<table>
<thead>
<tr>
<th>Integrated Resistance and Aerobic Training Study Sprint</th>
<th>Human Research Program Informed Consent Briefing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lori Ploutz-Snyder, Ph.D.</td>
</tr>
</tbody>
</table>

### Integrated Resistance and Aerobic Training Study- Sprint

#### Exercise Physiology Laboratory/SK
- Lori Ploutz-Snyder, Ph.D.
- Alan Moore, Ph.D.
- Jeffrey Ryder, Ph.D.
- Meg Everett, M.S.

#### Neuroscience Laboratory/SK
- Jacob Bloomberg, Ph.D.

#### Bone Laboratory/SK
- Jean Sibonga, Ph.D.
- Linda Shackelford, MD

#### Cardiovascular Laboratory/SK
- Steven Platts, Ph.D.
- David Martin, B.A.

#### Research Statistician/SK
- Robert Ploutz-Snyder, Ph.D.

#### ASCR/SD
- Mark Guilliams, M.A., CSCS

### University Partners
- Scott Trappe, Ph.D. – Ball State Univ
- Todd Trappe, Ph.D - Ball State Univ
- Wendy Kohrt, Ph.D. – Univ of Colorado
- Ed Coyle, Ph.D. – Univ of Texas
Background

Space flight causes reductions in fitness/health:

- Cardiovascular - reduced VO$_2$ max, cardiac output
- Bone – reduced bone mineral density
- Muscle - reduced mass, strength and endurance

Exercise is the primary countermeasure to protect against these changes and was made operational before completely mature; research continues to identify most effective/efficient exercise programs.

Crew medical tests (cardio, muscle, bone) do not yield sufficient information to fine tune the effectiveness of exercise programs, thus there is a need for more detailed testing aimed at identifying the most effective training program.
Fitness declines with ISS missions (n=24)

% Decline

-20 -18 -16 -14 -12 -10 -8 -6 -4 -2 0

Knee extension strength  Knee flexion strength  Knee extension endurance  Knee flexion endurance  Maximal aerobic capacity  Bone mineral density
Background

- NASA has spent millions of dollars over past decade to fund new exercise equipment and research on exercise effectiveness.
- Ground research clearly shows that intensity is the most important factor related to maintenance of fitness
  - Duration and frequency can be dramatically reduced only if intensity is kept high
- ARED and T2 allow for more variety and higher intensities
Background

- June and October 2008 workshops identified the need for an optimized exercise prescription.
  - ASCR, ExPC, HRP management, flight surgeons, medical operations, external experts in muscle, bone and cardiovascular function.

- 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.
Objective

• Obtain detailed information about crew physical fitness pre- and post-flight.
  – Participation involves pre- and post-flight testing (modifications to standard medical & new tests).

• Evaluate new evidence based exercise prescription with higher intensity, lower duration and frequency.
## Participation Options

- **Active subject** - Full participation of all pre-, in-, and post-flight data collection and in-flight exercise program
- **Control subject** - Pre- and post-flight testing only
- **Data Sharing subject** – Agree to share medical pre, in, and post bone and exercise data
- **Muscle biopsy**
In-flight exercise program

• Higher intensity, lower frequency and duration

• Muscle
  – Bedrest and unloading studies show 2-3 days/week of training is sufficient if the contractions during resistance exercise are maximal or nearly maximal
  – Aerobic intervals optimal for affecting muscle aerobic metabolism/endurance

• Bone
  – Evidence suggests multiple daily sessions required
  – High magnitude and rate of strain
  – Site specificity

• Cardiovascular
  – Need high intensity, best achieved with intervals
# Integration of Resistance and Aerobic

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Resistance</strong></td>
<td>35-60 min</td>
<td>35-60 min</td>
<td>35-60 min</td>
<td>35-60 min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Aerobic Interval</strong></td>
<td>32 min</td>
<td></td>
<td>15 min</td>
<td></td>
<td>35 min</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Aerobic Continuous</strong></td>
<td>30 min</td>
<td>30 min</td>
<td>30 min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

- **Short Sprint** - 10 minute warm up at 50% of HRmax, followed by 7-8 sets of near-maximal exercise for 30 seconds, followed by 15 seconds rest. Increase load after 9 sets (Burgomaster et al., 2008; Gibala & McGee, 2008; Gibala et al., 2008; Tabata et al., 1996)
  - Increases mitochondrial function, peripheral cardiovascular adaptations such as muscle enzymes and capillary density.

