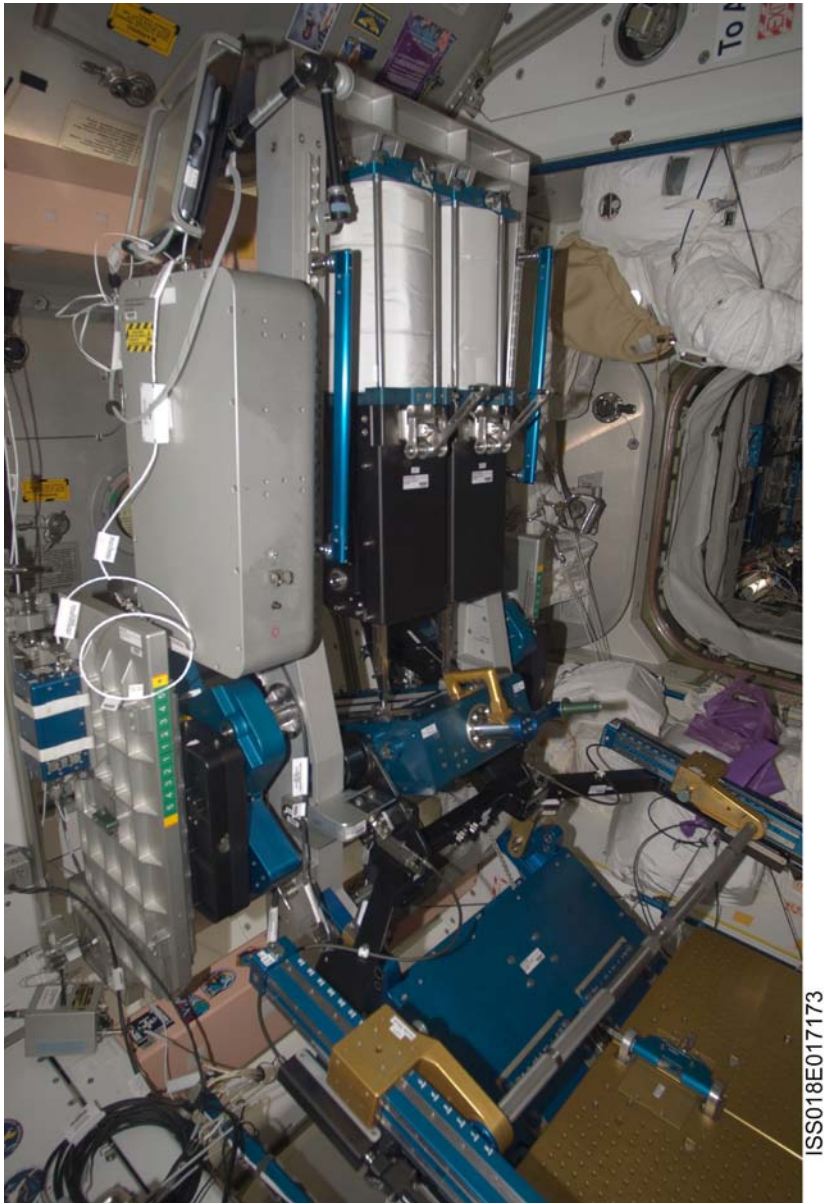
# ARED Update

- Being used for exercise
- Surprising amount of movement & VIS
- Squat exercise performed
  - Very similar to ground exercises, impressed
- No load data yet
- Working out issues with data/calibration



