# Isokinetic Strength Changes Following Long-Duration Spaceflight on the ISS

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**INTRODUCTION:** Long-duration spaceflight results in a loss of muscle strength that poses both operational and medical risks, particularly during emergency egress, upon return to Earth, and during future extraterrestrial exploration. Isokinetic testing of the knee, ankle, and trunk quantifies movement-specific strength changes following spaceflight and offers insight into the effectiveness of in-flight exercise countermeasures.

**METHODS:** We retrospectively evaluated changes in isokinetic strength for 37 ISS crewmembers (Expeditions 1–25) following 163 ± 38 d (mean ± SD) of spaceflight. Gender, in-flight resistance exercise hardware, and preflight strength were examined as potential modifiers of spaceflight-induced strength changes.

**RESULTS:** Mean isokinetic strength declined 8–17% following spaceflight. One month after return to Earth, strength had improved, but small deficits of 1–9% persisted. Spaceflight-induced strength losses were not different between men and women. Mean strength losses were as much as 7% less in crewmembers who flew after the Advanced Resistive Exercise Device (ARED) replaced the interim Resistive Exercise Device (iRED) as the primary in-flight resistance exercise hardware, although these differences were not statistically significant. Absolute and relative preflight strength were moderately correlated ($r = -0.47$ and $-0.54$, respectively) with postflight strength changes.

**DISCUSSION:** In-flight resistance exercise did not prevent decreased isokinetic strength after long-duration spaceflight. However, continued utilization of ARED, a more robust resistance exercise device providing higher loads than iRED, may result in greater benefits as exercise prescriptions are optimized. With reconditioning upon return to Earth, strength is largely recovered within 30 d.

**KEYWORDS:** ARED, gender, disuse, iRED, ISS, microgravity, muscle.

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Long-duration spaceflight results in a loss of muscle mass and strength, primarily in the locomotor and postural muscles of the legs and trunk.[17,31] Strength deficits represent both an operational and a medical risk to individual crewmembers. Despite the microgravity environment of the International Space Station (ISS), high levels of force production are occasionally required of crewmembers when moving large objects or freeing jammed hardware either inside the ISS or outside during extravehicular activities (EVA). The individual risk can be particularly acute upon return to Earth. Successful egress in an emergency landing scenario would likely require optimal muscular fitness. Even a nominal landing and subsequent return to daily functioning in a 1-g environment is potentially compromised by large deficits in muscular strength due to its essential contribution to balance and locomotion.[12,13] Importantly, results from ISS missions will be the main evidence base used to determine important exercise requirements for future, much longer duration exploration missions. While some strength and function loss may be acceptable on ISS missions, will continued muscle decline be acceptable when applied over a much longer time frame, such as a 3-yr microgravity/partial gravity exposure?

ISS crewmembers routinely participate in exercise countermeasures to counteract the effects of microgravity on muscle performance. Pre- and postflight strength testing thus provides

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insight into the effectiveness of these in-flight exercise countermeasures (both prescription and hardware). Although ISS crewmembers are prescribed exercise on an individual basis, they generally perform resistance exercise 4–6 d/wk during spaceflight.[23,31] Two pieces of hardware served as the primary resistance exercise devices during the first 25 ISS expeditions: the interim Resistive Exercise Device (iRED; Expeditions 1–17), and the Advanced Resistive Exercise Device (ARED; Expeditions 18–25). ARED is a more robust device with enhanced loading characteristics designed to address iRED's limitations and thus better mitigate spaceflight-induced strength loss.[21]

To better understand the effects of spaceflight on muscle strength and endurance and the recovery from microgravity, the National Aeronautics and Space Administration's (NASA) Space Medicine Division requires standardized pre- and postflight isokinetic testing of the locomotor and postural muscles of the legs and trunk for all its ISS crewmembers. Crewmembers are tested twice prior to launch (~180 d and ~60 d before launch; L-180 and L-60) to establish the preflight baseline and once soon after landing (~5 d after return; R+5) to assess the effectiveness of the in-flight countermeasures. Two follow-up tests (R+14 and R+30) are conducted in the first month after landing as an independent assessment of recovery from spaceflight. Flight surgeons and exercise specialists can utilize these standardized test results, along with results from other medical tests, to evaluate the relative efficacy of current and future countermeasures.

The overall objective of this report is to describe the results of isokinetic strength and endurance testing in the astronauts assigned to ISS Expeditions 1–25, the first 10 yr of the ISS. In doing so, we also set out to address several operationally relevant questions that might guide the development of future countermeasures and the planning for exploration missions. First, we sought to evaluate the influence of exercise hardware on changes in isokinetic strength, focusing on resistance exercise hardware because resistance exercise likely has a greater impact on strength than aerobic exercise. Also, the capabilities of the resistance exercise hardware improved significantly during the first 10 yr on the ISS. Second, we evaluated gender as a possible modifier of isokinetic strength changes to determine if there was a differential loss of strength between men and women following spaceflight, and whether current exercise countermeasures were equally protective for both genders. Women currently comprise 22% of the NASA astronaut corps as well as 22% of the crewmembers evaluated in this report. Some research has shown a gender-biased differential rate of strength loss and recovery following a period of disuse.[3,35] Third, we intended to determine whether the preflight muscular fitness of the astronauts would have an effect on the postflight strength changes. It could be hypothesized that high initial levels of strength would be more difficult to maintain with in-flight exercise, or alternatively that those with higher initial strength might be more likely to comply with prescribed exercise in flight. Because standardized isokinetic strength testing is a medical operations requirement and not hypothesis-driven research, we present a retrospective evaluation of isokinetic strength parameters with consideration of potentially influential factors; namely, the utilization of particular resistance exercise hardware during the mission, gender, and preflight isokinetic strength.

