



# An Evidence-Based Approach To Exercise Prescriptions on ISS

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# Summary of the Presentation

- Current exercise countermeasures
- New ISS exercise equipment
- Strategy for evaluation of evidence
- Proposed new ExRx



# ISS Exercise

- 2.5 hrs/day, 6 days/wk
- Resistance exercise
  - iRED
  - Predominantly high reps low loads
- Aerobic exercise
  - TVIS & CEVIS
  - 30 min continuous at ~70% HRmax
  - Some interval work – “Greenleaf protocol”

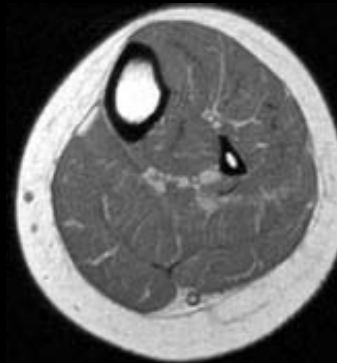


# Limitations of ISS Exercise Hardware

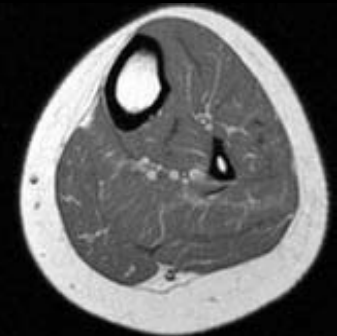
- iRED
  - Maximal load 300 lbs
  - Elastic bungee resistance not constant
  - Limited eccentric component
- CEVIS
  - Maximal load 300 Watts
- TVIS
  - Speed limitations
  - Subject loading limitations

# Exercise Not Fully Effective

- ISS crewmembers (expeditions 1-15, n=18)
  - Isokinetic knee extensor and flexor strength decrease 11% and 17%, respectively.
  - Isokinetic knee extensor and flexor endurance decrease 10% and 9%.
  - Maximal aerobic capacity (estimated from submaximal test) 10% reduction
  - Bone mineral density (BMD) 2-7% decrease depending on site.



PRE



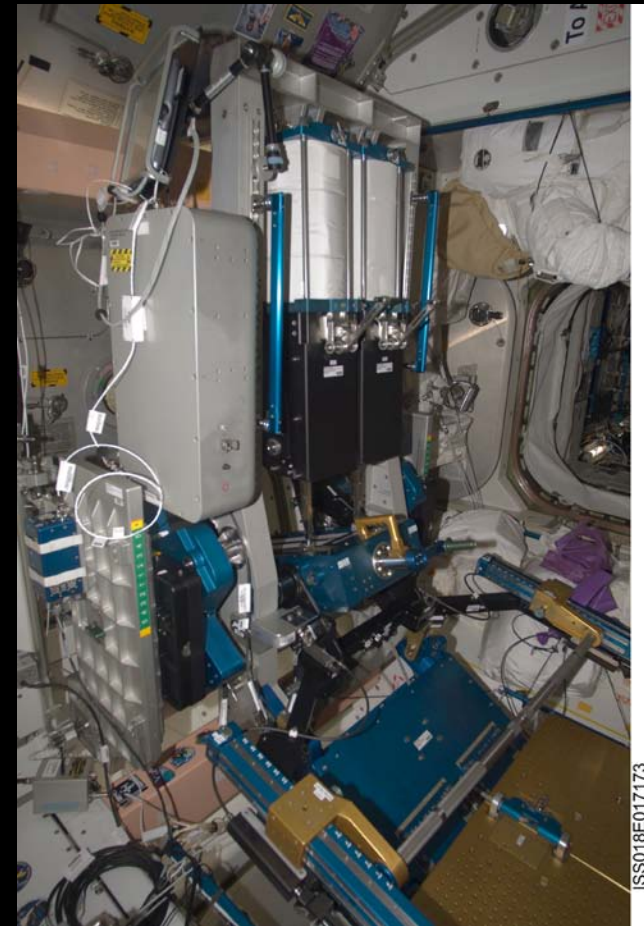
POST

# Why?

- ISS exercise hardware does not allow for sufficient intensity of exercise
- Inadequate ExRx
- Crew member noncompliance with ExRx
- Other

