Human Research Program Informed Consent Briefing

Lori Ploutz-Snyder, Ph.D.



Integrated Resistance and Aerobic Training Study- Sprint



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Background

Space flight causes reductions in fitness/health:

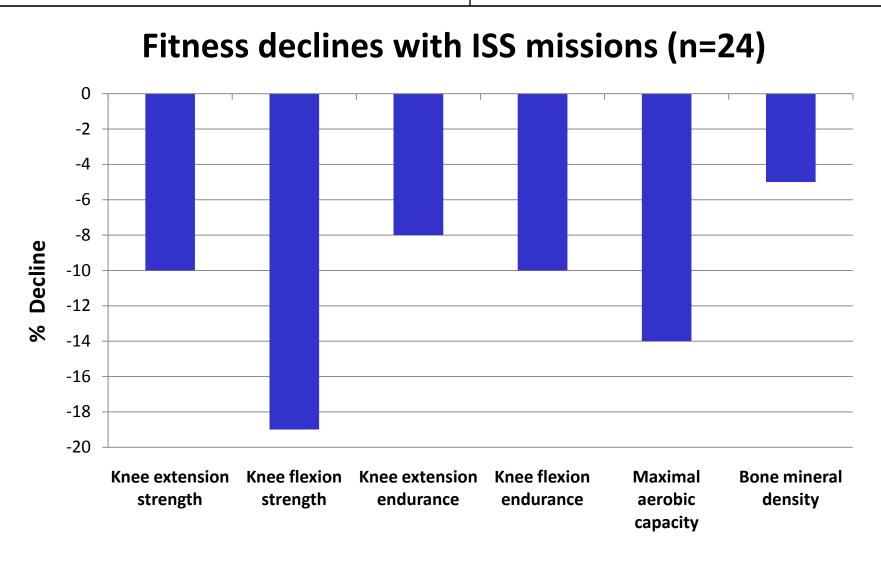
- •Cardiovascular reduced VO₂max, cardiac output
- •Bone reduced bone mineral density
- •Muscle reduced mass, strength and endurance

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.

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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 postflight 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

	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

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% 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. (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

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Sprint Resistance Exercise

	Day 1	Day 2	Day 3
	Squat, Bench Press, Romanian Dead Lift, Upright Row, Heel Raise	Dead lift, Shoulder Press, Bent-over Row, Single Leg Squat, Heel Raise	Front Squat, Bent-over Row, Dead lift, 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

Sprint Resistance Exercise – session detail

	Weel	ks 1-6	
	Light	Moderate	Heavy
	3	3	3
Reps	12	8	5
Rest (sec)	90	120	120
Total time (min)	35	40	40
	Week	s 7-12	
	Light	Moderate	Heavy
Sets	3	3	3
Reps	10	6	3
Rest (sec)	90	150	180
Total time (min)	35	60	40

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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
- VO₂max every 30 days
- Muscle size with ultrasound every 30 days

• Prescription can be adjusted accordingly based on in-flight measurements

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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.

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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
- VO₂max test for ventilatory threshold (L-270, L-80, L-50; R+1-3, 8-10, 30)
 - Peak: 3 min warmup, then 1 min25 W increments to max
 - Allows for evaluation of ventilatory threshold which has never before been assessed with spaceflight but is more functionally important than VO₂max

