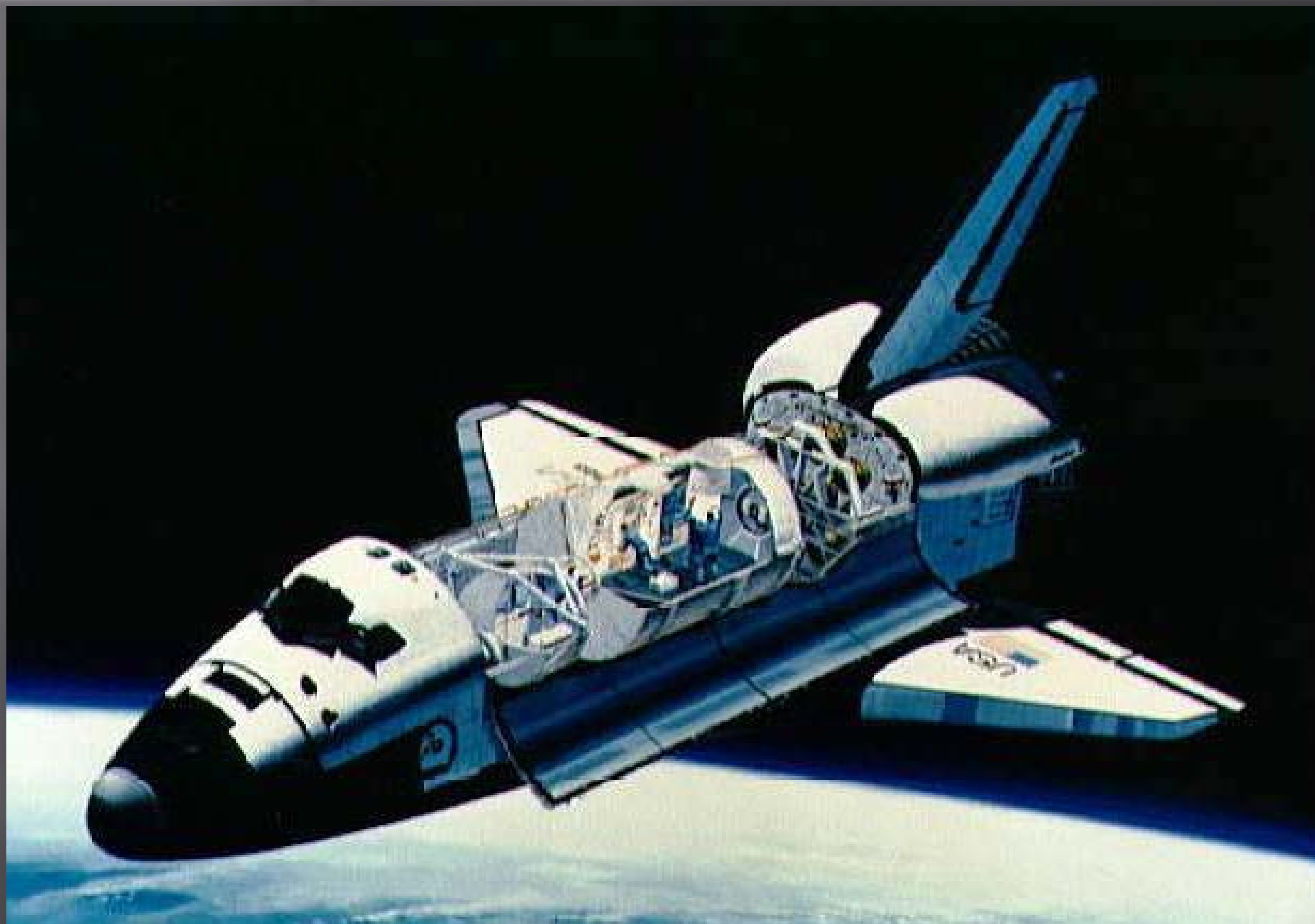
From the Bluegrass to Beyond the Blue

A Curiosity-Driven Career in Applied Spaceflight Biomedical Research

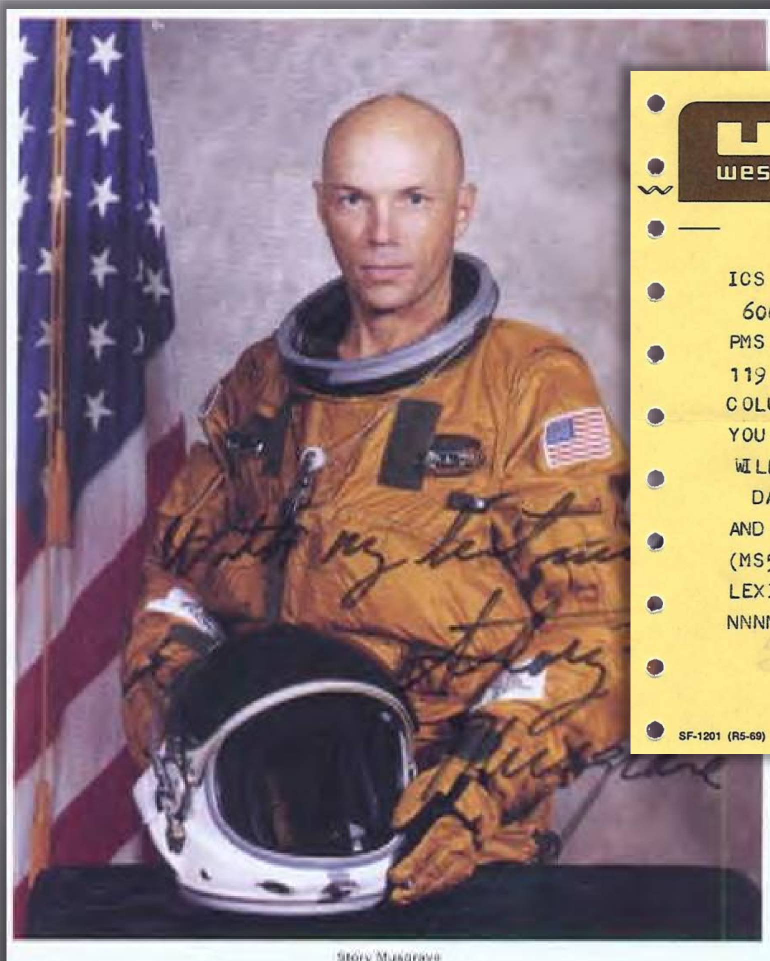
John B. Charles, Ph.D.
Gill Heart Lecture
Lexington KY
November 3, 2017

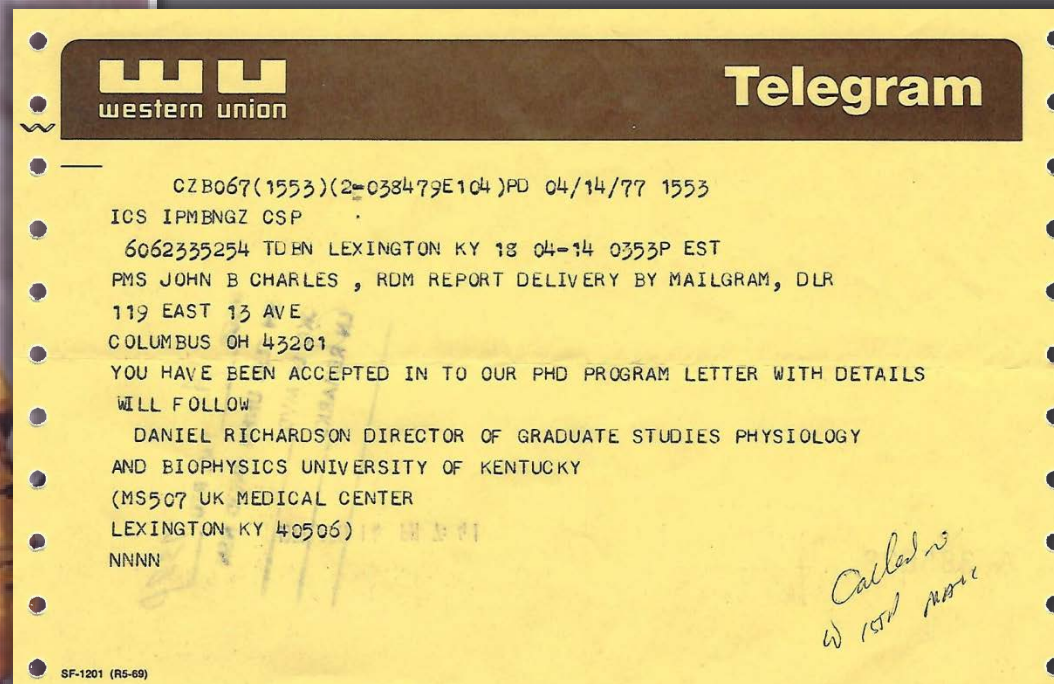
International Space Station (1999-2024)