# New ISS Hardware - ARED

- More exercises (29 different ones)
- Instrumented for data acquisition
  - Sets
  - Reps
  - Ground reaction forces
  - Load at the bar
- Improved loading
  - 600 lbs
  - Ecc-Con Ratio ~90%
  - Constant load
  - Simulated inertia



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# New ISS Hardware – T2

- Better harness & subject loading system
- Instrumented to allow ground reaction force data
- Improved speed





# HRP Integrated Research Plan

## Risks and Gaps

- Risk of impaired performance due to reduced muscle mass, strength and endurance.
  - Gap M7: Can the current in-flight performance be maintained with reduced exercise volume?
  - Gap M8: What is the minimum exercise regimens needed to maintain fitness levels for tasks?
  - Gap M9: What is the minimum set of exercise hardware needed to maintain those (M8) levels?
- Risk of reduced physical performance capabilities due to reduced aerobic capacity.
  - Gaps M7-9: (above)
  - Gap M2: What is the current status of in-flight and post-flight performance capability?
  - Gap CV2: What is  $VO_{2max}$  in-flight and immediately post-flight?

# More Risks/Gaps

- Risk of accelerated osteoporosis.
  - Gap B15: Can exercise hardware and protocol be designed to provide loads necessary to maintain bone health?

# Workshops

- June and October 2008 workshops suggested enough ground-based evidence existed to move forward with a flight ExRx study.
  - ASCR, ExPC, HRP management, flight surgeons, medical operations, external experts
- Major recommendations
  - Higher intensity, less frequent resistance exercise
  - More variety of resistance exercises
  - Alternate days of moderate intensity continuous aerobic exercise with higher intensity interval aerobic exercise
  - Monitor in-flight exercise performance using instrumented hardware
  - Include more robust physiological outcome measurements to document the efficacy of the exercise program.
- March 2009 proposal submitted for NAR

# Strategy for ExRx

- Identify exercise training programs that have been shown to maximize adaptive benefits of people exercising in both 0 and 1 g environments.
- Priority order of evidence
  - ISS or spaceflight information
  - Human flight analog studies (bedrest, unilateral lower limb suspension (ULLS)).
  - Human 1-g exercise training studies
  - Animal flight analogs or 1 g studies only in the rare cases where no human data exist.

# Cardiovascular Fitness

- “Capacity of the heart and lungs to supply oxygen-rich blood to the working muscles and the capacity of the muscles to use oxygen to produce energy.”

[www.health.qld.gov.au/npag/glossary.asp](http://www.health.qld.gov.au/npag/glossary.asp)

- Evaluation should include more than  $\text{VO}_2\text{max}$

# Intensity Is The Key Factor

- Trained for 10 weeks
  - High intensity (90-100% max HR) interval cycle (6x 5min, 2 min rest) exercise alternated with continuous running as fast as possible for 40 min.
- Divided subjects into 3 maintenance groups where one factor was reduced: intensity, duration or frequency.

(Hickson et al, 1981, 1982, 1985)

# Maintenance Groups

- Intensity
  - Work rate reduced by  $1/3$  or  $2/3$
- Duration
  - Reduced from 40 to 26 or 13 min/day
- Frequency
  - Reduced from 6 to 4 or 2 days/week

(Hickson et al, 1981, 1982, 1985)

# Which Group Would You Choose?

- Physiological adaptations were most robust to a **decrease in training frequency** as evidenced by a maintained  $\text{VO}_2\text{max}$  with as little as 2 days/week of high intensity exercise.
- Most physiological adaptations were maintained despite a **decreased duration**, even with as little as 13 min/day of training. The exception was that long-term (~2hr) endurance was not maintained in the shortest duration (13 min/day) group, however short term (~5 min) endurance was maintained.