## METHODS

### Participants

A total of 39 long-duration crewmembers flew under NASA's medical supervision (including several Japan Aerospace Exploration Agency, Canadian Space Agency, and European Space Agency astronauts) on ISS Expeditions 1–25. Of these 39 crewmembers, 2 were not included in these analyses; 1 crewmember refused to participate, and data from the other were excluded from our analyses due to highly variable and inconsistent test results. The resultant cohort for these analyses was 37 crewmembers ($N = 37$). Three crewmembers (two men, one woman) completed two ISS flights; measurements from both flights of these individuals are included as independent data sets. Descriptive data are provided in **Table I**. All subject characteristics data were measured at the final preflight test.

### Equipment and Testing

As specified in NASA's Medical Volume B 5.3 (Isokinetic Testing), astronauts were scheduled to perform two tests before flight [L-180: 209 (178–229) d and L-60: 60 (44–68) d; median (interquartile range)] and three tests following flight [R+5: 6 (5–7) d; R+14: 14 (13–16) d; R+30: 34 (31–37) d]. Crew surgeons may request additional, discretionary testing of individual crewmembers or they may waive part or all of a test protocol for various reasons, including excessive postflight fatigue, busy schedule, or joint pain. Preflight testing was conducted at NASA Johnson Space Center (JSC) in Houston, TX. Postflight testing was conducted either at JSC or the Gagarin Cosmonaut Training Center (GCTC) in Star City, Russia. Subjects wore laboratory-provided athletic shoes to maintain standardized footwear and completed a 5-min warm up on a cycle ergometer (Lode, Groningen, Netherlands) at 50 W before all test sessions. All isokinetic testing utilized a Humac Norm dynamometer (CSMi, Stoughton, MA). Calibration was performed before each test session per manufacturer instructions.

**Table I.** Subject Characteristics (Mean ± SD).

| | | MEN ($N = 29$) | | WOMEN ($N = 8$) | |
|---|---|---|---|---|---|
| | ALL ($N = 37$) | iRED ($N = 18$) | ARED ($N = 11$) | iRED ($N = 4$) | ARED ($N = 4$) |
| Age (yr) | 45.9 ± 4.4 | 46.4 ± 4.8 | 47.4 ± 4.1 | 42.5 ± 2.5 | 43.3 ± 2.5 |
| Body weight (kg) | 78.7 ± 11.0 | 81.7 ± 9.1 | 84.0 ± 9.1 | 68.1 ± 4.6 | 61.6 ± 2.0 |
| Flight duration (d) | 163 ± 38 | 164 ± 41 | 161 ± 38 | 185 ± 13 | 142 ± 37 |

At the first preflight session, the dynamometer was fit to each subject, and position settings were recorded so that they could be replicated for future test sessions. An anatomic reference (knee = 90°, ankle = 0°, trunk = 0°) was measured with a hand-held goniometer during subject set-up for each joint tested. Knee testing was conducted in the seated position over a range of 95° (flexion) to 20° (extension). Ankle testing was performed prone over a subject's maximal active range of motion rounded down to the nearest 5°. For example, if a subject could attain −18° of ankle flexion and 37° of ankle extension, range of motion was set at −15° (flexion) to 35° (extension). Trunk testing was conducted while standing using the Trunk Modular Component (CSMi, Stoughton, MA) from 0° (extension) to 90° (flexion). Trunk testing was not performed on R+5 due to concerns about post-spaceflight low back pain. Trunk testing also was not conducted for any subject too short to fit properly in the device or whose flight surgeon waived the test due to lower back pain (trunk testing: L–60, $N = 30$; R+14, $N = 25$). Testing was always performed in the order depicted in **Table II**. The right leg was used for all testing unless previous injury indicated the use of the contralateral limb.

Initially, subjects performed five warm-up repetitions of knee extension/flexion ($60° \cdot s^{-1}$, concentric/concentric) at 50% of their perceived maximum effort followed by two repetitions at near maximal effort. After a 1–2 min rest, subjects performed five maximal, discrete knee extension repetitions in which the leg was passively returned to the flexed knee position before each repetition. Knee flexion testing ($60° \cdot s^{-1}$) was completed in the same discrete fashion. Subsequently, subjects performed three warm-up repetitions of knee extension/flexion ($180° \cdot s^{-1}$, concentric/concentric) at 50% of their perceived maximum effort followed by a 2-min rest. Then they completed 21 consecutive maximal repetitions ($180° \cdot s^{-1}$, concentric/concentric) of knee extension/flexion; repetitions 2–21 were used for analysis.

Ankle testing was performed in a similar manner. After an initial warm-up (five repetitions at 50% of perceived maximum, two repetitions at near-maximum), subjects completed five maximal repetitions ($30° \cdot s^{-1}$, concentric) of discrete ankle extension (plantar flexion) followed by five maximal repetitions ($30° \cdot s^{-1}$, concentric) of discrete ankle flexion (dorsi flexion). The final pair of ankle tests was also ankle extension/flexion ($30° \cdot s^{-1}$), but these tests were completed eccentrically with subjects maximally resisting the movement of the dynamometer. After one warm-up repetition at 50% of perceived maximal effort, subjects completed five maximal repetitions of discrete ankle extension followed by a set of five maximal repetitions of discrete ankle flexion.

Last, subjects performed five warm-up repetitions of trunk flexion/extension ($60° \cdot s^{-1}$, concentric/concentric) at 50% of their perceived maximum followed by two repetitions at near maximal effort. After a 1–2 min rest, subjects performed five maximal, discrete trunk flexion repetitions followed by five maximal, discrete trunk extension repetitions.

### Subject Constraints

Subjects were requested not to eat a large meal for at least 2 h before testing but could eat a light snack up to 1 h before testing. No nicotine or alcohol was allowed for 8 h before testing; caffeine was restricted to one cup of coffee or its caffeine equivalent that was permitted up to 1 h before testing. Additionally, subjects could not perform a neutral buoyancy dive (training for EVA) for 72 h before testing, maximal exercise for 24 h before a scheduled evaluation, or any exercise 8 h before testing.

