

Bed Rest Exercise Protocols.

Exercise protocols were performed horizontally for logistical purposes as detailed in companion paper (15). Continuous cycle ergometer exercises were conducted on a Lode® supine cycle ergometer for 30 min on the same day as resistance exercise, but separated by at least six hours. Study personnel adjusted workloads to maintain target heart rates. Target workload was a heart rate corresponding to 75% of VO_{2peak} that was measured during their first session. Resistance exercise was conducted using an undulating periodization protocol that for the first six weeks cycled between days with three sets of 12 Repetition Maximum (RM), 8 RM, and 3 RM exercise within each week. After six weeks, three sets of 10 RM, 6 RM, and 3 RM were performed. Each resistance day included squats on a horizontal squat device (alternating days of standard width stance, wide stance, and single leg), single leg curls, leg press (alternating days of standard width stance, wide stance, and single leg), and calf press. Interval treadmill exercise was performed on a vertical treadmill (Standalone Zero-Gravity Locomotion Simulator, sZLS) that was used to simulate terrestrial ambulation while preserving axial unloading. Subjects were suspended on a cradle system in the horizontal position and pulled onto the treadmill belt via a harness system and a pneumatic subject-loading device to keep the subject in contact with the motorized treadmill and provide a ground reaction force at their feet. Subjects were targeted to be loaded from 75-80% body weight as tolerable by the subject (15). Following warm up on the treadmill, subjects performed the interval exercise protocol. Three different interval protocols were performed once each week. These protocols consisted of 6 x 2 min pyramid intervals (70%, 80%, 90%, 100%, 90%, 80% of VO_{2peak} target HR) with 2 min recovery periods; 4 x 4 min intervals (90% of VO_{2peak} target HR) with 3 min recovery periods; and 8 x 30 s sprint intervals with 15 s

recovery periods. Please note a potential limitation that aerobic exercise prescription in terms of HR at a certain % of VO2 max does not take into account nonlinearities between VO2 and work rate in different exercise domains.

SDC Table 1: Bed rest exercise protocol

	Day 1 (min)	Day 2 (min)	Day 3 (min)	Day 4 (min)	Day 5 (min)	Day 6 (min)	Day 7 (min)
Resistance	35-60		35-60		35-60		0
Aerobic Interval		32		15		35	0
Aerobic Continuous	30		30		30		0