(Hickson et al, 1981, 1982, 1985)



# Intensity Most Important Factor

- Little maintenance of physiologic adaptations with even the 1/3 reduction in training intensity.
  - Despite training 6 days/week for 40 min/day  $\text{VO}_2\text{max}$ , long-term endurance, and left ventricular mass were not maintained with 1/3 reduction in training work rate.
  - Alarming, all training-induced increases in left ventricular mass were completely lost when work rate was reduced by 1/3.
  - Training HR from 180 to 150 beats/min.
- To minimize crew time spent on exercise, exercise frequency and duration may be reduced but intensity must be maintained at as high of levels as reasonably possible.

(Hickson et al, 1981, 1982, 1985)

# ISS Aerobic Exercise

- Currently 30-40 min at 70-85% HRmax on CEVIS or TVIS.
- Research overwhelmingly shows higher intensity is required for physiologic adaptations.
- Interval work suggested.

# Aerobic Intervals

- 20-30 second “all out sprints”
  - Shortest well documented training
  - Elicits CV adaptations primarily at peripheral sites
    - Increased muscle oxidative enzymes and mitochondrial biogenesis
  - Very short exercise durations
    - 8 sets of 20 sec sprint with 10 sec recovery takes 4 min + warmup/cool down.

# Medium Intervals

- 2-3 minute intervals
  - Bedrest evidence of maintenance of  $\text{VO}_2$  max
  - 2 min interval sometimes used on ISS
    - 7 minute warm up at 40% of  $\text{VO}_2$ max, followed by 5x2 minute stages at 60,70,80,90,80%  $\text{VO}_2$ max, 5 min cool down
    - Well tolerated by crew, anecdotal evidence

# Long Intervals

- 4 minutes
  - Large number of ground based training studies support 4 min intervals
  - Best results when intensity is maintained ~90%

# Bone

- Bedrest studies - exercise interventions effective in reducing some, but not all bone loss.
  - Linearly periodized resistance exercise program and increased bone mineral density (BMD) in the lumbar spine, preserved bone in the heel, femoral neck and total hip, but was effective at the trochanter in only those subjects with dynamic loading of the hip on single heel raises (Shackelford et al., 2004).
  - Fixed traditional training program of leg and calf press using a flywheel device combined with low body negative pressure (LBNP) treadmill exercise alleviated about half of the bone loss in the trochanter and total hip (Smith et al., 2008).

# ISS Exercise and Bone

- Evidence from missions on ISS (expeditions 1-15; n=19) show modest correlations ( $r=0.4-0.55$ ) with bone mineral density and time/intensity of exercise.
- Trochanter, lumbar spine, and whole body BMD with total aerobic exercise time above 70% HRmax.
- Trochanter and pelvis BMD with total number of total exercise sessions.
- Femoral neck and lumbar spine BMD with total treadmill exercise time.
- Pelvis BMD showed with IRED deadlift load used during training, but other IRED correlations were much lower (unpublished internal data).

# Bone

- High magnitude (Rubin & Lanyon, 1985) and rate of dynamic (not static) strain (Hsieh & Turner, 2001).
  - Periodized resistance training program where the magnitude and rate of strain is regularly altered.
- Diverse strain distributions as bone adaptations are well documented to be site specific in humans as evidenced by both *in vitro* (Bass et al., 2002) and *in vivo* investigations (Maple et al, 1997; Winters-Stone & Snow, 2006).
  - Periodized resistance training whereby the resistance exercises are varied to yield diverse strain distributions.