Space Shuttle (1981-2011)
Spacelab (1983-1998)

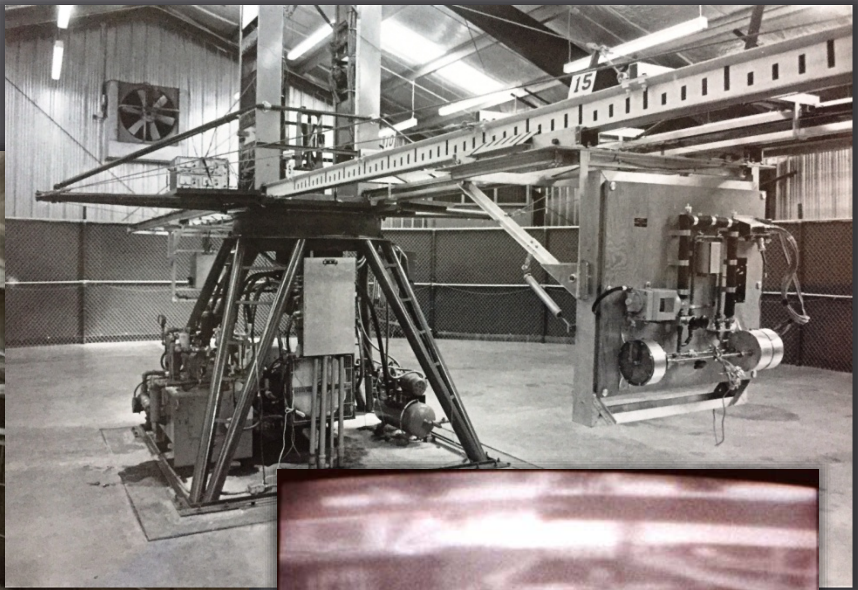


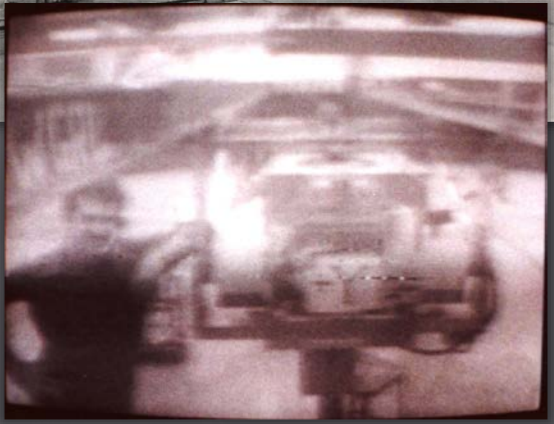
UKMC: launch pad to NASA





Wenner Gren Research Lab 1977-1983



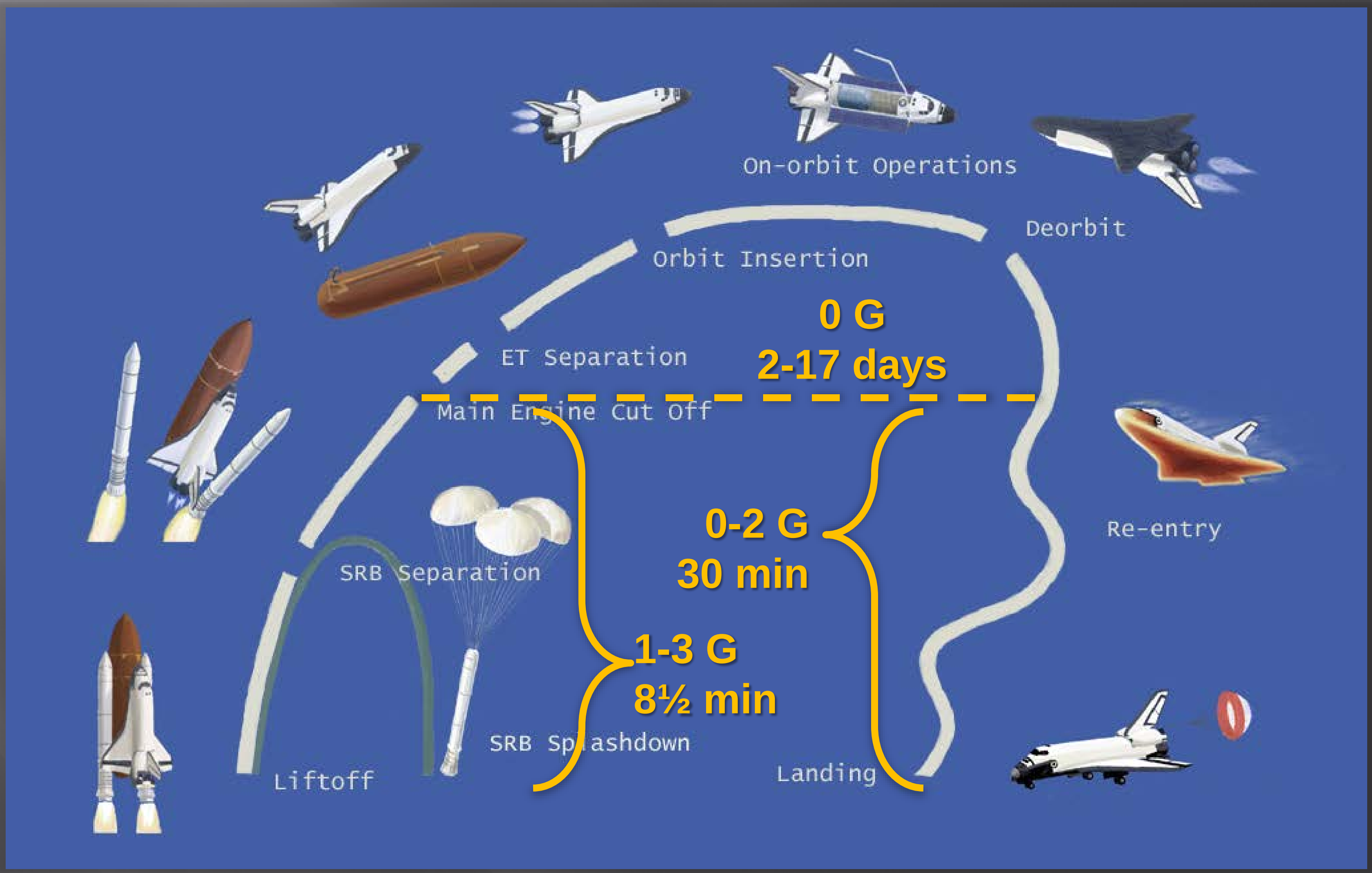


Cardiovascular Responses of Untrained and Endurance-Trained Dogs to Oscillatory Blood Volume Shifts (funded by AFOSR)

Wenner Gren Research Lab 1977-1983

To NASA Johnson Space Center in Houston to do cardiovascular research as NRC Postdoctoral Fellow (1983-1985) and a Civil Service scientist (since 1985)

Space Shuttle (1981-2011)