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</p>

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

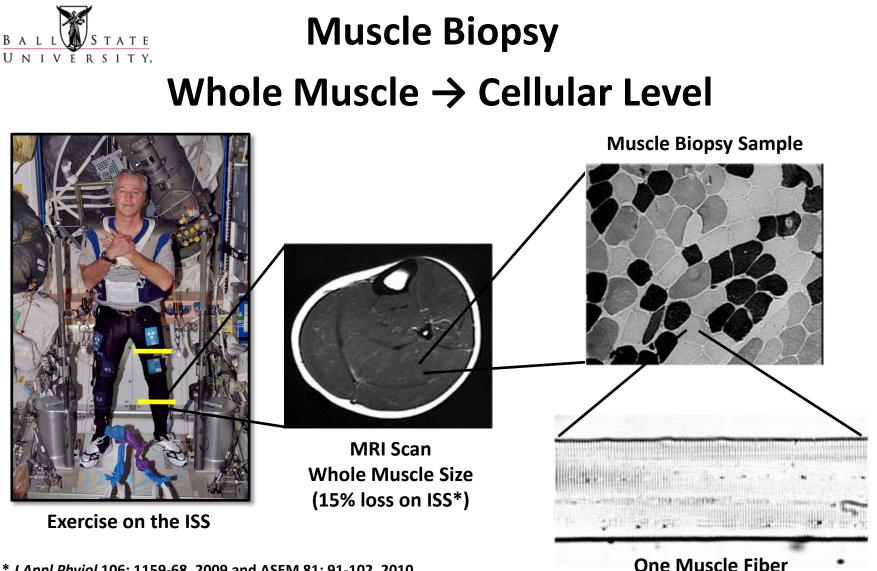


Integrated Resista	nce and Aerobic Training Study	Human Research Program Informed Consent B		
Sprint		Lori Ploutz-Snyder, Ph.D.		
	Pre-flight		Post-flight	
	L<365: DXA*, QCT†		R+0/1: Ultrasound, Muscle Biopsy	
	L-270: Peak Cycle (VO2max)*		R+1: Muscle Performance ⁺ , MRI, VO2max**	
	L-180: Isokinetic Testing*, Muscle Performance†		R+5-7: Isokinetic Testing*	
	L-80: Isokinetic Testing*, Muscle Perform MRI, Ultrasound, VO2max**	ance†,	R+6: Muscle Performance ⁺	
 * Nominal Medical testing requirement 	* Nominal Medical Isokinetic Testing, Muscle Performance ⁺ , V		R+8-10: VO2max ⁺	
 ** Testing replaces existing nominal medical testing 	existing nominal Muscle Biopsy (optional) medical testing		R+30: Isokinetic Testing*, Muscle Performance†, VO2max**	
requirement (either Functional Fit or Submax)			<r+30: DXA*, QCT+</r+30: 	
 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	

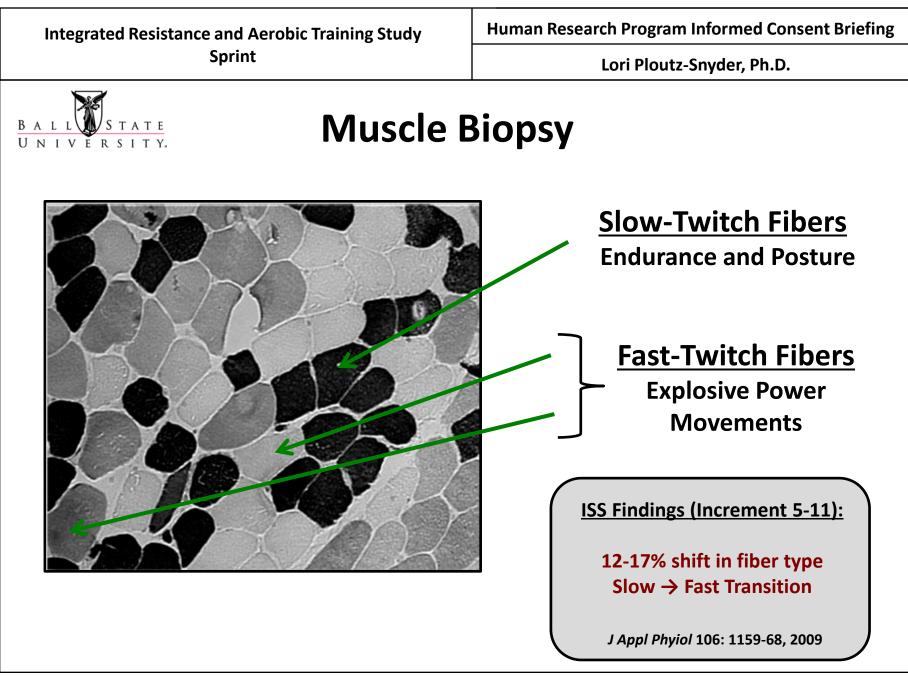
ntegrated Resistance and Aerobic Training Study	Human Research Program Informed Consent Brie Lori Ploutz-Snyder, Ph.D.		
Sprint			
Inflight Medical Requirements/Activities	Inflight Sprint		
 Periodic Fitness Evaluation (PFE): FD 14 and about every 30 days after (6 sessions/1.5 hrs per session) 9 hrs total 	 VO2max (replaces PFE): FD 14 and about every 30 days after (6 sessions/3.6 hrs per session) 21.5 hrs total 		
	 Muscle ultrasound: FD 14, 30 and about every 30 days after (7 sessions/1.75 hrs per session) 12.25 hrs total 		
Throughout mission:2.5 hrs per day of exercise training	Throughout mission:15-90 min per day of exercise training*		
Total testing time (PFE) = 9 hrs	Total testing time = 33.75 hr		