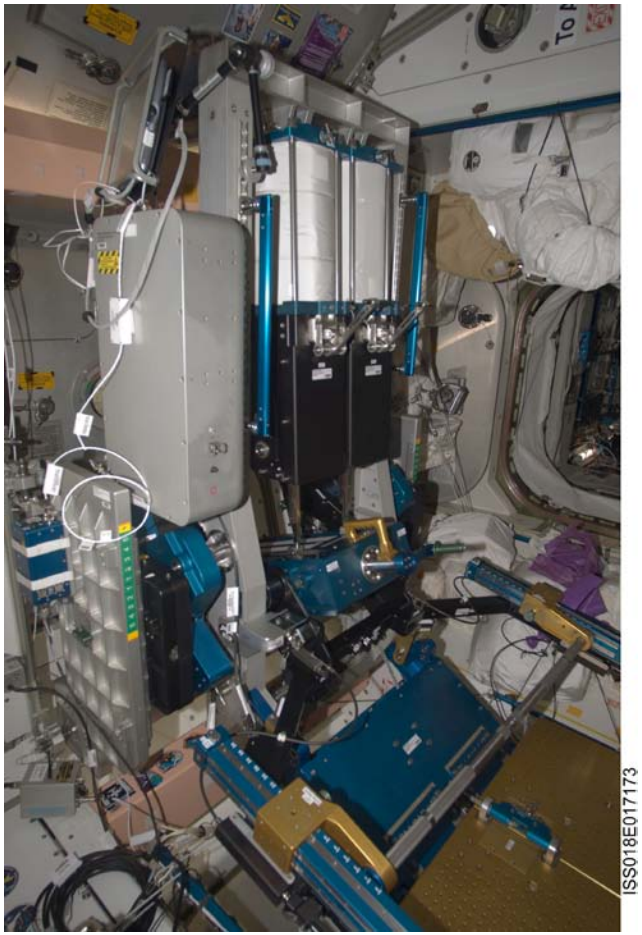
# Evidence-Based Exercise Prescription For Use On The ISS (EB-ExRx)

**PI - L. Ploutz-Snyder, Ph.D.**

- Developed as a result of 2 NASA workshops with internal & external scientists
  - Muscle Workshop in June 2008
  - ISS Exercise Prescription Workshop October 2008
- Utilizes evidence from ground based flight analogs and exercise training studies to prevent loss of muscle mass & function, cardiovascular function and bone health.
- Significant input from Astronaut Strength, Conditioning, and Rehabilitation (ASCR) team
  - Plan to implement this exercise protocol instead of “typical” ASCR protocol
- Extramural consultants involved:
  - Dr. Wendy Kohrt – Univ. of Colorado-Denver Health Sciences Center (bone inputs)
  - Dr. Ed Coyle – Univ. of Texas-Austin (aerobic, functional test inputs)
  - Drs. Todd and Scott Trappe – Ball State Univ. (muscle inputs) – leveraging Earmark funds

# Evidence-Based Exercise Prescription for use on the ISS (EB ExRx)

- **New exercise hardware**
  - ARED resistance exercise
    - Higher loads (600 vs 150 lbs)
    - More exercises (29 different ones)
    - Instrumented to allow data acquisition – LOADS!
  - T2 treadmill
    - Better harness & subject loading system
    - Instrumented to allow ground reaction force data
- **Basic Changes**
  - Higher intensity, less exercise time
  - 3 days/week resistance exercise
    - 3-12 RM periodized
    - Standard care is 6 days/week
  - Aerobic exercise every day
    - Also periodized
    - 30 min continuous on resistance days
    - High intensity intervals on alternate day (15-35 min)
- **Better physiological outcomes**
  - Typical medical tests
  - Muscle CSA (US/MRI)
  - Full battery of muscle function
  - $VO_2$max
  - Muscle biopsy option



# Specific Aims & Hypotheses

- **Hypothesis 1** – Three days/week of resistance training using ARED at a higher intensity will better protect skeletal muscle mass and function, and equally protect bone health compared to resistance exercise on ARED 6 days/week at a lower intensity. Both ARED protocols will be more effective than the IRED exercise program (historic data set).
- **Aim 1** – This hypothesis will be tested by comparing two ARED protocols, the new EB-ExRx and the standard care ExRx care from Space Medicine's Astronaut Strength, Conditioning and Rehabilitation (ASCR) group. Dependent variables under comparison include muscle mass, isometric and isokinetic muscle strength, endurance, power, central activation ratio, single fiber muscle function, oxidative and glycolytic muscle enzymes, and bone mineral density. The new protocols will be compared to the historic IRED data set using only the standard medical tests assessed on all astronauts and thus common to all three groups (isokinetic knee, ankle, back strength, general fitness test, and bone mineral density).