Recent events in 1983

STS-6
APRIL 4-9, 1983

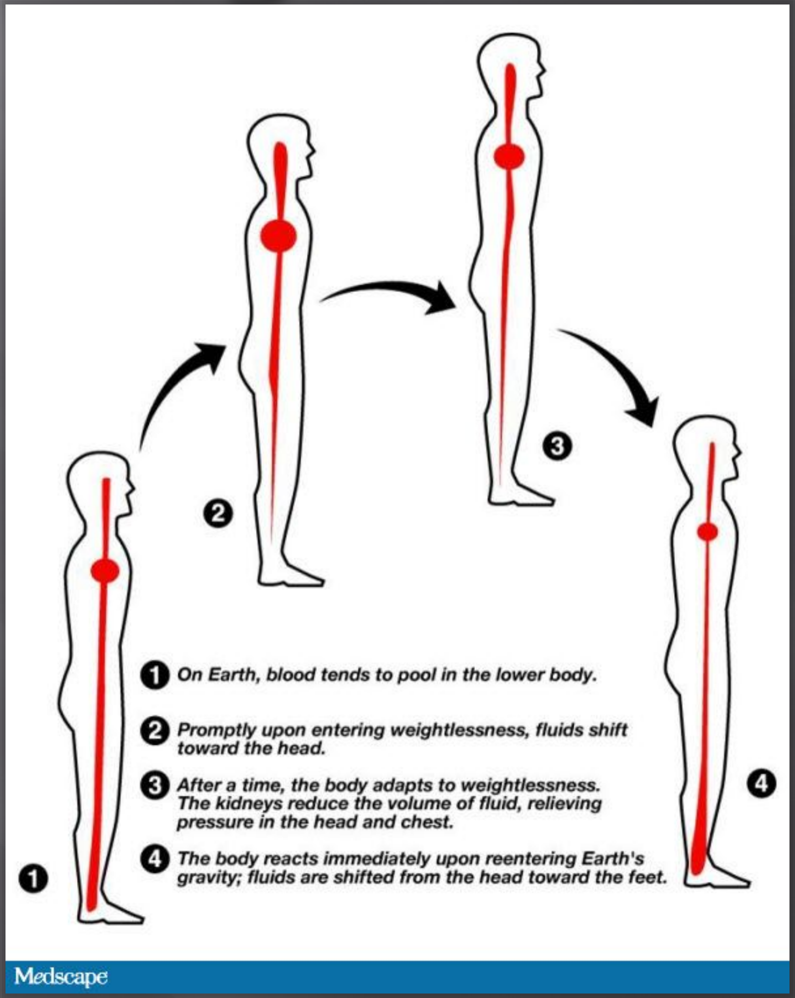
APRIL 4, 1:30 PM EST

Current events in 1983

STS-7
JUNE 18-24

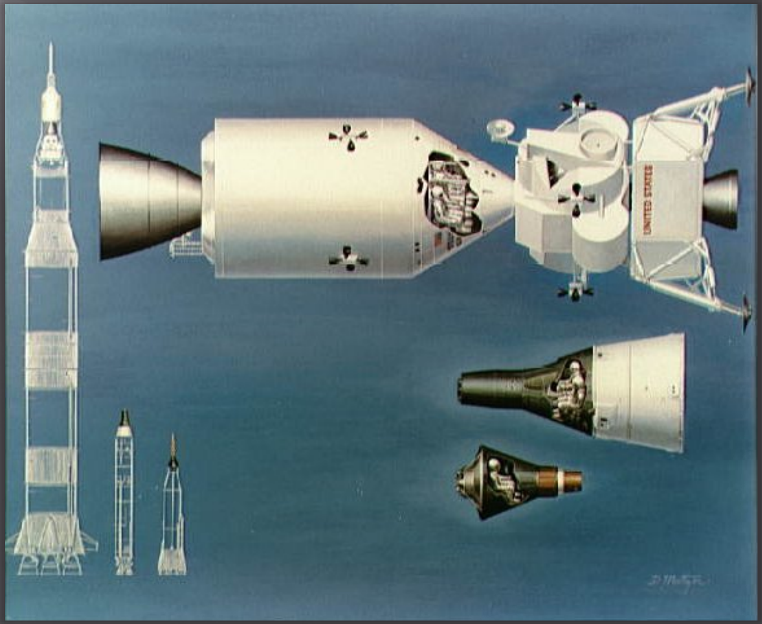
STS-8
AUG. 30 - SEP. 5

Cardiovascular response to weightlessness



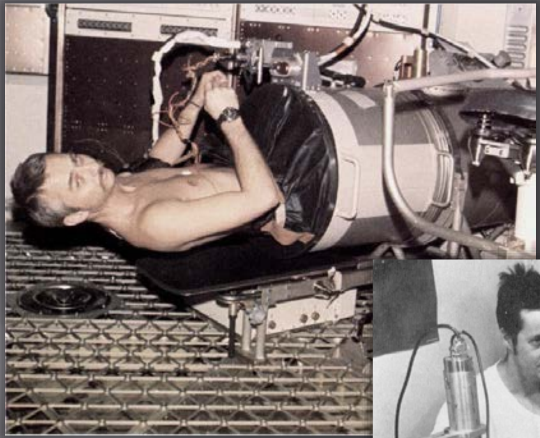
What was known about cardiovascular function during and after spaceflight?

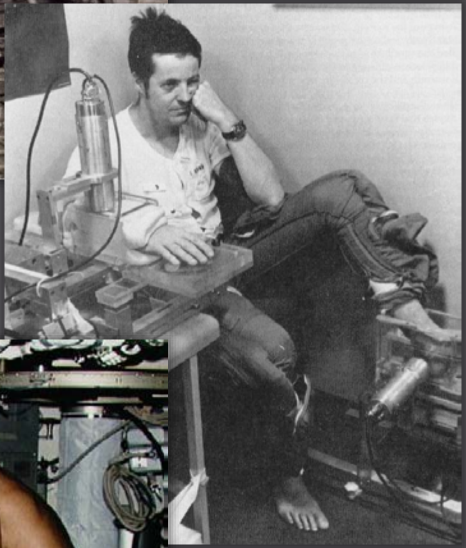
- Mercury: 6 flights, 6 men, 15 minutes-34 hours
  - Demonstrated basic survivability, functionality
- Gemini: 10 flights, 16 men (4 twice), 5 hours-14 days
  - Demonstrated operational proficiency, recovery in preparation for Apollo
    - Moderate post flight orthostatic intolerance
    - Moderate post flight loss of exercise capacity
    - Moderate RBC mass loss
- Apollo: 12 flights (9 lunar), 31 men (5 twice), 6-13 days
  - Demonstrated operational proficiency, recovery in implementing Apollo
    - Decreased postflight orthostatic tolerance
    - Post flight dehydration, weight loss
    - Reduced post flight exercise tolerance
    - Apollo 15 cardiac arrhythmia
    - Decreased RBC mass, plasma volume



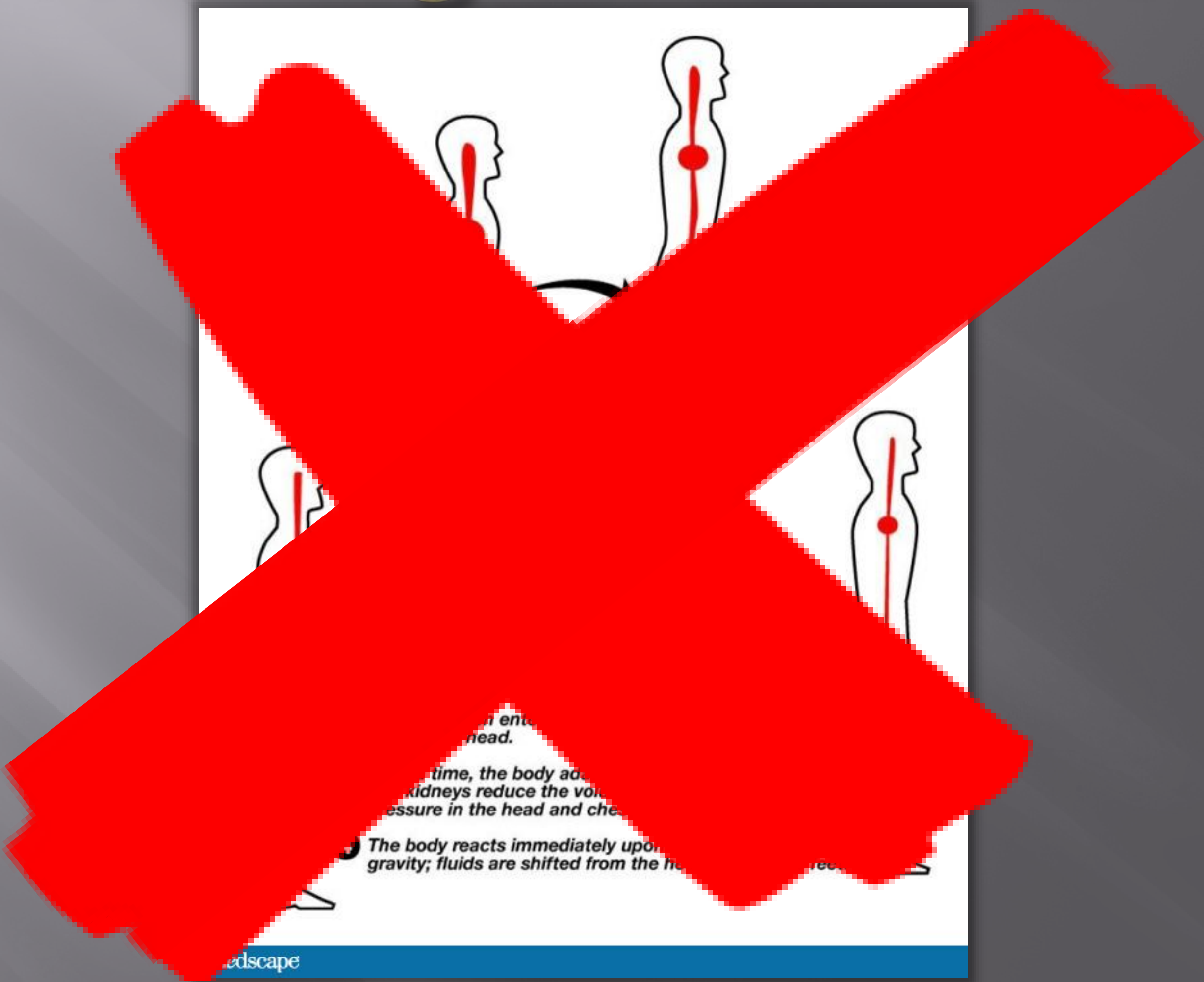
What was known about cardiovascular function during and after spaceflight?