- **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. (Greenleaf et al., 1989)
  - Maintain maximal aerobic capacity, similar protocol well tolerated on ISS

- **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. (Helgerud et al 2007)
  - Cardiac adaptations, cardiac output and stroke volume
### Sprint Resistance Exercise

<table>
<thead>
<tr>
<th>Week</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Light Squat, Bench Press, Romanian Dead Lift, Upright Row, Heel Raise</td>
<td>Light Dead lift, Shoulder Press, Bent-over Row, Single Leg Squat, Heel Raise</td>
<td>Light Front Squat, Bent-over Row, Dead lift, Bench Press, Heel Raise</td>
</tr>
<tr>
<td>2</td>
<td>Light Squat, Bench Press, Romanian Dead Lift, Upright Row, Heel Raise</td>
<td>Light</td>
<td>Light</td>
</tr>
<tr>
<td>3</td>
<td>Moderate Dead lift, Shoulder Press, Bent-over Row, Single Leg Squat, Heel Raise</td>
<td>Light</td>
<td>Heavy</td>
</tr>
<tr>
<td>4</td>
<td>Heavy Front Squat, Bent-over Row, Dead lift, Bench Press, Heel Raise</td>
<td>Moderate</td>
<td>Light</td>
</tr>
<tr>
<td>5</td>
<td>Light Front Squat, Bent-over Row, Dead lift, Bench Press, Heel Raise</td>
<td>Heavy</td>
<td>Moderate</td>
</tr>
<tr>
<td>6</td>
<td>Moderate Front Squat, Bent-over Row, Dead lift, Bench Press, Heel Raise</td>
<td>Light</td>
<td>Heavy</td>
</tr>
<tr>
<td>7</td>
<td>Heavy Front Squat, Bent-over Row, Dead lift, Bench Press, Heel Raise</td>
<td>Moderate</td>
<td>Light</td>
</tr>
<tr>
<td>8</td>
<td>Light Front Squat, Bent-over Row, Dead lift, Bench Press, Heel Raise</td>
<td>Heavy</td>
<td>Moderate</td>
</tr>
<tr>
<td>9</td>
<td>Moderate Front Squat, Bent-over Row, Dead lift, Bench Press, Heel Raise</td>
<td>Light</td>
<td>Heavy</td>
</tr>
<tr>
<td>10</td>
<td>Heavy Front Squat, Bent-over Row, Dead lift, Bench Press, Heel Raise</td>
<td>Moderate</td>
<td>Light</td>
</tr>
<tr>
<td>11</td>
<td>Light Front Squat, Bent-over Row, Dead lift, Bench Press, Heel Raise</td>
<td>Heavy</td>
<td>Moderate</td>
</tr>
<tr>
<td>12</td>
<td>Moderate Front Squat, Bent-over Row, Dead lift, Bench Press, Heel Raise</td>
<td>Light</td>
<td>Heavy</td>
</tr>
</tbody>
</table>
## Sprint Resistance Exercise – session detail

### Weeks 1-6

<table>
<thead>
<tr>
<th></th>
<th>Light</th>
<th>Moderate</th>
<th>Heavy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sets</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Reps</td>
<td>12</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Rest (sec)</td>
<td>90</td>
<td>120</td>
<td>120</td>
</tr>
<tr>
<td>Total time (min)</td>
<td>35</td>
<td>40</td>
<td>40</td>
</tr>
</tbody>
</table>

### Weeks 7-12

<table>
<thead>
<tr>
<th></th>
<th>Light</th>
<th>Moderate</th>
<th>Heavy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sets</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Reps</td>
<td>10</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Rest (sec)</td>
<td>90</td>
<td>150</td>
<td>180</td>
</tr>
<tr>
<td>Total time (min)</td>
<td>35</td>
<td>60</td>
<td>40</td>
</tr>
</tbody>
</table>
Exercise Logs

- Complete in-flight exercise logs outlining the exercise performed
  - Aerobic
  - Treadmill & cycle speed, load, duration, HR
  - Resistance
    - Exercise, load, reps, sets & rest between sets
In-flight data collection

- Muscle strength
  - Monitor training loads and adjust prescription as needed
- VO$_2$max every 30 days
- Muscle size with ultrasound every 30 days

- Prescription can be adjusted accordingly based on in-flight measurements
Pre and post-flight data collection

- Muscle
  - Muscle Function
  - Imaging
  - Muscle Biopsy
- Cardiovascular
  - Pre-, in-, post-flight VO₂max
  - Ventilatory threshold
  - Cardiac ultrasound
- Bone
  - DEXA, qCT
Testing – Muscle Function

• Leg Press
  • **Maximal Isometric Force**: Push against fixed footplate.
  • **Power/Endurance**: Push weight away as fast as possible (40% max. force, 21 repetitions). Leg extension push only; weight caught by a braking system.