### Data Analysis

Data analyses were performed using Stata 11.2 statistical software (StataCorp LP, College Station, TX) and Excel 2007 (Microsoft Corp, Redmond, WA). Data in tables are expressed as mean (95% CI) unless otherwise specified. The L-180 test was considered a familiarization session; percentage changes in strength were calculated in reference to L-60 testing values. Due to large inter-individual differences in strength, box and whisker plots were used to depict the data distribution of several representative variables. The top and bottom of the shaded boxes represent the 75$^{th}$ and 25$^{th}$ percentiles (interquartile range, IQR), respectively, while the solid line in the box represents the median (50$^{th}$ percentile). Whiskers equal the 25$^{th}$ percentile – (1.5 × IQR) and the 75$^{th}$ percentile + (1.5 × IQR) or the lowest/highest datum that lies within this calculated value. Any data points greater than the upper whisker or less than the lower whisker are plotted as individual outliers.[34] Peak torque values (in nanometers) were

**Table II.** MEDB 5.3 Isokinetic Testing Protocol.

| JOINT/MOVEMENT | SPEED | CONTRACTION | REPS | VARIABLE | ABBREVIATION |
|---|---|---|---|---|---|
| Knee extension | $60° \cdot s^{-1}$ | Concentric | 5 | Peak torque | Knee extension-60 |
| Knee flexion | $60° \cdot s^{-1}$ | Concentric | 5 | Peak torque | Knee flexion-60 |
| Knee extension | $180° \cdot s^{-1}$ | Concentric | 20 | Peak torque, total work | Knee extension-180<br>Knee extension work-180 |
| Knee flexion | $180° \cdot s^{-1}$ | Concentric | 20 | Peak torque, total work | Knee flexion-180<br>Knee flexion work-180 |
| Ankle extension | $30° \cdot s^{-1}$ | Concentric | 5 | Peak torque | Ankle extension con-30 |
| Ankle flexion | $30° \cdot s^{-1}$ | Concentric | 5 | Peak torque | Ankle flexion con-30 |
| Ankle extension | $30° \cdot s^{-1}$ | Eccentric | 5 | Peak torque | Ankle extension ecc-30 |
| Ankle flexion | $30° \cdot s^{-1}$ | Eccentric | 5 | Peak torque | Ankle flexion ecc-30 |
| Trunk flexion | $60° \cdot s^{-1}$ | Concentric | 5 | Peak torque | Trunk extension-60 |
| Trunk extension | $60° \cdot s^{-1}$ | Concentric | 5 | Peak torque | Trunk flexion-60 |

reported for all tests; total work (in nanometers) was also reported for 20 repetitions of the $180° \cdot s^{-1}$ knee test.

Comparisons were also made between genders (men vs. women) and between crewmembers who used two different resistance exercise devices. Specifically, comparisons were made between Expeditions 1–17, during which iRED was the primary resistance exercise hardware, and Expeditions 18–25, during which ARED served as the primary resistance exercise hardware. We compared the pre/post changes in isokinetic strength variables by exercise hardware using mixed-effects linear regression methods. Mixed-effects analyses are recent extensions of repeated measures ANOVA/OLS regression commonly referred to as mixed-effects modeling, higher level modeling (HLM), or multilevel modeling (MLM). These techniques have distinct advantages over traditional methods in longitudinal research where multiple observations per subject are evaluated, including better accommodation for occasional missing data. Our models included fixed-effects coefficients evaluating the pre/post change, exercise hardware (iRED and ARED), and importantly, the interaction term enabling us to determine whether the pre/post changes for iRED were significantly different from the pre/post changes for ARED. The models also included a random intercept to account for the repeated measures nature of this dataset. Alpha was set at $P \leq 0.05$. Pearson's correlation coefficients were calculated for knee extension-60 to assess the association between both absolute preflight strength and absolute strength loss following spaceflight as well as relative preflight strength and relative strength loss following spaceflight.

Data are presented in these various forms in an attempt to provide a comprehensive view of the dataset as we recognize that mean values, percent changes, and *P*-values will be of primary interest to many readers whereas others will appreciate the graphical representations of other measurements of central tendency and variance.

## RESULTS

The ISS crewmembers exhibited isokinetic strength losses in the locomotor and postural muscles of the legs and trunk following long-duration spaceflight (**Table III**). At R+14, some isokinetic strength parameters had modestly improved, while others decreased further. For all measurements, mean strength and total work improved at R+30 compared to R+5, but mean values remained somewhat below preflight values (Table III).

On R+5, the greatest strength losses were seen in knee flexion–60 (16.6%), knee flexion–180 (16.2%), knee extension–180 (15.6%), and ankle extension con–30 (13.6%). More moderate losses of 8–11% occurred in all other tests performed.

Mean knee strength tended to moderately improve by R+14 (knee extension–180, knee extension work–180, knee flexion–60, knee flexion–180) or slightly worsen (knee extension–60, knee flexion work–180) in comparison to R+5 changes. Mean ankle strength also improved somewhat on R+14 with one measurement (ankle extension ecc–30) returning to near preflight levels (–3.3%). Trunk strength, tested for the first time postflight on R+14, exhibited moderate losses of 6–8%.

Knee strength improved further by R+30 with residual deficits ranging from 4–9%. Ankle strength seemed to more fully recover than the knee with deficits of only 1–4% persisting at R+30 testing. Trunk extensor strength was essentially restored to preflight levels while trunk flexor strength was still 6% below preflight values.

### Gender

Mean strength losses on R+5 appear greater for women than men (by percent change from preflight) for all but two parameters (ankle flexion con–30 and ankle flexion ecc–30) (**Table IV**). However, 95% CI for all variables overlapped, suggesting that there was no significant gender effect.

Differences between the genders were greatest for knee extension–60, knee flexion–180, knee flexion work–180, ankle extension con–30, ankle extension ecc–30, and trunk extension–60; the strength losses were ~5–8% greater in women.