- CVD during flight appeared adaptive, stabilized after 4-6 weeks, did not impair health or performance
- LBNP reliably predicted post flight CV status, recovery associated with amount of personal exercise
- No significant inflight decrement in work capacity, physiological responses to exercise
- Cardiac electrical activity by VCG not significantly altered, WNL
  - Single episode of significant arrhythmia during exercise in one crewman early in flight
- Decreased CO post flight, due to reduced venous return

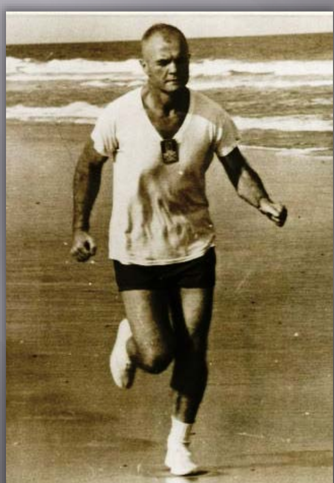




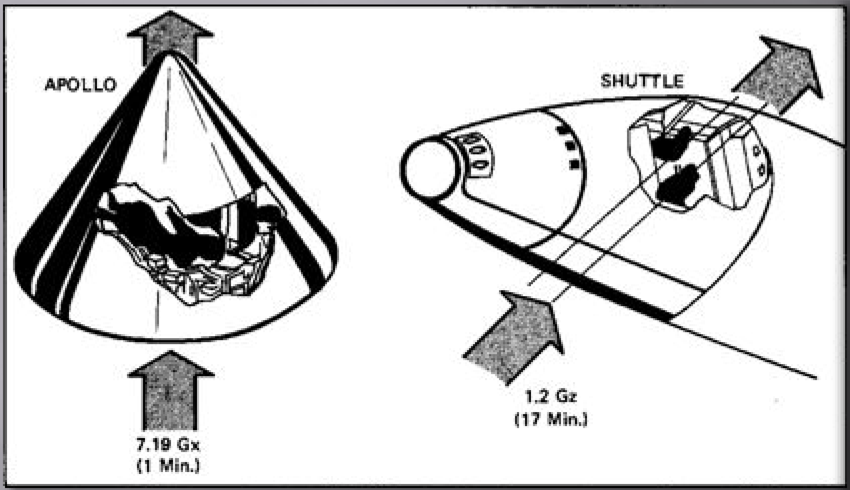
Cardiovascular response to weightlessness

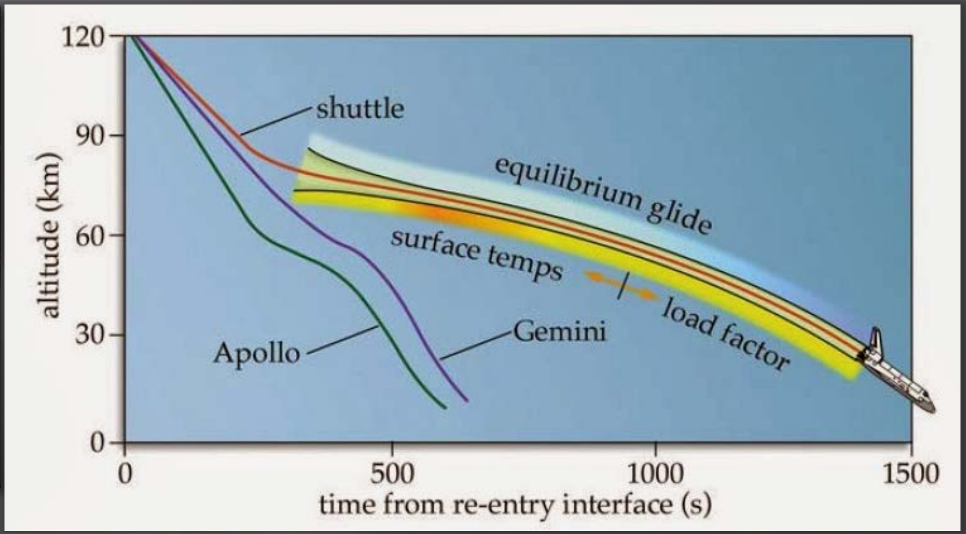


What really happens



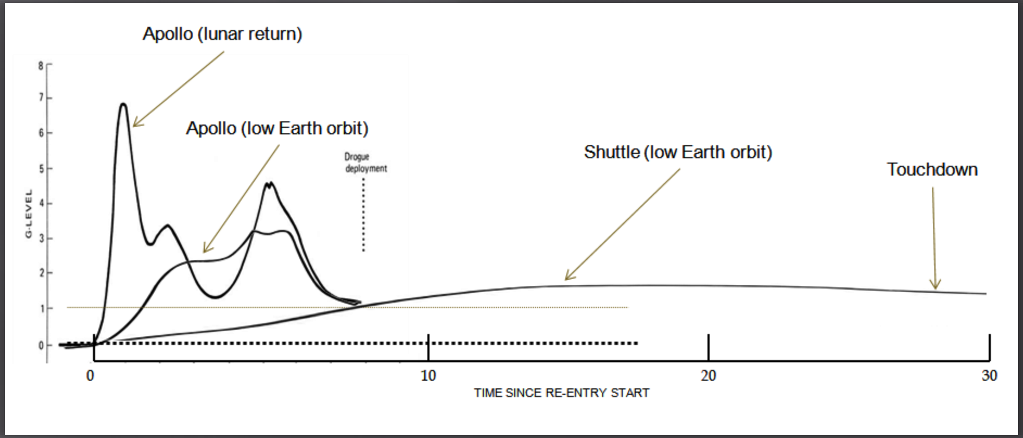
Cardiovascular implications of Space Shuttle Orbiter re-entry





