



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

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Introduction

- Its long been hypothesized that VGE detectable by 2D ultrasound or Doppler begin as smaller microbubbles, but the technology to measure these small bubbles has not been available
- Using dual frequency ultrasound (DFU) we can detect microbubbles in both tissue and blood
- We hypothesized that we would be able to detect microbubbles in the bloodstream after decompression using DFU

Questions

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

Dual Frequency Ultrasound

- Dual-Frequency Ultrasound (DFU) involves "pumping" bubbles at their resonant frequency and "imaging" the bubbles using a second frequency (Figure 1)
- When bubbles of resonant size are present, mixing (sum and difference) signals are produced

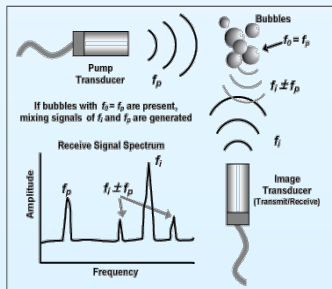


Figure 1. Dual-frequency ultrasound looks for the nonlinear mixing of two different ultrasound frequencies to detect and size resonating bubbles.

Methods

- Lipid-stabilized microspheres (Definity™) were used as a nonlinear source to determine if DFU could detect injected microbubbles
- Definity™ was injected intravenously into swine and measurements were made over the carotid, brachial, femoral vascular areas

Methods (con't)

- In a separate experiment, swine (n = 12; 20kg) were exposed to 4.0-4.5 ATA with a compression/decompression rate of 10 psi/min
- VGE and DFU were assessed pre- and post-dive
- Measurements were taken at 3 vascular sites: carotid, femoral, brachial
- The transducers were held in a stable configuration via a custom built holder

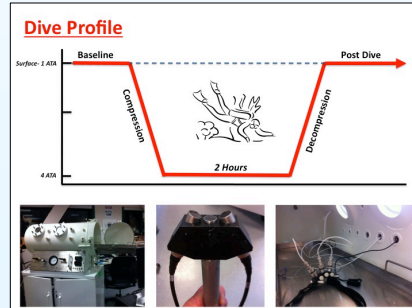


Figure 2. Clockwise from top: Dive profile, CDFI transducer for in chamber monitoring, CDFI transducer for out of chamber monitoring, and Reimers 20-48 hyperbaric chamber.

Results: Injected microbubble detection at vascular sites

Can injected microbubbles be detected at vascular sites?

- Rapid increase in difference signal following injection, followed by a gradual return to baseline (Figure 3)
- Injected microbubbles can be detected at vascular bundles

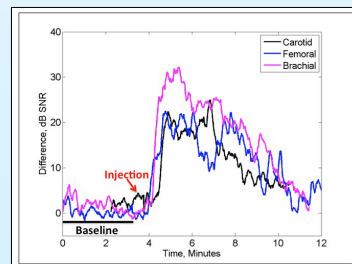


Figure 3. Injected microbubbles produce increased difference signal after injection into the bloodstream.

Results: Decompression-induced microbubble detection at vascular sites

Can microbubbles be detected at vascular sites following decompression?

- Figure 4 shows the results from one swine after decompression. Figure 5 shows the results from a sham dive. In 8 swine, no VGE were detected, but microbubbles were seen (Figure 6)
- After decompression, microbubbles can be detected over vascular bundles.

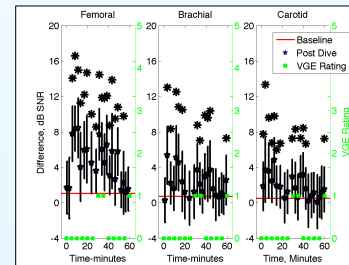


Figure 4. Microbubble detection following decompression.

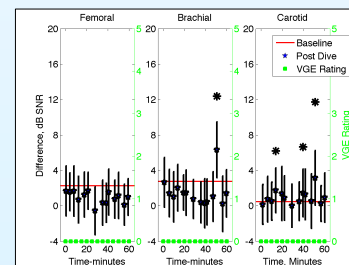


Figure 5. Microbubbles are not seen after a sham dive.

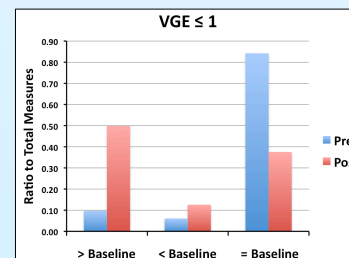


Figure 6. Change in the distribution of difference signal following decompression in swine with VGE ≤ 1 (p < 0.01 pre vs. post).

Results: Timing of Microbubble Appearance

Do decompression-induced microbubbles precede the appearance of VGE?

- In a swine with late onset VGE, microbubbles appeared before VGE (Figure 7)
- Microbubble signal decreases with presence of VGE (Figure 8)

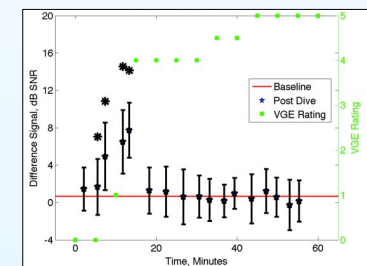


Figure 7. The disappearance of microbubbles with the onset of VGE over the carotid vascular bundle (*, p < 0.01).

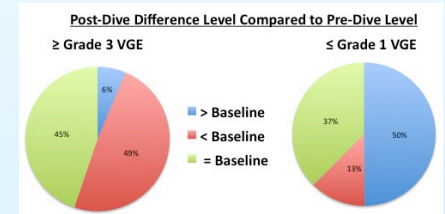


Figure 8. Once VGE were detected (left) the percentage of sites showing increased microbubble signals over baseline decreased markedly (blue regions)

Conclusions

- DFU detects microbubbles in the bloodstream
- Microbubbles are produced by decompression
- Microbubble detection is inversely correlated to VGE
- The presence of microbubbles may indicate impending decompression stress
- We are currently exploring whether microbubbles could be used as an early marker of decompression stress

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