### Exercise Hardware

For expeditions during which iRED was the primary resistance exercise device (Exp 1–17), mean losses were generally greater than those after ARED became operational (Exp 18–25; **Table V**). This was particularly the case for knee extension–60, knee

**Table III.** Isokinetic Strength Changes (%) Following Spaceflight (L-60 TO R+5, 14, 30).

| | R+5 | | R+14 | | R+30 | |
|---|---|---|---|---|---|---|
| | N | Mean (95% CI) | N | Mean (95% CI) | N | Mean (95% CI) |
| Knee extension-60 | 37 | -11.0 (-7.2, -14.8) | 34 | -12.2 (-8.8, -15.6) | 36 | -8.5 (-5.2, -11.8) |
| Knee flexion-60 | 37 | -16.6 (-13.1, -20.2) | 34 | -12.8 (-9.3, -16.3) | 36 | -6.6 (-2.6, -10.6) |
| Knee extension-180 | 37 | -15.6 (-12.4, -18.8) | 34 | -10.6 (-7.0, -14.2) | 36 | -4.6 (-1.8, -7.5) |
| Knee flexion-180 | 37 | -16.2 (-11.7, -20.6) | 34 | -12.9 (-9.2, -16.6) | 36 | -3.9 (0.8, -8.6) |
| Knee extension work-180 | 34 | -7.9 (-3.8, -12.0) | 31 | -7.8 (-4.4, -11.1) | 33 | -5.2 (-2.3, -8.0) |
| Knee flexion work-180 | 34 | -8.5 (-4.6, -12.3) | 31 | -11.1 (-7.6, -14.6) | 33 | -4.4 (-0.3, -8.5) |
| Ankle extension con-30 | 37 | -13.6 (-9.7, -17.4) | 34 | -8.4 (-3.7, -13.1) | 36 | -3.5 (0.7, -7.7) |
| Ankle flexion con-30 | 37 | -10.7 (-6.5, -14.8) | 34 | -9.0 (-5.3, -12.7) | 36 | -4.0 (-0.4, -7.6) |
| Ankle extension ecc-30 | 32 | -11.4 (-4.6, -18.1) | 31 | -3.3 (2.8, -9.3) | 32 | -1.3 (5.0, -7.5) |
| Ankle flexion ecc-30 | 31 | -8.7 (-5.9, -11.6) | 30 | -6.7 (-2.9, -10.4) | 32 | -4.3 (-1.6, -7.1) |
| Trunk extension-60 | | Not tested | 25 | -6.3 (-1.9, -10.7) | 27 | -0.8 (4.0, -5.6) |
| Trunk flexion-60 | | Not tested | 25 | -8.1 (-3.3, -12.9) | 27 | -5.6 (-1.9, -9.4) |

**Table IV.** Isokinetic Strength Changes (%) by Gender Following Spaceflight (L-60 To R+5 for Knee and Ankle; L-60 to R+14 for Trunk).

| | MEN | | WOMEN | |
|---|---|---|---|---|
| | N | Mean (95% CI) | N | Mean (95% CI) |
| Knee extension-60 | 29 | -10.0 (-5.5, -14.4) | 8 | -15.0 (-8.2, -21.7) |
| Knee flexion-60 | 29 | -16.2 (-13.2, -19.2) | 8 | -18.3 (-5.3, -31.3) |
| Knee extension-180 | 29 | -15.1 (-12.3, -17.8) | 8 | -17.6 (-6.1, -29.0) |
| Knee flexion-180 | 29 | -14.6 (-10.1, -19.0) | 8 | -21.9 (-9.0, -34.8) |
| Knee extension work-180 | 27 | -7.4 (-2.4, -12.5) | 7 | -9.6 (-5.7, -13.5) |
| Knee flexion work-180 | 27 | -6.7 (-2.3, -11.2) | 7 | -15.1 (-9.3, -20.9) |
| Ankle extension con-30 | 29 | -12.0 (-8.0, -16.1) | 8 | -19.1 (-9.6, -28.7) |
| Ankle flexion con-30 | 29 | -10.8 (-6.0, -15.5) | 8 | -10.4 (-1.1, -19.6) |
| Ankle extension ecc-30 | 25 | -10.3 (-2.0, -18.7) | 7 | -15.1 (-6.2, -23.9) |
| Ankle flexion ecc-30 | 25 | -9.2 (-5.8, -12.5) | 6 | -7.0 (-1.4, -12.6) |
| Trunk extension-60 | 19 | -5.1 (-0.4, -9.8) | 6 | -10.0 (0.9, -21.0) |
| Trunk flexion-60 | 19 | -7.3 (-1.5, -13.2) | 6 | -10.6 (-2.3, -18.9) |

flexion–60, and knee extension work–180. However, no significant differences were found (Table V). Comparisons of median (IQR) values of selected tests are displayed in **Fig. 1–5**.

### Strength Correlations

Correlations between absolute preflight strength and changes in strength are shown in **Fig. 6**. Pearson's product moment correlation for preflight absolute strength (knee extension at $60° \cdot s^{-1}$; nm) and change in absolute strength (nm) was $r = -0.47$ ($P = 0.003$); the coefficient of determination was $r^2 = 0.22$. Correlations between relative preflight strength (normalized for bodyweight) and relative changes in strength are shown in **Fig. 7**. Pearson's product moment correlation for preflight relative strength (knee extension at $60° \cdot s^{-1}$; $nm \cdot kg\ bodyweight^{-1}$) and change in relative strength ($nm \cdot kg\ bodyweight^{-1}$) was $r = -0.54$ ($P < 0.001$); the coefficient of determination was $r^2 = 0.29$.

## DISCUSSION

The purpose of this report is to retrospectively review isokinetic strength and endurance data from 37 astronauts who completed long-duration missions aboard the ISS. These measurements were initiated as a means to monitor the health of individual crewmembers and to document the effectiveness of current and future exercise countermeasures to offset the deconditioning effects of spaceflight. Our primary findings are that postflight strength losses were apparent in all tested postural and locomotor muscles, but there was no effect of gender upon these results. Also, although not statistically significant, mean postflight strength losses for most measures were less in crewmembers who utilized ARED during flight. Finally, preflight strength was moderately associated with postflight strength changes.