# Bone

- Only a few repetitions are required (Rubin & Lanyon, 1984).
  - 36 cycles of loading per day is as effective as 360 cycles/day when the strain rate is high.
  - Minimal number of repetitions is dependent on the load, with higher loads requiring fewer repetitions (Cullen et al, 2001)
  - 2 shorter exercise sessions in one day as opposed to one longer session

# Bone

- Multiple daily exercise sessions optimize bone growth (Robling et al., 2000).
  - Resting ~4 h between bouts nearly doubled bone formation responses in rodents (Robling et al. 2001).
  - Significant correlations among trochanter and pelvis BMD and total number of exercise sessions on ISS.
  - Femoral neck and lumbar spine BMD correlated with total treadmill exercise time on an ISS.
  - 2 exercise sessions in one day as opposed to one longer session

# Bone

- **Longer rest intervals between sessions and sets is beneficial.**
  - Bone quickly sensitizes to the mechanical loading stimulus, allowing rest periods between sessions allows for restoration of the mechanosensitivity.
  - 8 hours of recovery is required to regain full mechanosensitivity of bone & 14 seconds is the optimal time between loading cycles within an exercise session in rodents. (Robling et al., 2001).
  - This supports the notion of having 2 exercise sessions in one day separated by several hours as opposed to one longer session

# Muscle

- >25 bedrest and ULLS studies evaluating exercise as a countermeasure for muscle size/strength
- Variety of exercises used
  - LBNP treadmill
  - Flywheel
  - Traditional weights
- All exercise programs that were effective in maintaining muscle size/strength used maximal or nearly maximal contractions.

# Examples of Effective Countermeasures

- Traditional weights
  - 21 day ULLS KE and PF
  - 10 reps at 40%, 2 MVIC, 10 reps at 80%, a final set of as many reps as possible of isotonic exercise at 80%.
  - Every 3 days
  - Total exercise time (including rest) was 6.5 min
  - KE and PF CSA and MVC were maintained

# Countermeasures

- Traditional weights
  - 14 Days Bedrest
  - 5 sets of leg press every other day at 8 RM
  - 1RM & CSA maintained, MVIC not

# Countermeasures

- Inertial flywheel
- 60 Day bedrest exercise for squat & calf press every 3 days beginning on day 2
- LBNP treadmill
- Effective to maintain VL size and strength but not SOL (28% vs 8% loss)

(Trappe et al., 2007, 2007, 2008)

## Common To Effective Countermeasures

- Use of maximal or nearly maximal contractions!
- Calf and thigh require different stimuli



# Countermeasures

- So...how do you design exercise programs for spaceflight?
- If it works in bedrest does it work with spaceflight?