+Gx

+Gz



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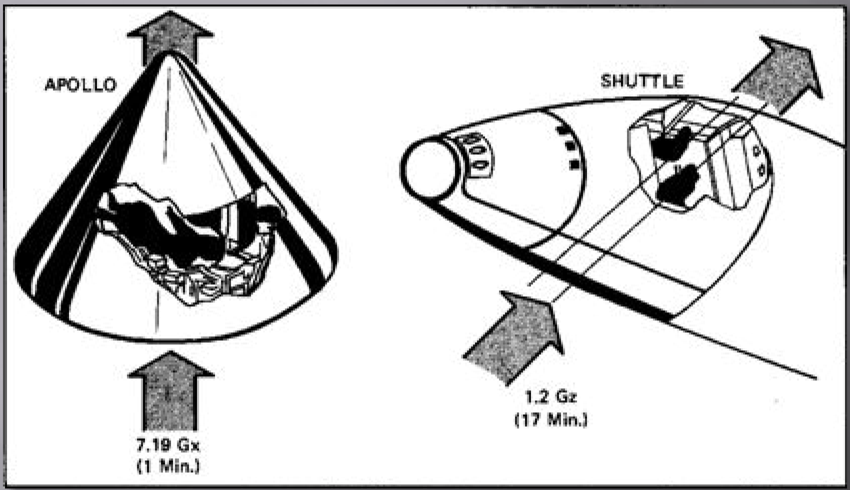
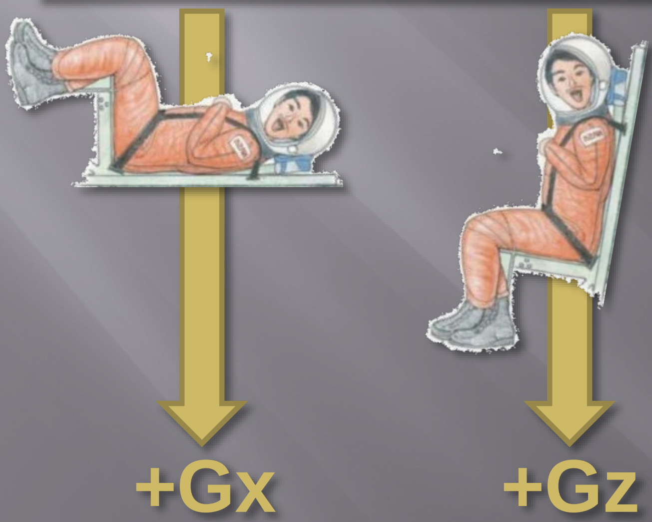


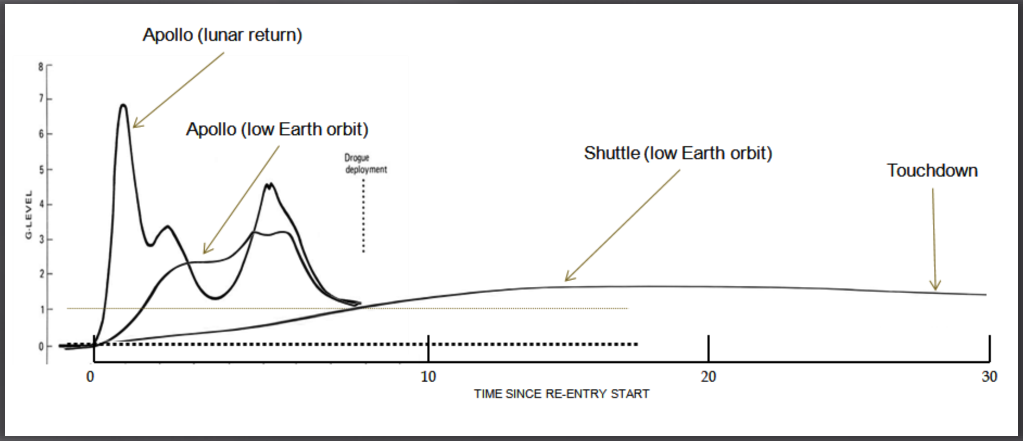
Increased risk of orthostatic intolerance

- Seated upright—parallel to G direction
- G load lower but lasted longer

Implication

- Fainting (GLOC) during piloting and landing
- Inability to execute emergency egress after landing





The incidence of post-spaceflight orthostatic hypotension

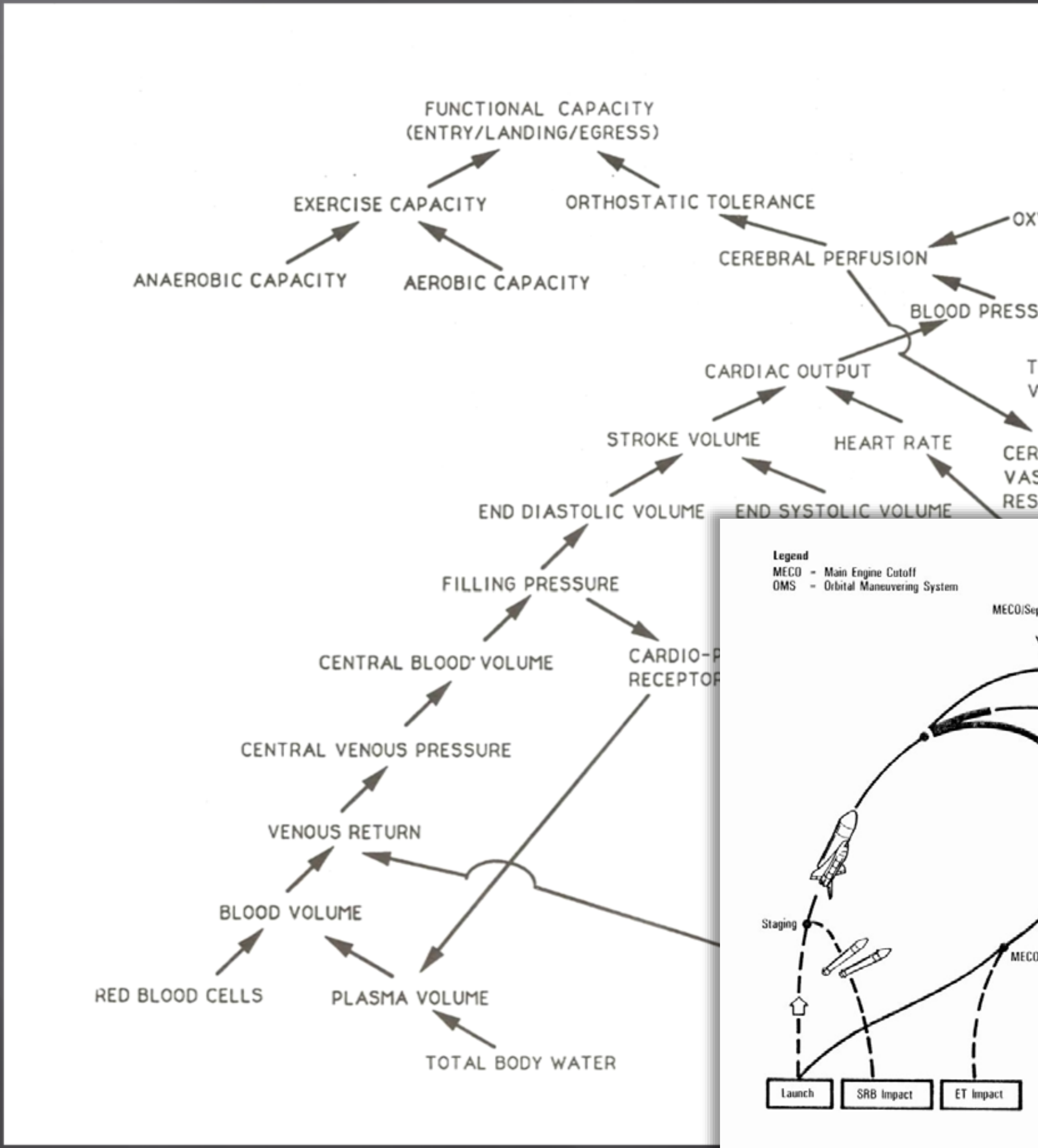
		Pre-Challenger	Post-Challenger
Pre-egress	% missions	25%	54%
	% crewpersons	6%	13%
In clinic	% missions	13%	39%
	% crewpersons	3%	10%
Number of missions		24	13
Average mission duration		6	5.5

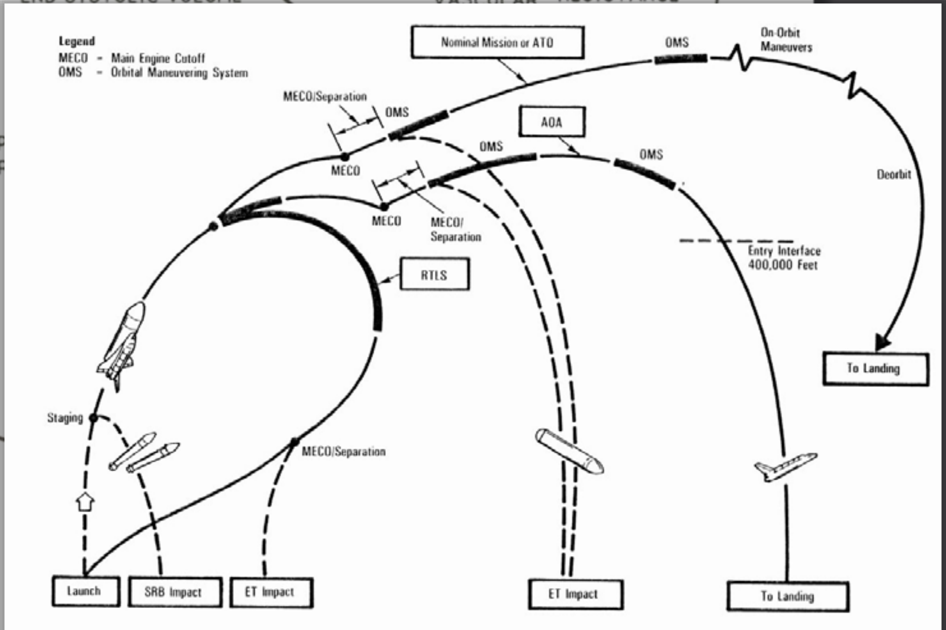
What changed after Challenger?