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* J Appl Phyiol 106: 1159-68, 2009 and ASEM 81: 91-102, 2010

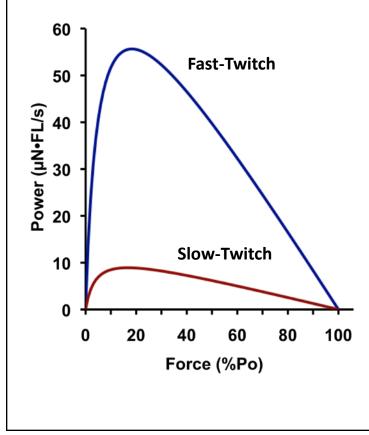


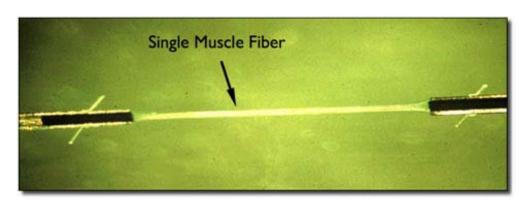
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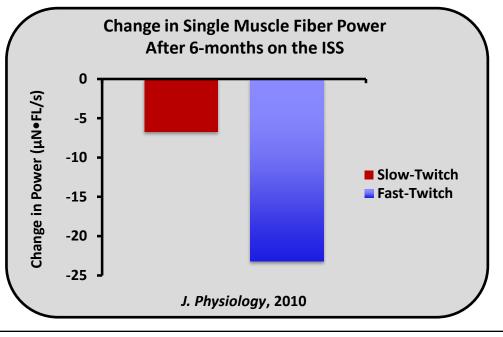


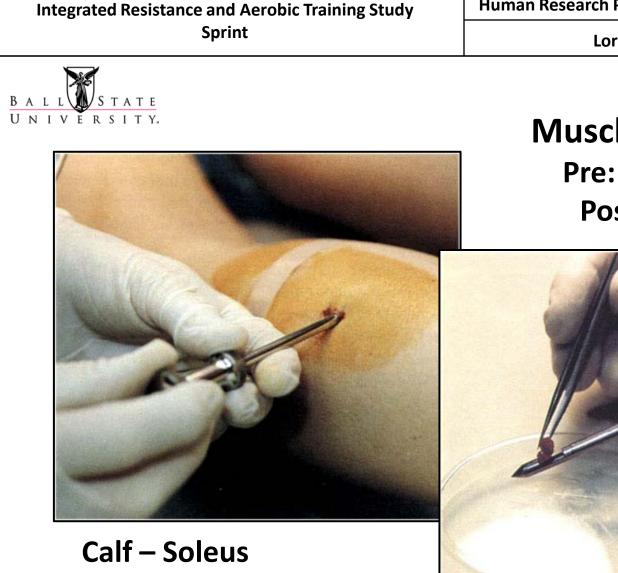
Muscle Biopsy











Thigh – Vastus Lateralis

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



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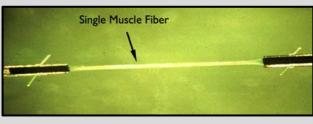
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Muscle Biopsy – Science

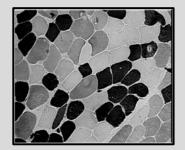
Function & Structure

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

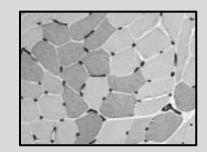
3. Aerobic and Anaerobic Enzymes



Muscle Biochemistry to determine metabolic profile which impacts energy transfer and metabolic health

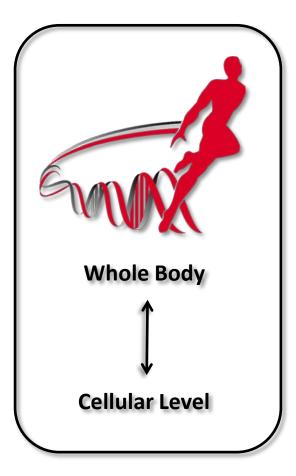
Mitochondria

4. Capillary Density



To determine capillary network which impacts blood flow, oxygen, and nutrition delivery

Muscle Biopsy – Science Application



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.



Recent ISS muscle publications: 1. Trappe et al. JAP 106: 1159-68, 2009 and 2. Fitts et al. J. Physiol. 2010.

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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)



R+0

biopsy in Star City



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