# Specific Aims & Hypotheses

- **Hypothesis 2 –** Alternating days of high intensity interval training with days of continuous aerobic exercise will be more effective than predominantly continuous aerobic exercise in the maintenance of cardiovascular function.
- **Aim 2** – This hypothesis will be tested by comparing the two exercise protocols, the new EB-ExRx and the standard care ExRx care from Space Medicine's Astronaut Strength, Conditioning and Rehabilitation (ASCR) group. Dependent variables under comparison include ventilatory threshold, HR at submaximal workload, and VO2max. The new protocols will be compared to the historic IRED data set using only the standard medical tests that are assessed on all astronauts and thus are common to all three groups (submaximal estimate of VO2max, HR at submax workload).

# Specific Aims & Hypotheses

- **Hypothesis 3** – Recovery of muscle function and VO2max will be most rapid in the EB-ExRx group, followed by standard care, followed by historic ISS group (who used old exercise hardware).
- **Aim 3** – Two different analyses will be performed to evaluate this hypothesis. First, all 3 groups will be compared using the standard medical tests common to all 3 groups. The EB-ExRx and standard care groups will be compared using standard medical data plus the new measures unique to this project.

# Important Bone Parameters

- **High magnitude** (Rubin & Lanyon, 1985) **and rate of dynamic (not static) strain** (Hsieh & Turner, 2001).
- **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).
- Only a **few repetitions are required** (Rubin & Lanyon, 1984).
- **Multiple daily exercise sessions** optimize bone growth (Robling et al., 2000**).**
- **Longer rest intervals between sessions and sets** is beneficial (Robling et al., 2001).

# Important Muscle Parameters

- Evidence for maintaining muscle mass and function during flight analogs comes from over 25 bedrest and ULLS published studies.
- Flywheel, LBNP treadmill, traditional weights
- Effective studies ALL used maximal or nearly maximal contractions

# Important Cardiovascular Parameters

- Intensity most important single factor affecting training maintenance
- 10 week high intensity training (90-100% max HR) interval cycle (6x 5min, 2 min rest) exercise alternated with continuous running as fast as possible for 30 min.
- After 10 weeks one training parameter was manipulated to see whether fitness could be maintained over the next 15 weeks with reductions in either exercise intensity, duration or frequency (Hickson et al, 1981, 1982, 1985).
- Intensity – decreased 1/3 or 2/3 in WR
- Duration – decreased from 40 min/day to 26 or 13
- Frequency - decreased from 6 day/week to 4 or 2

# Hickson Study Results

- Physiological adaptations were most robust to a decrease in training frequency as evidenced by a maintained $VO_2$max with as little as 2 days/week of high intensity exercise.
- Most physiological adaptations were maintained despite a decreased exercise 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.
- Despite training 6 days/week for 40 min/day $VO_2$max, long-term endurance, and left ventricular mass were not maintained with as little as a one-third reduction in training workrate. Alarmingly, all increases in left ventricular mass observed from the initial 10 weeks of training were completely lost when workrate was reduced by one-third.