# Flight Countermeasures Improving

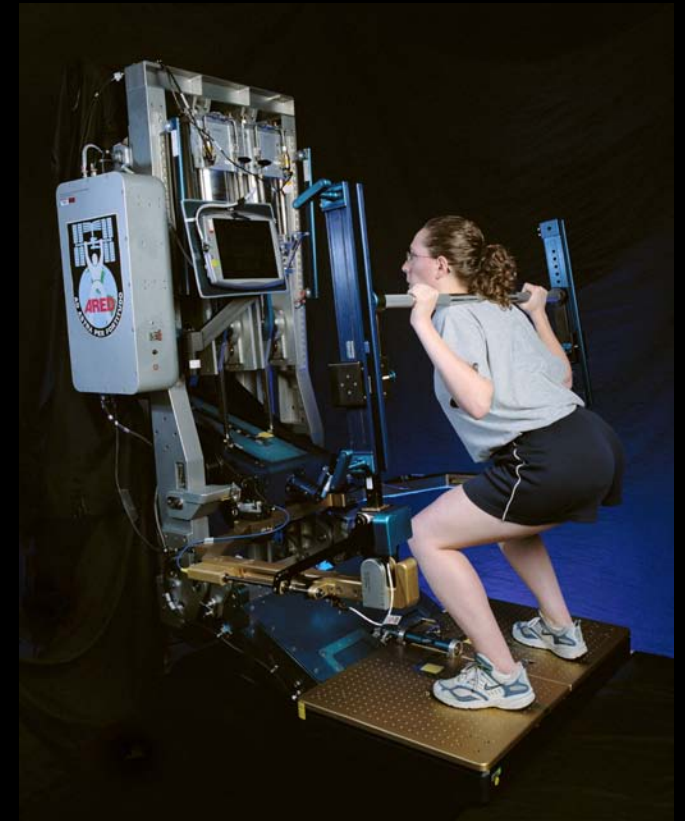
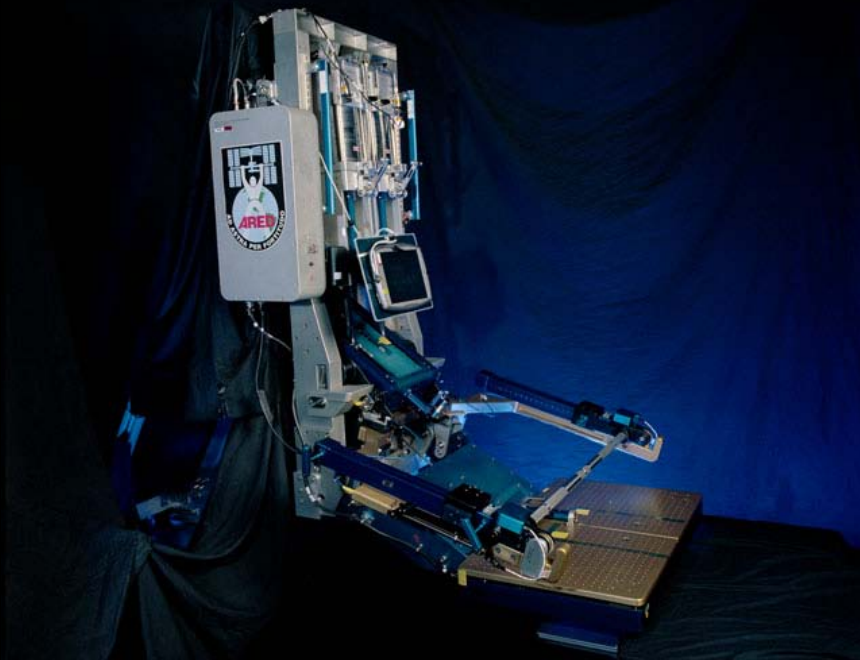
- NASA/MIR – elastic expanders
  - 16 crew, ~140 days, 10%, 13% loss in muscle **mass** in QF and calf
- ISS – IRED
  - 18 crew, ~180 days 11%, 18% loss QF, calf **strength**

# Bedrest vs. Spaceflight

- Length of study
  - Few bedrest studies as long as 90 days
  - ISS flights 180 days
- Presence of gravity in bedrest
  - Movements in bed still against gravity
  - Lumbar spine
  - Other stressors in flight, calm & safe in bedrest

