INTRODUCTION
Musculoskeletal activity accelerates inert gas elimination during oxygen breathing prior to decompression (prebreathe), but may also promote bubble formation (nucleation) and increase the risk of decompression sickness (DCS). The timing, pattern and intensity of musculoskeletal activity and the level of tissue supersaturation are likely critical to the net effect. Understanding the relationships is important to evaluate exercise prebreathe protocols and quantify decompression risk in gravity and microgravity environments. The NASA Prebreathe Reduction Program (PRP) combined oxygen prebreathe and exercise preceding a low pressure (4.3 psia; altitude equivalent of 30,300 ft [9,235 m]) simulation exposure of non-ambulatory subjects (a microgravity analog) to produce two protocols now used by astronauts preparing for extravehicular activity. One protocol included both upright cycling and non-cycling exercise (CEVIS: ‘cycle ergometer vibration isolation system’) and one protocol relied on non-cycling exercise only (ISLE: ‘in-suit light exercise’). CEVIS trial data serve as control data for the current study to investigate the influence of ambulation exercise in 1G environments on bubble formation and the subsequent risk of DCS.

METHODS
The current study replicates the CEVIS protocol, with single exceptions in each experiment, with metabolic output matched for all. Experiment 1 (E1) added controlled ambulation (stepping in place with a fixed cadence [80 steps per minute] and height [producing a 45° angle of the thigh indexed to the points of rotation of hip and knee]) at ground level (saturated inert gas state) and at 4.3 psia (spacesuit pressure; supersaturated state) instead of maintaining non-ambulation throughout. Experiment 3 (E3) restricted ambulation to the preflight period only. Decompression stress was assessed through subjective symptom reports and with non-invasive ultrasound measures recorded during each of 14 epochs of the four-hour microgravity simulation. Aural Doppler (TechnoScientific DBM 9000) was used to monitor venous gas emboli (VGE; Spencer grade 0-IV scale) passing through the pulmonary artery. Two-dimensional echocardiographic imaging (SonoSite SonoHeart 180) was used to look for left ventricular gas emboli (LVGE; the presence of which was a test termination criterion). Venous blood was collected at baseline, then following a transient partial depressurization-repressurization cycle that simulated a suit donning period, and finally upon the completion of the simulated spacewalk. The blood was assayed to determine if the established measures of decompression stress could be correlated with microparticle (cell fragment) accumulation. Fisher Exact Tests (one-tailed) were used to compare test and control groups. Significance was accepted at \( p \leq 0.05 \). The plan was to test 25-50 subjects in each experiment; suspending trials when the DCS or grade IV VGE observations reach 70% confidence of DCS risk >15% and grade IV VGE risk >20%.

RESULTS
CEVIS trials were concluded with 45 person-trials (35 male, 10 female; 0/45 [0%] DCS, 3/45 [7%] peak grade IV VGE). E1 trials were concluded with 21 person-trials (16 male, 5 female; 4/20 [20%] DCS, 6/21 [29%] peak grade IV VGE) since the statistical outcome would not change with additional trials to the minimum planned number. E3 trials continue with 38 person-trials completed (29 male, 9 female; 2/38 [5%] DCS, 4/38 [11%] peak grade IV VGE). The observed DCS in CEVIS was significantly lower than in E1 \( (p=0.004) \), but not different from E3 \( (p=0.109) \). The observed DCS in E3 is trending towards being lower than in E1 \( (p=0.058) \). The observed frequency of grade IV VGE in CEVIS was significantly lower than in E1 \( (p=0.014) \), but not different from E3 \( (p=0.279) \). The observed frequency of grade IV VGE in E3 was significantly lower than in E1 \( (p=0.0499) \). Microparticle patterns are widely variable and still under analysis.

DISCUSSION
The results of the current trials support the thesis that decompression stress is increased by ambulation exercise in a 1G environment, given the higher incidence of DCS and grade IV VGE when subjects ambulated both at ground level immediately prior to depressurization and during periods of depressurization. The lower frequency of observations of the highest grade of VGE and the trend towards less DCS when ambulation was conducted at ground level only suggests that exercise during periods of supersaturation plays a more important role in decompression risk.