# So What?

- The application of this work to the current proposal suggests that **to minimize crew time spent on exercise, that exercise frequency and duration may be reduced but intensity must be maintained at as high of levels as reasonably possible.**

# Current Exercise on ISS

- Current in-flight aerobic exercise consists of 30-40 min of continuous exercise at 70-85% of maximal heart rate (HRmax) with treadmill running at less than 1 full body weight of resistance.
- Research literature overwhemingly shows the greatest benefits in markers of cardiorespiratory fitness are realized with higher intensity (85-100%), lower duration exercise protocols such as intermittent or interval programs combining short sprints with short to medium rest periods for a wide variety of populations ranging from heart disease patients to endurance athletes (example reviews Gibala & McGee, 2007; Meyer et al, 1998; Midgley & McNaughton, 2006).

# Intervals

- **20-30 second intervals**. The shortest well documented protocols are 20-30 sec “all out” sprints such as those described by Tabata et al. and Gibala et al.

  dramatic increases in muscle oxidative capacity including increased oxidative enzymes citrate synthase and cytochrome oxidase, increased markers of mitochondrial carbohydrate (pyruvate dehydrogenase E1alpha protein content) and lipid (3-hydroxacyl CoA dehydrogenase) oxidation, and activation of signaling cascades linked to mitochondrial biogenesis (AMPK and p38MAPK).

## More intervals

- **2 minute intervals.** There are many studies documenting the effectiveness of 2 minute interval aerobic exercise programs for improving cardiovascular function. Importantly there are a series of bedrest studies utilizing interval LBNP treadmill exercises (3 min stages at 60-80% VO2max) that show a maintenance of VO2 max and sprint speed over 30 days of bedrest (Lee et al., 2008)

## Even More Intervals

- **4 minute and longer intervals.** There is a large body of literature documenting the superiority of  4 minute high intensity intervals to continuous exercise in training induced CV adaptations especially in special populations.

# Intervals Selected

- **Intensified Greenleaf** - 5 minute warm up at 50% VO2max, followed by 6x2 minute stages at 70, 80, 90, 100, 90%, 80% VO2max. The first 5 stages are separated by 2 minute active rest stages at 50% VO2 max. The final stage is a 5 min active rest at 40% VO2max.
- **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
- **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

# Intervals

| | Day 2 / Protocol 1 | Day 4 / Protocol 2 | Day 6 / Protocol 3 |
|---|---|---|---|
| | 6 x2 minute stages at 70, 80, 90, 100, 90, 80% $VO_2$max with 2 min rest in between; >50% of sessions on T2 = 32 min total time | 8 x 30 sec at maximal effort with 15 sec rest in between – all sessions passive treadmill =15 min total | 4x4 min at 90% HRmax with 3 min active rest; >50% of sessions on T2 = 35 min total |

# EB-ExRx
# Resistance

## Weekly Training 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, Sumo Dead Lift, Bench Press, Heel Raise |
| Week | | | |
| 1 | Light | Light | Light |
| 2 | Light | Moderate | Light |
| 3 | Moderate | Light | Heavy |
| 4 | Moderate | Light | Moderate |
| 5 | Heavy | Moderate | Light |
| 6 | Moderate | Light | Heavy |
| 7 | Light | Heavy | Moderate |
| 8 | Heavy | Light | Heavy |
| 9 | Moderate | Heavy | Moderate |
| 10 | Heavy | Light | Moderate |
| 11 | Heavy | Moderate | Light |
| 12 | Moderate | Light | Heavy |

## Program Variables for the Resistance Training Intervention

| Weeks 1-6 | | | |
|---|---|---|---|
| | Light | Moderate | Heavy |
| Sets | 3 | 3 | 3 |
| Reps | 12 | 8-10 | 6-7 |
| Rest (sec) | 90 | 120 | 120 |
| Total Time (min) | 35 | 40 | 40 |
| | | | |
| Weeks 7-12 | | | |
| | Light | Moderate | Heavy |
| Sets | 3 | 4 | 4 |
| Reps | 12 | 6-8 | 3-5 |
| Rest (sec) | 90 | 150 | 180 |
| Total Time (min) | 35 | 50 | 60 |