STS-4 ➔ 51-L (25)

STS-26 ➔ 135

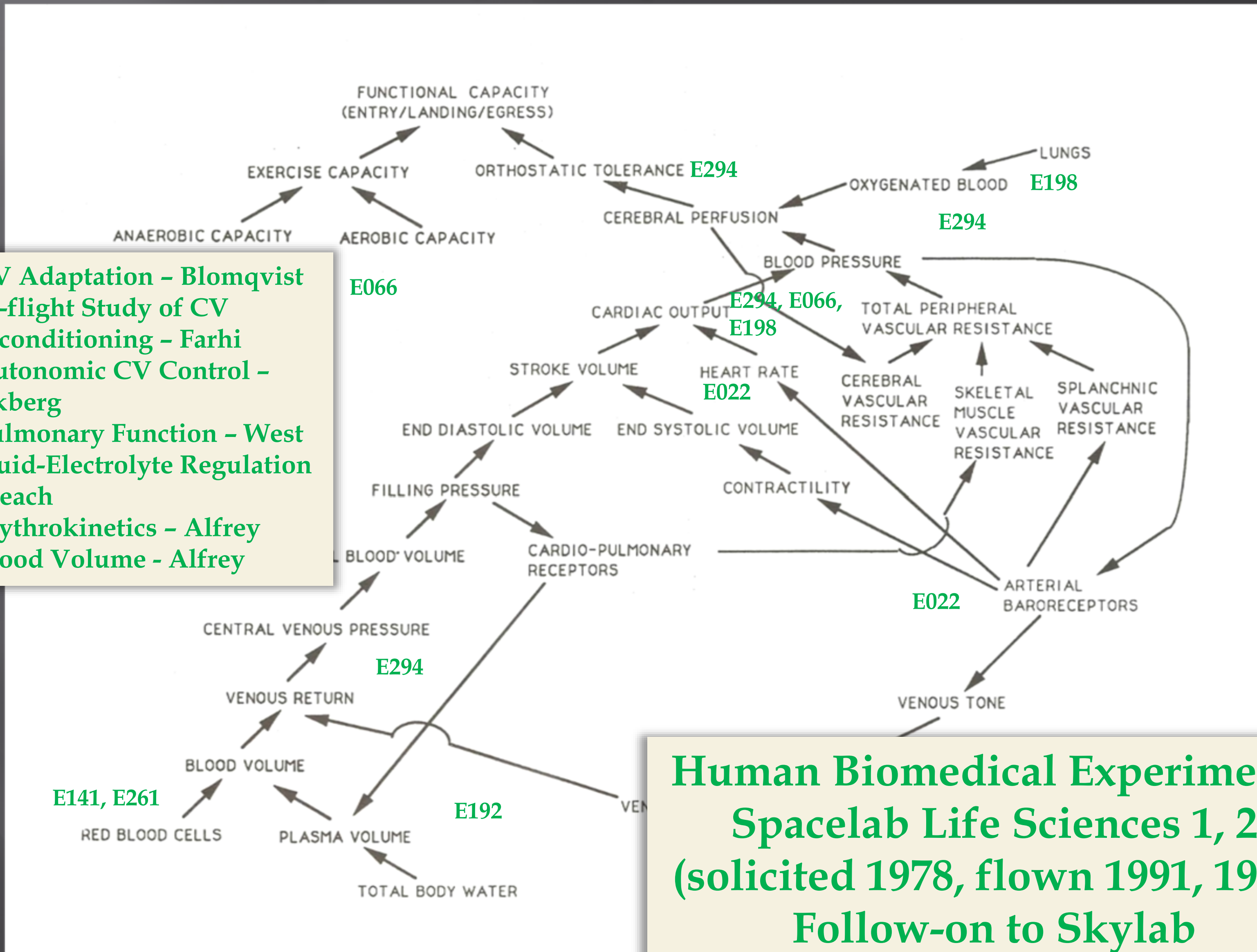
Factors influencing cardiovascular support of functional capacity in Space Shuttle astronauts





Abort and Normal Mission Profile

Factors influencing cardiovascular support of functional capacity in Space Shuttle astronauts



E294, CV Adaptation – Blomqvist
E066, In-flight Study of CV Deconditioning – Farhi
E022, Autonomic CV Control – Eckberg
E198, Pulmonary Function – West
E192, Fluid-Electrolyte Regulation – Leach
E261, Erythrokinetics – Alfrey
E141, Blood Volume - Alfrey

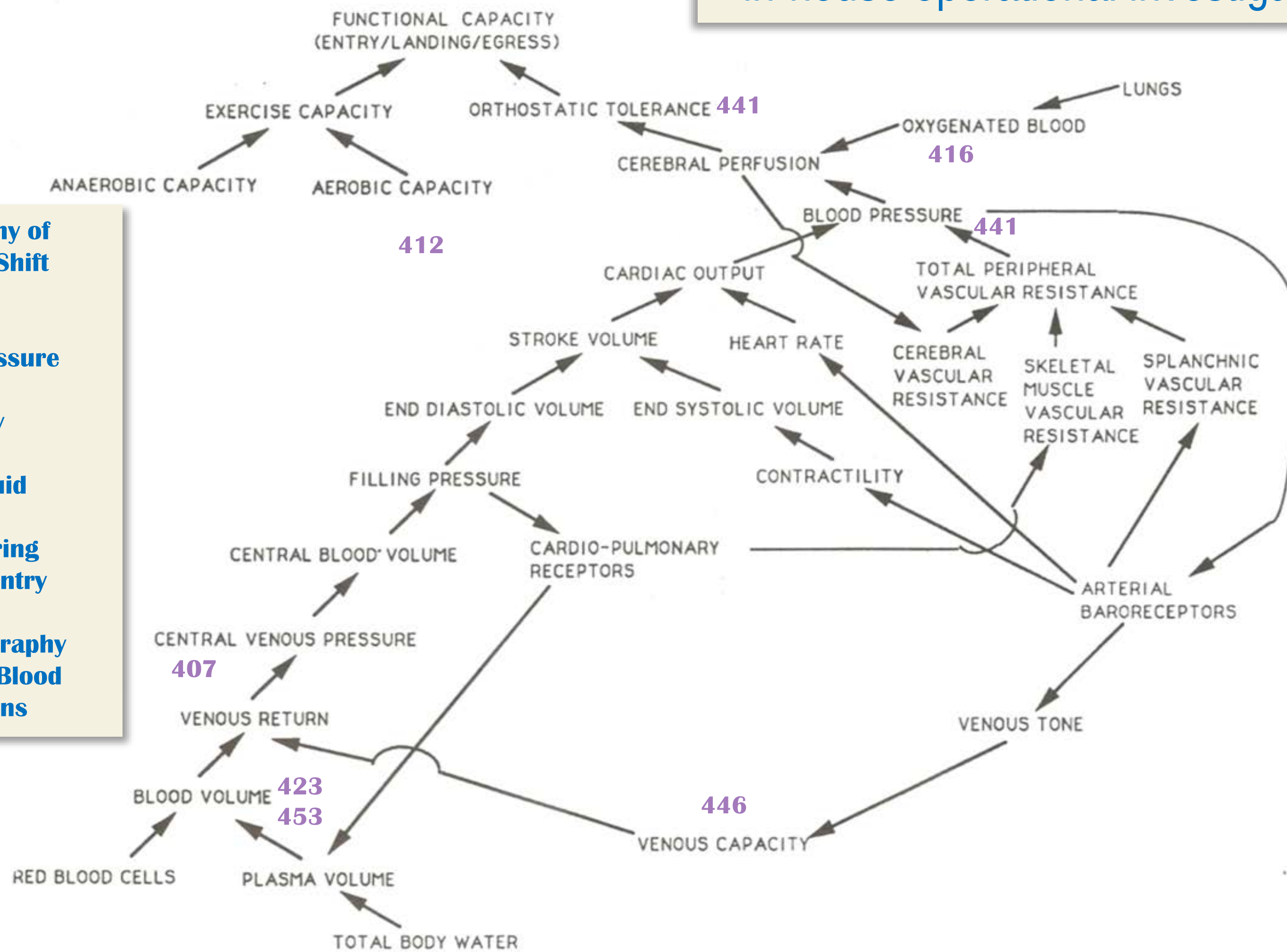
Human Biomedical Experiments
Spacelab Life Sciences 1, 2
(solicited 1978, flown 1991, 1993)
Follow-on to Skylab

