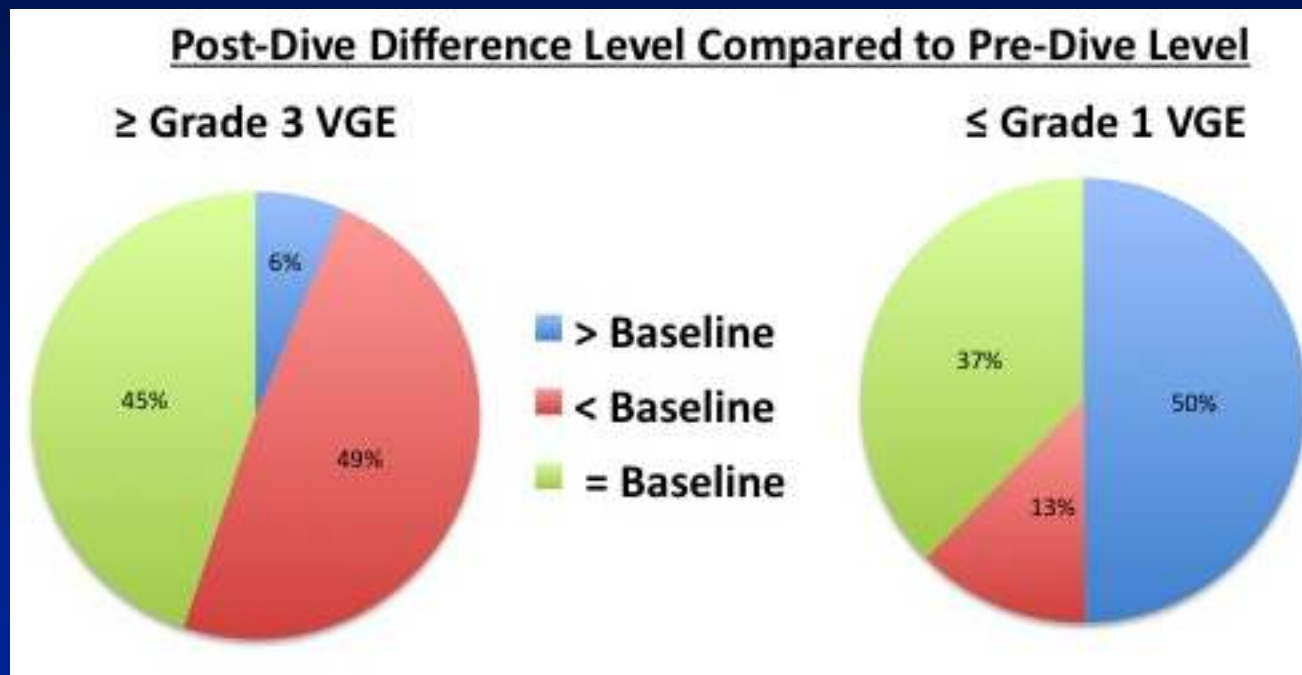
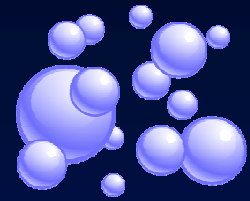


4.0 ATA Dive; VGE \approx 3.5

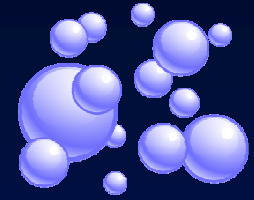


Decrease in microbubbles detection with increased VGE (*, $p < 0.01$)

Microbubble Detection-*Decompression Results*

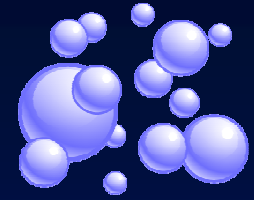


When VGE are present, the percentage of sites showing microbubble signals above baseline (blue region) decreases markedly



Microbubble Detection-*Conclusions*

- **DFU is sensitive to microbubbles in tissue and in the bloodstream**
- **Microbubbles appear after decompression, and are seen prior to detection of VGE via 2D ultrasound**
- **Microbubble detection is inversely correlated to VGE (i.e. once VGE appear, microbubble signals decline)**
- **The presence of microbubbles may be an early indicator of decompression stress**



Microbubble Detection-*Next Steps*

- **We are currently developing the technology to measure microbubbles while in the chamber**
- **Examine the effects of interventions on microbubble formation**
- **Examine whether individualized interventions based on real-time microbubble detection could be used**