In Response:

Thank you for these interesting comments. We fully agree that the "life expectancy" of venous gas emboli (VGE) detected in the right cardiac chambers is short, since, as you point out, they will predominantly be carried with the blood to the pulmonary circulation and efficiently filtered away in the pulmonary capillaries. Thus, it was of course not the same specific bubbles detected during subsequent cardiac ultrasound imaging. The ultrasound technique used to detect VGE in the two studies^{1,2} does not allow us to discern the origin of the bubbles. It must, however, be assumed that VGE observed in the cardiac chambers stem from peripheral systemic veins, since, as mentioned in our articles, 1,2 unloaded knee bends/extensions provoke an almost immediate (within seconds) surge of bubbles in the right cardiac atrium. Thus, whether already detached from the endothelium or still attached to, for example, an active hydrophobic spot, the bubbles must have been readily available to be mobilized by the movements; in the conditions where knee bends induced high ultrasound scores, a pool of bubbles must have been present in the peripheral veins. However, it might have been more appropriate to term such gas formations in peripheral veins "bubbles" than "emboli", since they to a large extent may be attached to the endothelium.

Regardless, our observation that knee bends induced a similar, albeit smaller, surge in right atrial gas emboli also immediately following recompressions from 24,000 to 15,000 ft² suggests that the pressure elevation was not sufficient to compress all gas bubbles in the peripheral veins. An excursion to 900 ft, by contrast, virtually abolished the occurrence of cardiac gas emboli. Furthermore, upon return to 24,000 ft following an excursion to 15,000 ft, the appearance of cardiac gas emboli reassumed at pre-excursion levels within a few minutes. This seems to favor the notion of regrowth of already existing bubbles in peripheral veins as the major contributor to the observed cardiac bubbles upon return to 24,000 ft from 15,000 ft, if as you

say, it may take more than 20 min for a bubble to develop from a precursor in a peripheral vein and eventually appear in the right heart. In fact, at 15,000 ft, neoformation of gas bubbles detectable by cardiac ultrasound imaging is virtually nonexistent, as shown in the present¹ and previous studies,⁴ suggesting that VGE observed at 15,000 ft² reflected bubbles "surviving" the compression from 24,000 ft. We do, however, agree that following the excursions to 900 ft,¹ more cardiac gas bubbles might have occurred at 24,000 ft with a prolongation from 20 to 30 min at this altitude.

Finally, we wish to emphasize that our in vivo observations do not allow us to pinpoint the origin of the VGE observed in the right cardiac chambers. Therefore, it would be of interest to have the present or similar pressure and gas profiles tested in the in vitro systems used to study bubble formation at endothelial hydrophobic spots.³

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REFERENCES:

- Ånell R, Grönkvist M, Eiken O, Gennser M. Nitrogen washout and venous gas emboli during sustained vs. discontinuous high-altitude exposures. Aerosp Med Hum Perform 2019; 90(6):524–530.
- Ånell R, Grönkvist M, Gennser M, Eiken O. Evolution and preservation of venous gas emboli at alternating high and moderate altitude exposures. Aerosp Med Hum Perform 2020; 91(1):11–17.
- Arieli R. Nanobubbles form at active hydrophobic spots on the luminal aspect of blood vessels: consequence for decompression illness and possible implications for autoimmune disease. An overview. Front. Physiol. 2017; 8:591.
- Webb JT, Pilmanis AA, O'Connor R. An abrupt zero-preoxygenation altitude threshold for decompression sickness symptoms. Aviat Space Environ Med. 1998; 69(4):335–340.

Erratum

Pettijohn KA, Geyer D, Gomez J, Becker WJ, Biggs AT. Postural instability and simulator seasickness. Aerosp Med Hum Peform. 2018; 89(7):634–641. DOI: https://doi.org/10.3357/AMHP.4998.2018

At the end of the sentence beginning "In order for successful adaptation ..." on page 635 an additional citation was inadvertently omitted. A citation should appear at the end of that sentence, reading: "Littman EM, Adaptation to Simultaneous Multi-Dimensional Distortions, Ph.D. dissertation, Miami University, 2011."

We sincerely apologize for the error and any inconvenience this may cause.