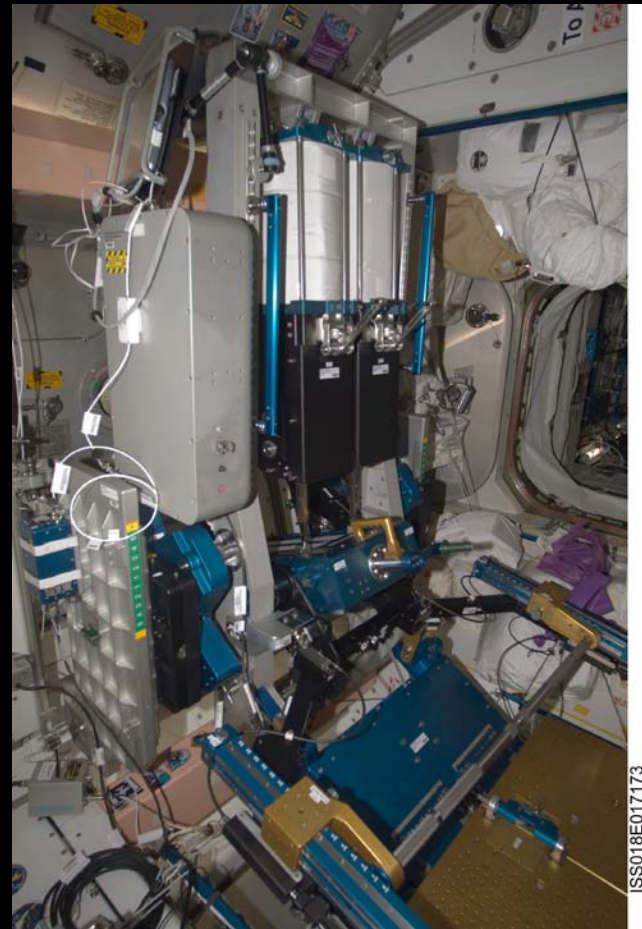
# Exercise Equipment on ISS

- Advanced Resistance Exercise Device (ARED)



# ARED

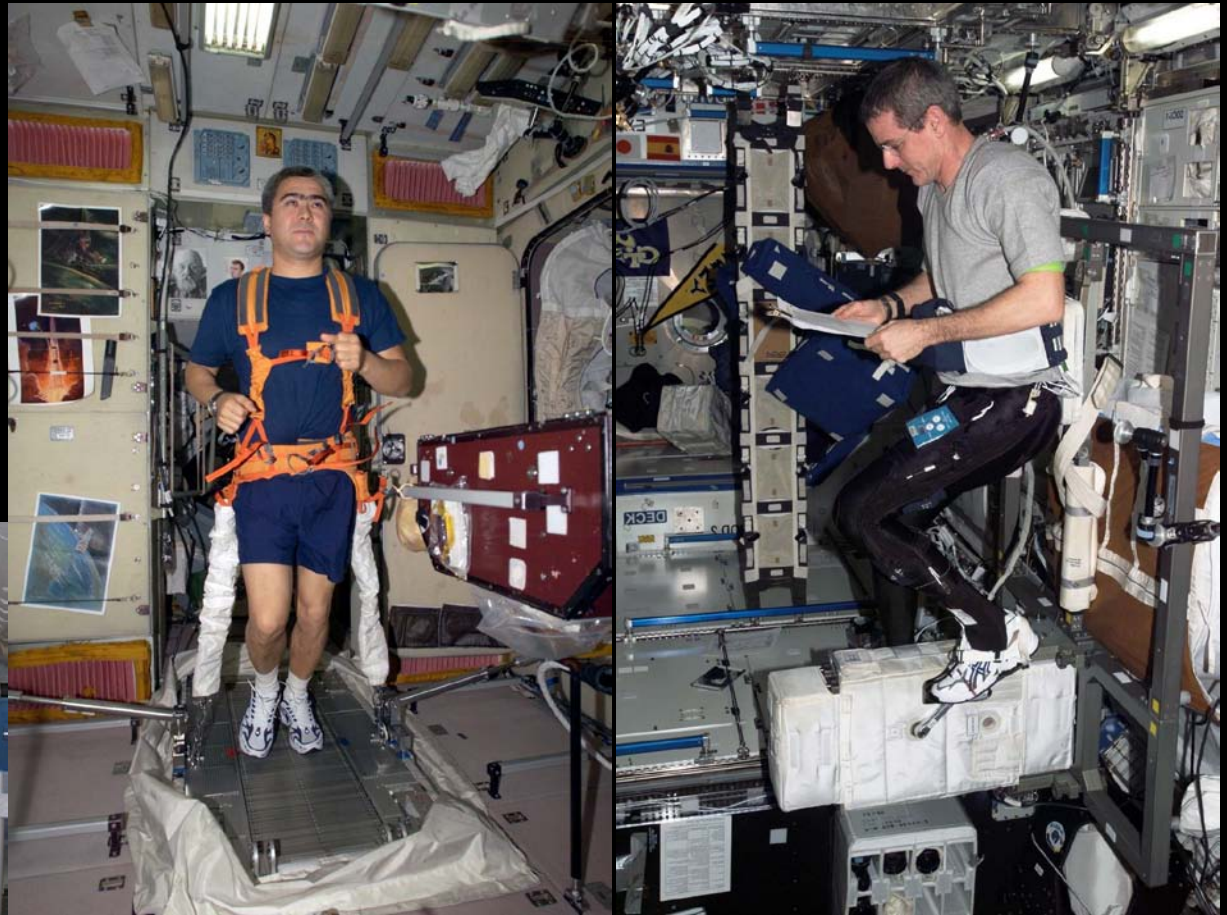
- Greater loads – 600 lbs
  - Pneumatic cylinders
    - Constant load
    - Ecc-Con ratio ~90%
  - Flywheels
    - Simulated inertia
- 29 different exercises
- Instrumented