• Knee Extension
  • **Force Control**: Match leg force with a reference force displayed on a computer screen during isometric leg extension (5% maximal force).
  • **Neuromuscular Drive**: Brief, electrical muscle stimulus provided to thigh muscle during isometric leg extension.
• **Bench Press**

  • **Maximal Isometric Force:** Push against fixed bar.

  • **Power/Endurance:** Push weight away as fast as possible (30% max force, 21 repetitions) Arm extension only; weight caught by a braking system.

  • **Muscle Force Control:** Match isometric arm force with a reference force displayed on a computer screen (5% maximal force).
Testing – mods to standard medical

- Cycle Test MEDB 4.1

- VO\textsubscript{2}max test for ventilatory threshold (L-270, L-80, L-50; R+1-3, 8-10, 30)
  - Peak: 3 min warmup, then 1 min 25 W increments to max
  - Allows for evaluation of ventilatory threshold which has never before been assessed with spaceflight but is more functionally important than VO\textsubscript{2}max
Bone – density and architecture

• Bone densitometry MEDB 1.11
  – DEXA scan, L-<365, R+30, R+180, then yearly

• Add qCT for bone density and geometry of hip and spine
  – L-<365 and R+30
Imaging- MRI for muscle size

- MRI of the legs for muscle size/volume of thigh and calf (L-80, L-50; R+ 1-3)
  - 30 min supine rest
  - 8 min scan of calf
  - 8 min scan of thigh
Imaging- Ultrasound

- Ultrasound of the leg muscles (L-80, 50; R+0-1)
- Cardiac ultrasound
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<tr>
<td><strong>Pre-flight</strong></td>
<td><strong>Post-flight</strong></td>
</tr>
</tbody>
</table>
| L<365:  
  DXA*, QCT†                                       | R+0/1:  
  Ultrasound, Muscle Biopsy                      |
| L-270:  
  Peak Cycle (VO2max)*                              | R+1:  
  Muscle Performance†, MRI, VO2max**             |
| L-180:  
  Isokinetic Testing*, Muscle Performance†          | R+5-7:  
  Isokinetic Testing*                            |
| L-80:  
  Isokinetic Testing*, Muscle Performance†, MRI, Ultrasound, VO2max** | R+6:  
  Muscle Performance†                              |
| L-50 (as close to departure as possible):  
  Isokinetic Testing, Muscle Performance†, MRI, Ultrasound, VO2max | R+8-10:  
  VO2max†                                         |
| L-45:  
  Muscle Biopsy (optional)                          | R+30:  
  Isokinetic Testing*, Muscle Performance†, VO2max** |
|                                                        | <R+30:  
  DXA*, QCT†                                     |

* Nominal Medical testing requirement

** Testing replaces existing nominal medical testing requirement (either Functional Fit or Submax)

† Possible Data Share with existing experiments

6.25 hrs shared medical  
10 hrs study specific and possible experiment data sharing

6 hrs shared medical  
6.5 hrs study specific and possible experiment data sharing
### Inflight Medical Requirements/Activities

<table>
<thead>
<tr>
<th>Periodic Fitness Evaluation (PFE):</th>
</tr>
</thead>
<tbody>
<tr>
<td>• FD 14 and about every 30 days after</td>
</tr>
<tr>
<td>(6 sessions/1.5 hrs per session)</td>
</tr>
<tr>
<td>• 9 hrs total</td>
</tr>
</tbody>
</table>

VO2max (replaces PFE):
- FD 14 and about every 30 days after
- (6 sessions/3.6 hrs per session)
- 21.5 hrs total

<table>
<thead>
<tr>
<th>Muscle ultrasound:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• FD 14, 30 and about every 30 days after</td>
</tr>
<tr>
<td>(7 sessions/1.75 hrs per session)</td>
</tr>
<tr>
<td>• 12.25 hrs total</td>
</tr>
</tbody>
</table>