### Resistance Exercise on the ISS

Previous reports from long-duration spaceflight missions (Skylab, Mir) documented strength losses despite the performance of exercise countermeasures.[16,19,25,30] Countermeasures performed on those missions, however, were primarily aerobic in nature although some components included comparatively low intensity resistance exercise. Resistance exercise devices that could provide higher loading intensities than on previous missions were in use on the ISS since Expedition 1. The capabilities of the first resistance exercise device to be flown on the ISS, however, were limited by the space and power available on the ISS at the time, and thus iRED did not meet the requirements of an ideal resistance exercise device for use in microgravity.[18] iRED was designed to fit in Node 1 of the ISS, to remain partially deployed when not in use, and to require no power to operate. iRED was thus limited in several crucial ways. First, the maximum resistance that it could provide (136 kg) was quite low.[18,26] The gravitational weight of a crewmember's body in space does not contribute to loading during an exercise such as the squat (as bodyweight would on Earth) and a resistance exercise device designed for use in space must compensate for this fact. Consequently, iRED provided a maximum additional load of 46 kg (~0.5 bodyweight of additional loading) relative to what a 90-kg astronaut would experience when doing the same exercise on Earth. Such maximal loads are far below those previously shown to provide an effective resistance exercise countermeasure in bed rest as a model of spaceflight.[27] Second, iRED provides eccentric loading equivalent to ~72% of a given concentric load.[1] In contrast, free weights provide ~95% eccentric loading.[1] Eccentric loading is an essential component to elicit optimal strength adaptations from resistance training.[4,6,15,24] Further, as a result of the low loading capabilities of iRED, many astronauts were capable of lifting with the full load of iRED after a few months of spaceflight, and the only way to further increase the exercise training stimulus was to increase the volume, rather than the intensity.[20]

Thus, it is not surprising that the results from our tests indicate

**Table V.** Isokinetic Strength Changes (%) by Countermeasures Hardware Following Spaceflight (L-60 to R+5 for Knee and Ankle; L-60 to R+14 for Trunk).

| | iRED | | ARED | | SIGNIFICANCE |
|---|---|---|---|---|---|
| | N | Mean (95% CI) | N | Mean (95% CI) | (Pre/post × group) |
| Knee extension-60 | 22 | -13.7 (-8.1, -19.3) | 15 | -7.1 (-3.1, -11.2) | 0.14 |
| Knee flexion-60 | 22 | -19.5 (-15.1, -23.9) | 15 | -12.4 (-7.1, -17.7) | 0.11 |
| Knee extension-180 | 22 | -17.4 (-12.8, -22.1) | 15 | -12.9 (-9.2, -16.6) | 0.43 |
| Knee flexion-180 | 22 | -17.3 (-10.5, -24.1) | 15 | -14.5 (-9.6, -19.4) | 0.57 |
| Knee extension work-180 | 19 | -10.7 (-6.6, -14.7) | 15 | -4.3 (3.2, -11.9) | 0.16 |
| Knee flexion work-180 | 19 | -8.9 (-4.4, -13.4) | 15 | -7.9 (-1.1, -14.8) | 0.54 |
| Ankle extension con-30 | 22 | -14.2 (-8.9, -19.6) | 15 | -12.6 (-7.1, -18.2) | 0.82 |
| Ankle flexion con-30 | 22 | -9.7 (-4.4, -15.1) | 15 | -12.0 (-5.3, -18.7) | 0.41 |
| Ankle extension ecc-30 | 19 | -11.3 (-0.3, -22.2) | 13 | -11.5 (-6.2, -16.8) | 0.82 |
| Ankle flexion ecc-30 | 17 | -8.5 (-4.1, -12.8) | 14 | -9.1 (-5.4, -12.7) | 0.66 |
| Trunk extension-60 | 12 | -7.4 (0.3, -15.2) | 13 | -5.3 (-0.5, -10.0) | 0.59 |
| Trunk flexion-60 | 12 | -8.0 (-1.4, -14.6) | 13 | -8.2 (-1.0, -15.4) | 0.70 |

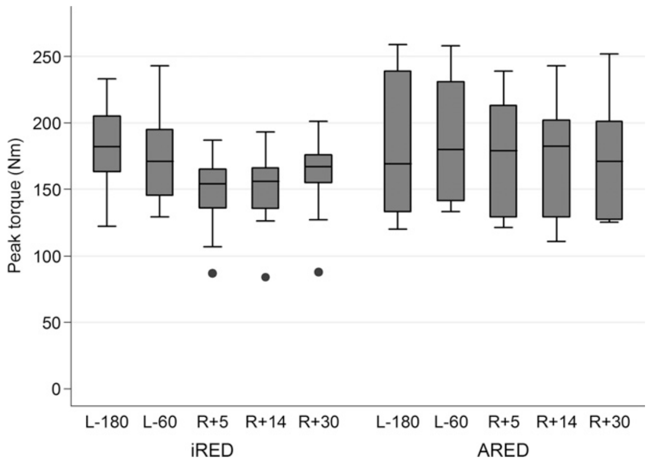


**Fig. 1.** Median (interquartile range) and outlier values of knee extensor isokinetic strength ($60° \cdot s^{-1}$) by countermeasures hardware.

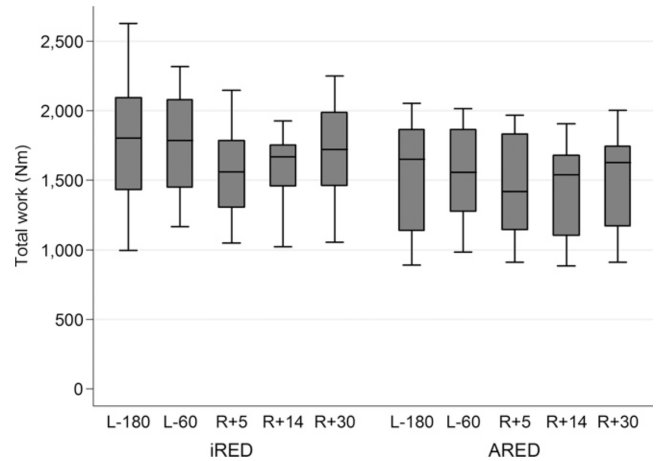


**Fig. 3.** Median (interquartile range) values of knee extensor total work ($180° \cdot s^{-1}$) by countermeasures hardware.