Factors influencing cardiovascular support of functional capacity in Space Shuttle astronauts

Factors influencing cardiovascular support of functional capacity in Sp… …ts

Thornton DSOs (1982-1986)
(Detailed Supplementary Objectives - in-house operational investigations)

- **407, Photography of Body Fluid Shift**
- **412, Treadmill Operation**
- **415, Tissue Pressure Tonometry**
- **416, Ambulatory Monitoring**
- **423, In-flight Fluid Changes**
- **441, BP Monitoring during Re-entry**
- **446, Leg Plethysmography**
- **453, Combined Blood Investigations**



Factors influencing cardiovascular support of functional capacity in Sp... ...ts

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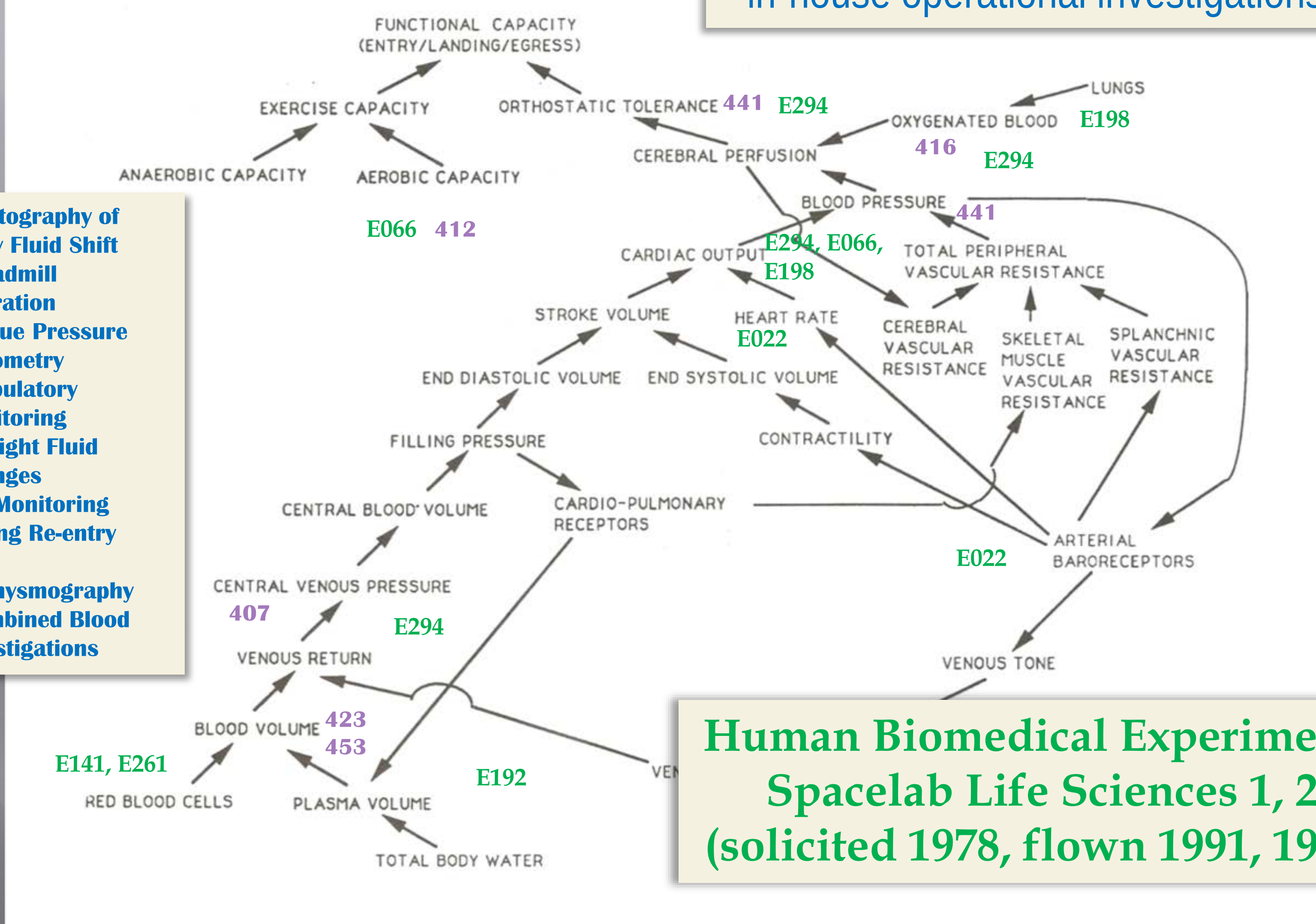

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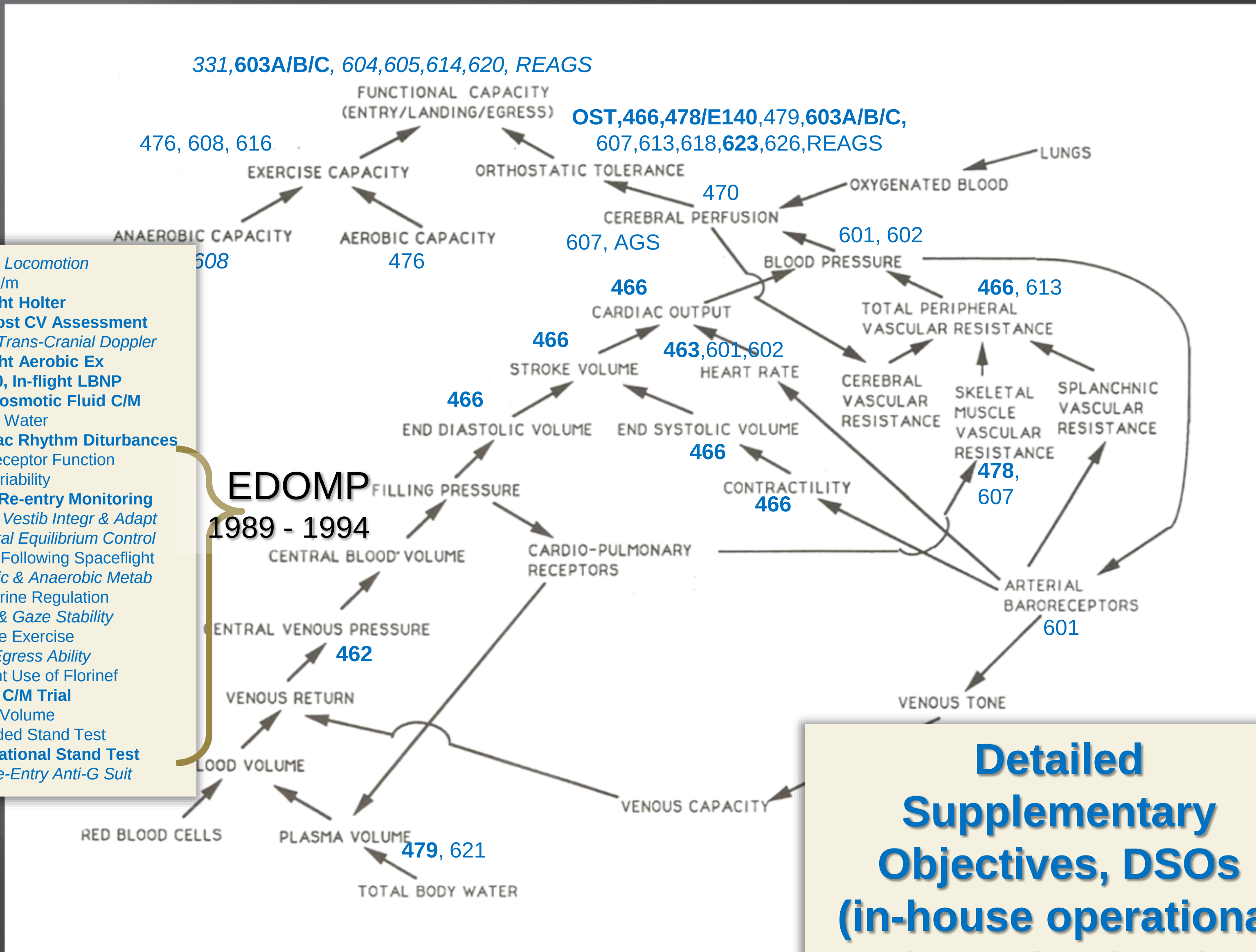
Human Biomedical Experiments Spacelab Life Sciences 1, 2 (solicited 1978, flown 1991, 1993)