# ISS Exercise Equipment

- TEVIS
- CEVIS
- T2 soon



# Resistance Exercises – Weekly Schedule

	Day 1	Day 2	Day 3
	Squat, Bench Press, Romanian Dead Lift, Upright Row, Heel Raise	Dead Lift, Shoulder Press, Single Leg Squat, Bent-over Row, Single Leg Heel Raise	Front Squat, Bent-over Row, Single Leg Knee Extension, Bench Press, Heel Raise
Week			
1	Light	Light	Light
2	Light	Light	Light
3	Moderate	Light	Heavy
4	Heavy	Moderate	Light
5	Light	Heavy	Moderate
6	Moderate	Light	Heavy
7	Heavy	Moderate	Light
8	Light	Heavy	Moderate
9	Moderate	Light	Heavy
10	Heavy	Moderate	Light
11	Light	Heavy	Moderate
12	Moderate	Light	Heavy

# Resistance Exercise Session Details

## Weeks 1-6

	Light	Moderate	Heavy
<b>Sets</b>	3	3	3
<b>Reps</b>	12	8	5
<b>Rest (sec)</b>	90	120	120
<b>Total Time (min)</b>	35	40	40

## Weeks 7-12

	Light	Moderate	Heavy
<b>Sets</b>	3	4	4
<b>Reps</b>	10	6	3
<b>Rest (sec)</b>	90	150	180
<b>Total Time (min)</b>	35	50	60



# Aerobic Interval Exercises

- **Short Sprint** - 10 minute warm up at 50% of HRmax, followed by 7-8 sets of maximal exercise for 30 seconds, followed by 15 seconds rest. Increase load after 9 sets
- **2 minute** - 5 minute warm up at 50%  $VO_2$ max, followed by 6x2 minute stages at 70, 80, 90, 100, 90%, 80%  $VO_2$ max. The first 5 stages are separated by 2 minute active rest stages at 50%  $VO_2$  max. The final stage is a 5 min active rest at 40%  $VO_2$ max.
- **4 minute** - 5 minute warm up at ~50% HRmax, followed by intervals of exercise at 90% HRmax. The exercise intervals will be 4x4 min bouts, with 3 min active rest periods.