Throughout mission:
- 2.5 hrs per day of exercise training

**Total testing time (PFE) = 9 hrs**

### Inflight Sprint

<table>
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<td>• FD 14 and about every 30 days after</td>
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<td>(6 sessions/3.6 hrs per session)</td>
</tr>
<tr>
<td>• 21.5 hrs total</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Throughout mission:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 15-90 min per day of exercise training*</td>
</tr>
</tbody>
</table>

**Total testing time = 33.75 hrs**

*2.5 hrs of exercise time will still be scheduled daily
Integrated Resistance and Aerobic Training Study
Sprint

Human Research Program Informed Consent Briefing
Lori Ploutz-Snyder, Ph.D.

Muscle Biopsy
Whole Muscle → Cellular Level

Exercise on the ISS

MRI Scan
Whole Muscle Size (15% loss on ISS*)

Muscle Biopsy Sample

One Muscle Fiber

Muscle Biopsy

Slow-Twitch Fibers
Endurance and Posture

Fast-Twitch Fibers
Explosive Power Movements

ISS Findings (Increment 5-11):
12-17% shift in fiber type
Slow → Fast Transition

J Appl Physiol 106: 1159-68, 2009
Muscle Biopsy

Single Muscle Fiber Power

![Graph showing single muscle fiber power for fast-twitch and slow-twitch muscles.](image)

- Fast-Twitch
- Slow-Twitch

Change in Single Muscle Fiber Power After 6-months on the ISS

- Slow-Twitch: -25
- Fast-Twitch: -20

*J. Physiology, 2010*
**Muscle Biopsy**

Pre: L-50-55
Post: R+0

- Calf – Soleus
- Thigh – Vastus Lateralis
Muscle Biopsy – Science

**Function & Structure**

1. **Single Muscle Fiber Function**
   - To determine size, strength, speed and power in slow-and fast-twitch muscle fibers which impacts muscle performance

2. **Muscle Fiber Type Transformations**
   - To determine changes in fiber type which impacts muscle performance, metabolic health, fuel use, and fatigue

**Metabolic Capacity**

3. **Aerobic and Anaerobic Enzymes**
   - Muscle Biochemistry to determine metabolic profile which impacts energy transfer and metabolic health

4. **Capillary Density**
   - To determine capillary network which impacts blood flow, oxygen, and nutrition delivery
1. The cellular data will complement the whole muscle assessment to provide a detailed profile of skeletal muscle health and the effectiveness of the current ISS hardware and new exercise prescription.

2. Our recently published ISS muscle biopsy research from Increment 5-11 in combination with new whole muscle and cellular information will provide a strong scientific platform to help guide future countermeasure programs.

Muscle Biopsy Team Experience

**Space Flight:** Shuttle & ISS
- 14 crewmembers
- 56 muscle biopsies total

**Bed Rest:** 17, 60 and 90-d

**Aging:** up to 93 years old

**Athletes:** Recreational, Competitive, and Olympic

Drs. Scott and Todd Trappe have performed >3,000 muscle biopsies
(Human Performance Laboratory > 10,000)
Experiment Training

- **L-18-12 months**
  - 1 hr overview familiarization

- **L-12-6 months**
  - 2 hr PPFS
  - 1.5 hrs VO2max nominal operations
  - 1 hr ultrasound

- **L-18 months (as soon after consent as possible)**
  - Sprint exercises during scheduled gym time
Possible Risks or Discomforts

• Reasonable risk

• Imaging
  • MRI – personal injury from magnetic objects, noise, claustrophobia
  • qCT – radiation exposure
  • Ultrasound – gel
  • Protections – screen for metal implants, earplugs, feet first scanning, monitor crew radiation exposure, ask about allergy to ultrasound gel.

• Muscle biopsy
  • Discomfort, bleeding, infection, scarring of skin

• Protections – use of standard sterile procedures, experienced investigator to obtain biopsy.
Possible Risks or Discomforts

- Exercise testing – typical risks associated with exercise
  - Muscle soreness, cramping, joint injury, strains, sprains, cardiovascular events, light-headedness after exercise, discomfort
  - Protections – warm up, supervision, concentric only contractions, subjects already screened for heart disease, cool down
### Participation Options

- **Active subject** - Full participation of all pre-, in-, and post-flight data collection and in-flight exercise program
- **Control subject** - Pre- and post-flight testing only
- **Muscle biopsy**