that resistance exercise has not been completely effective in preventing decreased muscle strength and endurance, particularly during the early ISS missions when iRED was in use. Our findings for lower limb and trunk muscles are generally similar to those recently reported by others.[10,31] For example, Trappe et al. observed decreased plantar flexor strength and power, coupled with muscle atrophy, in the nine ISS astronauts that they studied.[31] However, the magnitude of the mean decrease in plantar flexor isokinetic strength reported by Trappe et al. (−20%) appears somewhat larger than that observed in our subjects (–14%), some of whom participated in both sets of testing. It is tempting to speculate that some of the divergence in results is explained by differences in the resistance exercise devices in use at the time. All astronauts studied by Trappe et al. used iRED, whereas 40% of the astronauts in our cohort used ARED.[31] However, our data do not support a strong benefit of ARED exercise over iRED exercise for plantar flexor muscle strength.

ARED was designed, built, and deployed on the ISS during Expedition 18 in response to the perceived deficiencies of iRED, particularly to increase the exercise intensity and reliability of the hardware. ARED provides up to 273 kg of loading – more than enough for the typical crewmember.[21] Using the example above, a 90-kg crewmember would be able to exercise with up to 183 kg of resistance above the amount that would be required to replace bodyweight. Additionally, ARED provides ~90% of the concentric load during the eccentric phase of exercise and uses flywheels to replicate the inertia experienced during exercise in normal gravity.[21] Perhaps not surprisingly then, the decrease in knee extensor strength and endurance in astronauts who used ARED was about half of that observed in astronauts who used iRED during their mission. The selective protection of the knee extensor muscles may be related to the training emphasis upon near daily squat and deadlift exercises not only to protect against muscle atrophy but also against bone demineralization, particularly at the hip.[20] Unfortunately, the ability to detect any exercise device effects in trunk strength measures may have been masked by the long delay from landing to first postflight trunk tests or confounded by the common postflight complaint of lower back pain.

Attributing all the improvements in muscle strength and endurance to ARED may be problematic because the second

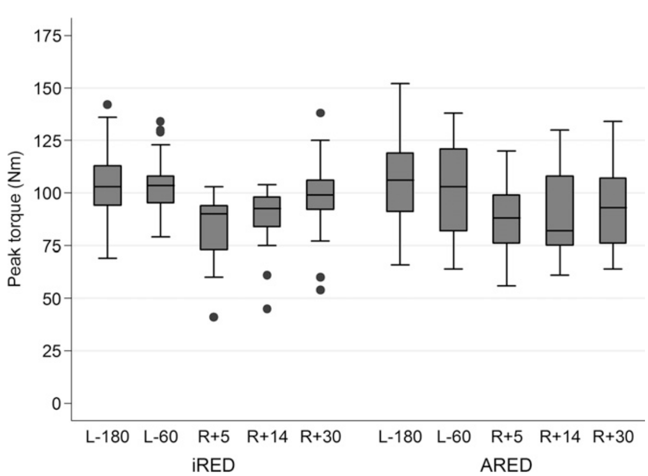


**Fig. 2.** Median (interquartile range) and outlier values of knee flexor isokinetic strength ($60° \cdot s^{-1}$) by countermeasures hardware.

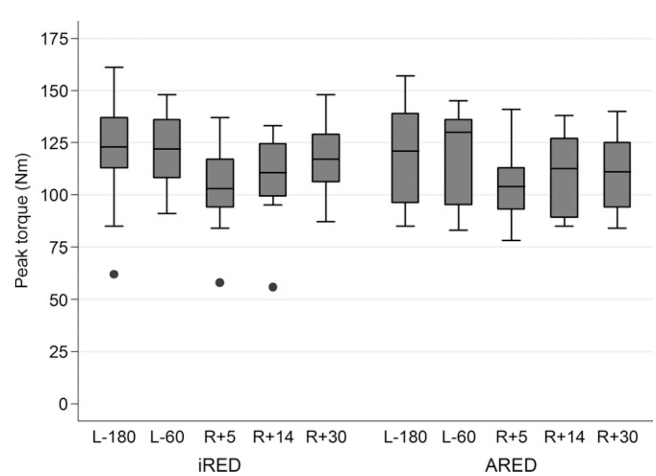


**Fig. 4.** Median (interquartile range) and outlier values of concentric ankle extensor isokinetic strength ($30° \cdot s^{-1}$) by countermeasures hardware.

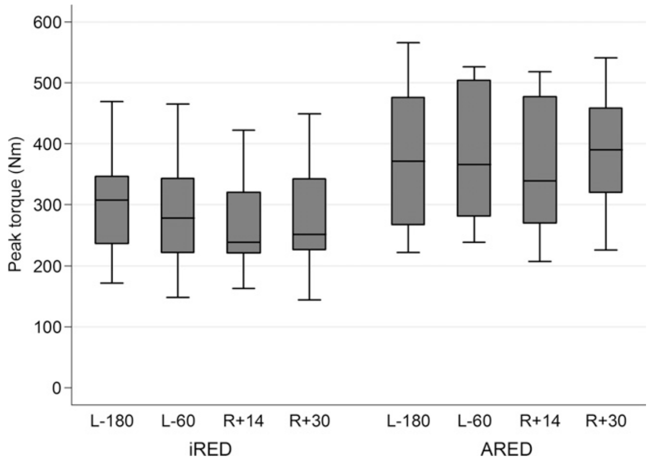


**Fig. 5.** Median (interquartile range) values of trunk extensor isokinetic strength (60° • $s^{-1}$) by countermeasures hardware.