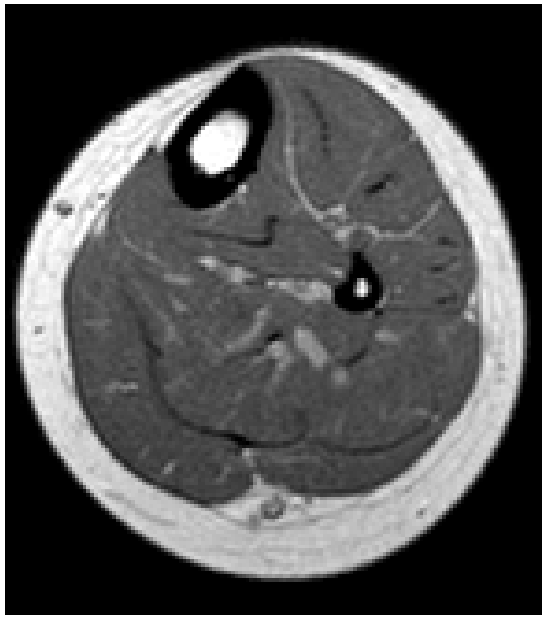
# Integration

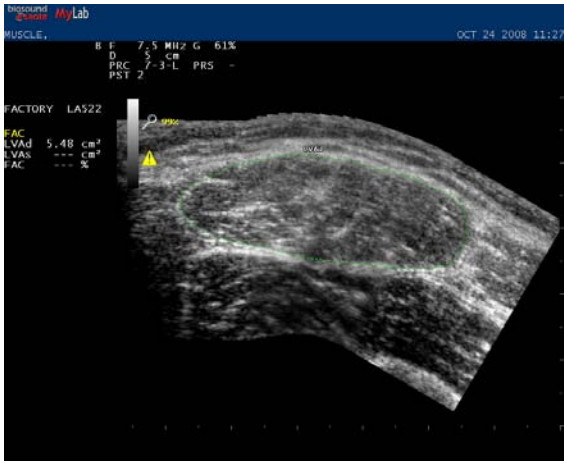
| | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 |
|---|---|---|---|---|---|---|---|
| Resistance | 35-60 min | | 35-60 min | | 35-60 min | | |
| Aerobic Interval | | 32 min | | 15 min | | 35 min | |
| Aerobic Continuous | 30 min | | 30 min | | 30 min | | |

Preferably 8 hours, but at least 4 hours will separate exercise bouts
Time savings – 3 hr/week

# Outcome Measurements

- Muscle CSA
  - Pre/Post-flight MRI
  - Pre/In/Post-flight Ultrasound
- Muscle Function FTT
- Single fiber size, contractile function, type
- Aerobic & glycolytic enzymes
  - Citrate synthase & PFK



# CV

- Pre/In/Post-flight VO2max
- Ventilatory threshold pre/post-flight
- HR response to submax load pre/in/post

## Standard Medical

- Bone – DEXA or qCT
- Isokinetic (quad, calf, back)
- Functional fitness
- Submax VO2 test

# 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-45-50 | Biopsy | 60 min |
| Preflight L-30-35 | MRI, Muscle, US, $VO_2$max | 60, 50, 30, 60 min |
| Postflight R+0 | US, Biopsy | 30 min, 60 min |
| Postflight R+2 | Muscle, $VO_2$max | 50, 60 min |
| Postflight R+5 | Isokinetic knee, ankle, functional fit | 60,60 min |
| Postflight R+6 | MRI, Muscle, US | 60, 40, 30 min |
| Postflight R+10 | $VO_2$max | 60 min |
| Postflight R+14 | Isokinetic knee, ankle, back | 60 min |
| Postflight R+29 | Muscle, $VO_2$max | 40, 60 min |
| Postflight R+30 | Isokinetic knee, ankle, back, functional fit | 60, 60 min |
| Postflight <R+30 | Bone | 60 min |

# EB ExRx Protocol: Integration of Aerobic & Resistance

| | 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