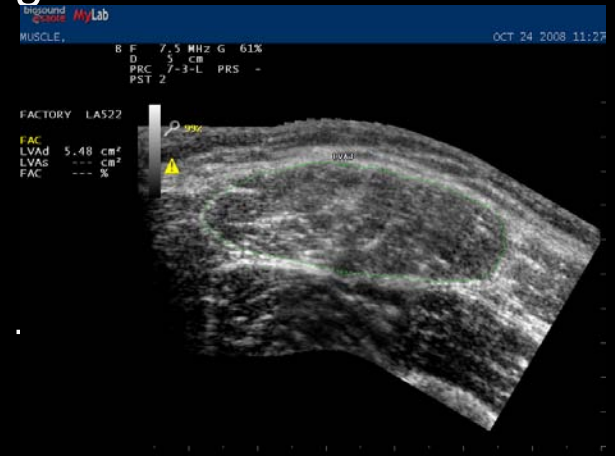
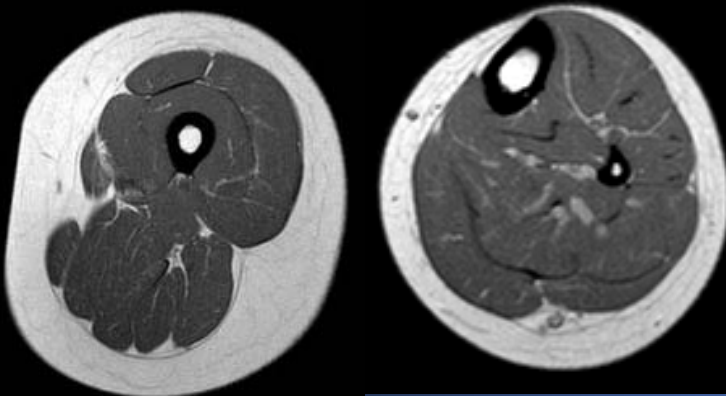
# Integration of Resistance and Aerobic

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

Note: Time savings up to 3 hours/week compared to current exercise time  
At least 4 hrs, preferably 8 hrs separating exercise sessions

# Pre- and Post-Flight Measurements

- Muscle CSA
  - Pre/Post-flight MRI – Availability at landing?
  - Pre/In/Post-flight Ultrasound – In-flight?
- Muscle Function Test from FTT
  - Power, endurance, CAR, steadiness
- Single fiber size, contractile function,
- Aerobic & glycolytic enzymes
  - Citrate synthase & PFK



# Pre- and Post-Flight Measurements

- Cardiovascular
  - Pre/In/Post-flight  $\text{VO}_2\text{max}$
  - Ventilatory threshold pre/post-flight using standard ramp cycle protocol
    - 50 Watts for 3 min then increased by 25 Watts/min thereafter
  - HR response to submax load pre/in/post
- Bone
  - QCT as a standard medical test. Structural parameters can be estimated from 2-d DXA scans by Hip Structure Analysis in the absence of QCT scans.
  - Request data sharing with with MedB8.1/Clinical Nutritional Assessment and the SMO 016E/Nutritional Status Assessment for bone markers.

# Pre-Post-Flight Test Schedule

Time	Test	Time Required
Preflight L<365	Bone	60 min
Preflight L-180	Isokinetic knee, ankle, back	75 min
Preflight L-60-90	Isokinetic knee, ankle, back	60 min
Preflight L-50-55	Biopsy	60 min
Preflight L-45-50	MRI, US, functional fit=Muscle, Cycle=VO <sub>2</sub> max	60, 50, 30, 60 min
Preflight L-10	MRI, Muscle, US, VO <sub>2</sub> max	60, 50, 30, 60 min
Postflight R+0	MRI or US, Biopsy	30 min, 60 min
Postflight R+1	Muscle, VO <sub>2</sub> max	50, 60 min
Postflight R+5	Isokinetic knee, ankle, functional fit =Muscle	60,60 min
Postflight R+6	MRI, US	60, 40, 30 min
Postflight R+10	Cycle =VO <sub>2</sub> max	60 min
Postflight R+14	Isokinetic knee, ankle, back	60 min
Postflight R+29	Cycle =VO <sub>2</sub> max	40, 60 min
Postflight R+30	Isokinetic knee, ankle, back, functional fit = Muscle	60, 60 min
Postflight <R+30	Bone	60 min

## •In-flight Data

### Muscle Strength

5 RM weeks 1-7  
3RM after week 7

### VO<sub>2</sub>max

Every 30 days

### Muscle Size??

Vastus lateralis via ultrasound

Pre-flight testing = 11 hrs

Post-flight testing = 14 hrs

# Summary

- New ISS exercise hardware should allow for exercise at intensities high enough to be expected to elicit adaptive responses.
- New ExRx should incorporate higher intensity exercises and seek to optimize intensity, duration and frequency to yield and efficient ExRx.