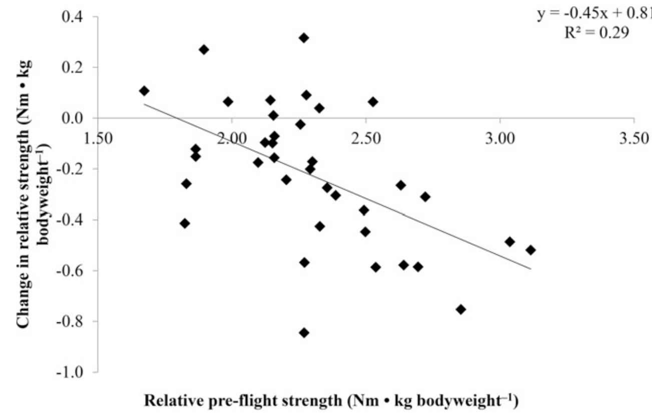


**Fig. 7.** Correlation between relative preflight isokinetic strength (60° • $s^{-1}$ knee extension, Nm • kg $\text{bodyweight}^{-1}$) and change in relative isokinetic strength (Nm • kg $\text{bodyweight}^{-1}$) following ISS spaceflight.

generation treadmill (T2) was delivered to the ISS during Expedition 20; treadmill exercise had a profound effect on the leg muscle function of the Skylab 4 astronauts,[30] and Trappe et al. observed a relationship between treadmill exercise time during flight and decreased postflight calf muscle size.[31] However, the only noteworthy performance improvement from the original treadmill to T2 was an increased peak running velocity (from $4.47\ \text{m} \cdot \text{s}^{-1}$ to $5.36\ \text{m} \cdot \text{s}^{-1}$).

The exercise prescriptions on ARED were designed in a periodized manner to challenge each astronaut by varying intensity within each week and increasing intensity each week of the mission. Because ARED operation in a microgravity environment was not well understood initially, subtle changes in exercise selection and prescription were made over time to reduce the risk of damage to the hardware and to increase the effectiveness of the exercise prescription. This might explain the modest improvement in muscle performance among the astronauts who used ARED compared to iRED users. Current research and further operational experience should continue to improve ARED exercise prescriptions and facilitate full utilization of its unique capabilities. In fact, a recent report by Smith et al. demonstrated that ARED exercise coupled with adequate dietary intake (specifically, total energy, protein, and Vitamin D) maintains lean tissue mass and bone mineral density in ISS astronauts.[28]

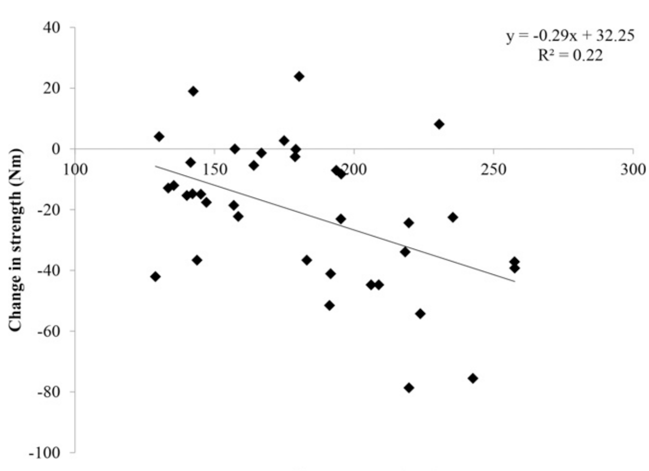


**Fig. 6.** Correlation between absolute preflight isokinetic strength (60° • $s^{-1}$ knee extension, Nm) and change in absolute isokinetic strength (Nm) following ISS spaceflight.

### Gender Effects on Strength Changes

The number of female astronauts has increased in recent years[11] as has the number of women who have flown long-duration missions. Thus, it is clear that the exercise countermeasures employed during spaceflight must be safe and effective for both genders, and we sought to determine whether there was an effect of gender on postflight muscle strength. There has been a recent suggestion that women may be at increased risk for muscle atrophy and decreased strength compared to men based upon bed rest results.[33] In the present sample, small differences in mean strength loss appear to exist between male and female crewmembers, with female crewmembers losing on average more than their male counterparts. However, given the small number of female crewmembers and the large interindividual differences in strength losses, potential gender differences are difficult to verify. Our observations are supported by a few studies that have reported gender differences in strength[35] and neuromuscular performance[14] following disuse of the lower extremities. Clark et al. found that women recovered muscle strength more slowly than men after 3 wk of upper extremity cast immobilization.[3] In contrast, recent bed rest data from our laboratory indicate that there are no differences in isokinetic strength losses for the knee, ankle, or trunk after 60 and 90 d of bed rest.[8] The difference in the response to spaceflight between women and men becomes particularly important if one assumes that their countermeasure performance was the same, but without clear recording of exercise history we cannot confirm this assumption.

### Effect of Preflight Strength on Strength Changes After Spaceflight

Spaceflight-induced strength loss was moderately correlated to preflight strength levels with greater preflight strength associated with greater strength loss. Absolute and relative preflight strength explained 22% and 29%, respectively, of the postflight strength loss in our astronaut sample. However, it would seem erroneous to suggest that in order to protect against large decreases in muscle performance, astronauts with lower fitness levels should be selected for long-duration flight. Despite the association between preflight strength and postflight strength loss, it seems prudent that crewmembers fly with reasonably high levels of preflight strength. This point is well-illustrated by a crewmember who flew two long-duration ISS missions. During one mission, the astronaut launched with notably higher preflight strength scores. Despite sustaining similar losses of relative strength (knee extension-60) during both missions, following the mission with greater preflight strength, the astronaut's postflight strength was still higher than the preflight strength of the measure before the other mission. Even if losses had been greater due to this crewmember's higher preflight strength, it is intuitive that when returning from long-duration flight, the astronaut would be better-equipped to respond to an emergency situation or to simply resume normal activities more quickly in a gravitational environment. Absolute and relative strength levels (regardless of losses sustained during flight) upon return to a gravitational environment (e.g., arrival on Mars) after a prolonged microgravity transit could be particularly critical as crewmembers may be required to immediately perform vigorous activities (e.g., habitat construction) on the terrestrial surface.

### Implications for Spaceflight and Exploration Missions

The question remains as to whether these changes in muscle strength will have a significant impact on an exploration mission or when astronauts return to Earth. Without a clear definition of the physical requirements of extraterrestrial EVA or postlanding activities,[23] we turned to recent medical literature to interpret these results. Relative isokinetic strength ($Nm \cdot kg$ $bodyweight^{-1}$) during $60° \cdot s^{-1}$ knee extension has been shown to predict the risk of incident severe mobility limitation.[22] Transition from low risk to moderate risk for this negative outcome occurred at 1.71 $Nm \cdot kg^{-1}$ bodyweight of peak torque in men and 1.34 $Nm \cdot kg^{-1}$ bodyweight in women.[22] Our data indicate that only one crewmember (a man) was below the gender-specific strength threshold before flight. However, after return to Earth (R+5), four crewmembers (all men) fell below this cut point; three of them flew during iRED's deployment. The crewmember who slipped below the 1.71 $Nm \cdot kg^{-1}$ bodyweight strength threshold while using ARED in-flight was at only 1.87 $Nm \cdot kg^{-1}$ bodyweight of relative knee extensor strength before flight; thus, his in-flight strength loss was a moderate 9%––just slightly above the ARED group mean.

We do not suggest that these crewmembers were at risk of severe mobility limitations due to a transient loss of muscle strength. However, our data, in combination with those of Manini et al. highlight the importance of muscular strength and the fact that a small subset of crewmembers, either due to low strength before flight or substantial losses during flight, dipped to strength levels associated with an elevated risk for severe mobility limitations in a large cohort of elderly people.[22] This problem may be compounded by the observation that the current EVA suit reduces the effective force output by ~50% in some cases due to the difficulty required to work against the suit and suit pressure.[9]

Thus, it seems prudent that all crewmembers should maintain strength levels above some specific threshold with an added safety factor. Specific relative thresholds for astronaut occupational task performance should be identified as opposed to the mobility limitation in elderly individuals in the example given above. Current research is addressing this important issue and developing thresholds of lower body muscular strength and power required for performance of mission related tasks.

Importantly for postflight recovery of astronauts on Earth and during exploration missions, strength improved during the first 30 d following return to Earth in these ISS astronauts, even though small deficits persisted. After landing on Earth, astronauts want to resume their normal activities of daily living as quickly as possible, such as returning to work, driving their car, and spending time with their families. To accomplish this, astronauts after ISS participate in a prescribed reconditioning program consisting first of bodyweight, mobility, and stretching exercises and progressing to increasing intensities of aerobic and resistance exercise as well as more complex coordination tasks.[20] These isokinetic test results suggest that the astronaut reconditioning program is effective, although it is not entirely clear why muscle strength and endurance do not improve greatly in the first 2 wk postflight. Trappe et al. observed a similar delay in muscle strength recovery, although the measured muscle volume recovered somewhat from immediate postflight.[31] They speculated that some of the delay in recovery might be accounted for by muscle damage and soreness secondary to reloading, which might have impacted the intensity and duration of reconditioning exercises. To date, no ISS astronaut has refused to participate in the postflight reconditioning program, but anecdotal information from several U.S. astronauts who flew on early NASA Mir missions and had little reconditioning time scheduled after landing indicated a prolonged recovery from flight due to the lack of a structured program. This is particularly important information for exploration mission planners who will need either to provide adequate countermeasures during transit in microgravity or allow for a prolonged recovery time upon arrival at the extraterrestrial destination.

### Limitations

There are several limitations to the interpretation and generalizability of the results presented in this report. First, the lack of a mandatory, standardized in-flight exercise prescription[20] makes it difficult to assess the effectiveness of ARED relative to iRED. However, the higher loading intensities used with ARED and anecdotal reports from ISS astronauts suggest that ARED will favorably impact muscle strength and endurance. Second, the time for these tests was limited due to other operational and research constraints (training, other medical testing, etc.) such that a complete depiction of muscle performance was not possible. Testing was limited to those regions in which we were most likely to observe changes in muscle performance, with no testing of the upper body; therefore we are unable to characterize the whole body response to microgravity. Further, the current isokinetic testing protocol could be augmented with tests of both slower (e.g., isometric) and faster (e.g., $300° \cdot s^{-1}$) movement velocities to provide further insight into spaceflight-induced changes and countermeasures effectiveness; these protocols have been used by others to study spaceflight- and bed rest-induced changes in strength.[2,32] Third, due to concerns with postflight exercise-induced muscle injury, we limited our testing protocols primarily to isokinetic concentric tests. The single eccentric test performed at the ankle was chosen because previous experience with long-duration astronauts indicated that this was most likely to provide safe, reliable data. Fourth, we have no information about the time course of the changes in muscle strength and endurance during spaceflight. In-flight isokinetic strength testing using the European Space Agency-developed Muscle Atrophy Research and Exercise System (MARES)[7] will be initiated in the future to provide insight into the time course of strength loss during spaceflight, which may be particularly rapid in the early days of unloading,[5,29] and to inform development of countermeasure exercise prescriptions. Last, we do not have the capability to routinely measure ground reaction forces during in-flight exercise on ARED. Although we have done this in parabolic flight during iRED exercise,[18] the inability to precisely characterize loading patterns during in-flight exercise hinders our efforts to more completely understand resistance exercise kinetics in microgravity.

## CONCLUSIONS

Isokinetic strength data from the first 10 yr of long-duration spaceflight onboard the International Space Station show that despite current in-flight exercise countermeasures, crewmembers lose moderate amounts of strength in the locomotor and postural muscles of the knee, ankle, and trunk. Strength is largely recovered within the first 30 d of return to Earth, although small deficits do persist. Current data do not support gender-specific differences in strength loss following long-duration spaceflight. Greater preflight strength is associated with greater in-flight strength loss. Preliminary results do suggest an apparent trend for improved strength preservation since ARED became operational as the primary resistance exercise hardware on the ISS, specifically in the knee extensor muscles. This trend is expected to continue as future research, operational experience, and engineering repairs/improvements lead to both better exercise prescriptions and better ability to measure and record ARED loading.

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