Extended Duration Orbiter Medical Project (1989-1995)

- Extended Duration Orbiter Project
  - 1988: Congress allocated $125M to extend STS from ~10 days maximum up to 16 days, potentially up to 30 days
  - 1992-2003: 14 EDO flights, 14-18 days
- Concerns
  - Astronaut Office
    - Unaided egress
    - Manual landing proficiency
  - Space Life Sciences
    - Cardiovascular (orthostatic intolerance)
    - Neuromuscular (input/output offset using hand controllers; post flight disequilibrium)
    - Neurosensory (vertigo)
    - Musculoskeletal (exercise capacity re: unassisted ambulation in 34-kg LES)
- Extended Duration Orbiter Medical Project
  - Dec. 1989-Sep. 1995: $40M
  - NASA civil service lead scientists, academic participants
  - Implementation via Detailed Supplementary Objectives (DSO)

Factors influencing cardiovascular support of functional capacity in Space Shuttle astronauts

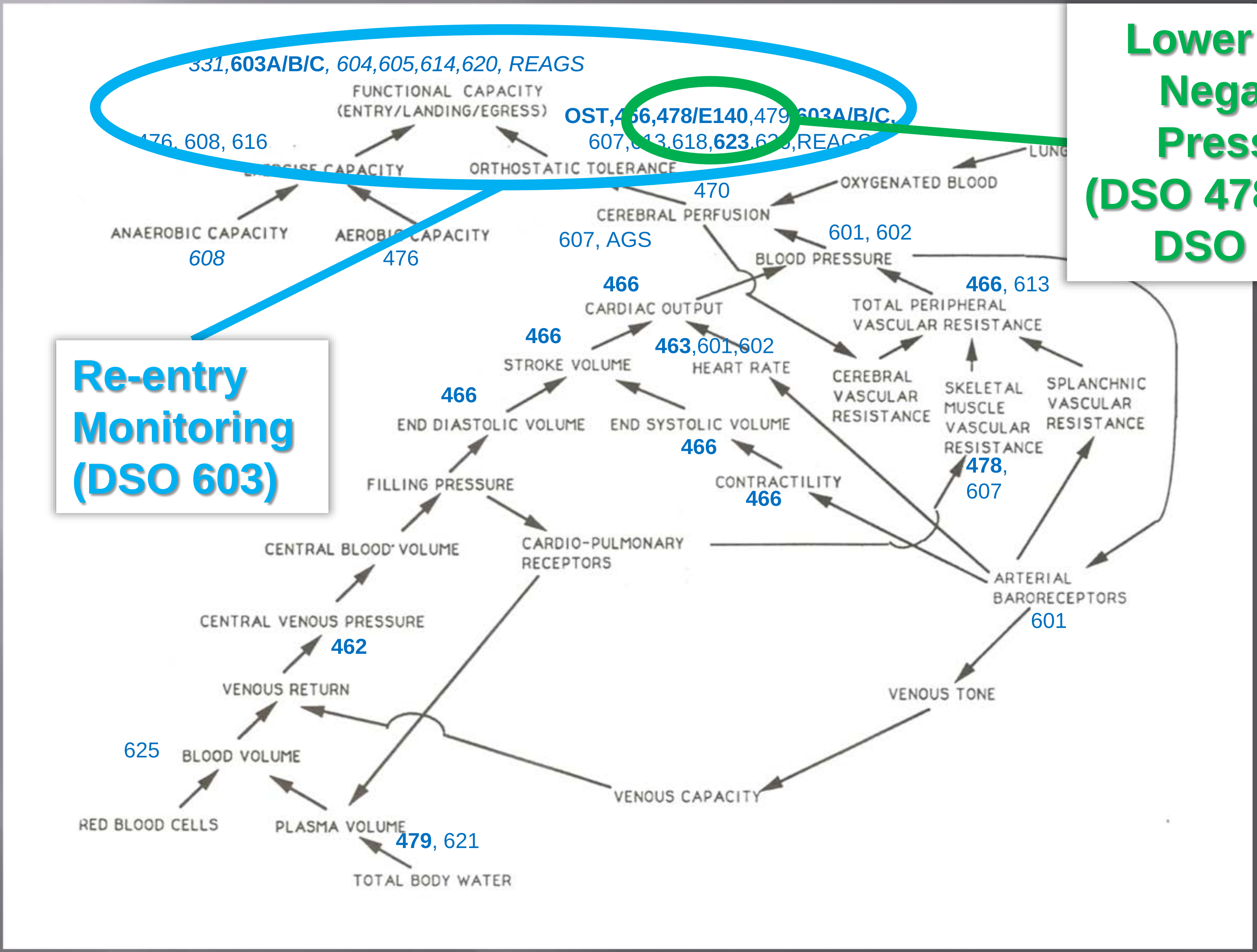


331, LES & Locomotion
402, CVD c/m
463, In-flight Holter
466, Pre/Post CV Assessment
470, TCD, Trans-Cranial Doppler
476, In-flight Aerobic Ex
478 & E140, In-flight LBNP
479, Hyperosmotic Fluid C/M
480, Heavy Water
482, Cardiac Rhythm Diturbances
601, Baroreceptor Function
602, BP Variability
603A/B/C, Re-entry Monitoring
604, Visual Vestib Integr & Adapt
605, Postural Equilibrium Control
607, LBNP Following Spaceflight
608, Aerobic & Anaerobic Metab
613, Endocrine Regulation
614, Head & Gaze Stability
618, Intense Exercise
620, Seat Egress Ability
621, In-flight Use of Florinef
623, LBNP C/M Trial
625, Blood Volume
626, Extended Stand Test
OST, Operational Stand Test
REAGS, Re-Entry Anti-G Suit

EDOMP
1989 - 1994

Detailed Supplementary Objectives, DSOs (in-house operational investigations)

Factors influencing cardiovascular support of functional capacity in Space Shuttle astronauts



Lower Body Negative Pressure (DSO 478, E140, DSO 623)

Re-entry Monitoring (DSO 603)

Orthostatic Function during Entry, Landing and Egress

Heart Rate, Blood Pressure, G-level and Posture Before, During and After Entry, Descent, Landing and Egress

DSO 603 re-entry monitoring

Heart rate during re-entry and postflight orthostasis and ambulation

Military Spaceflight

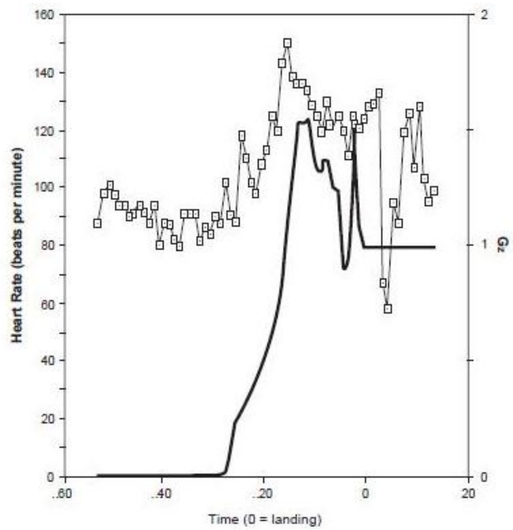
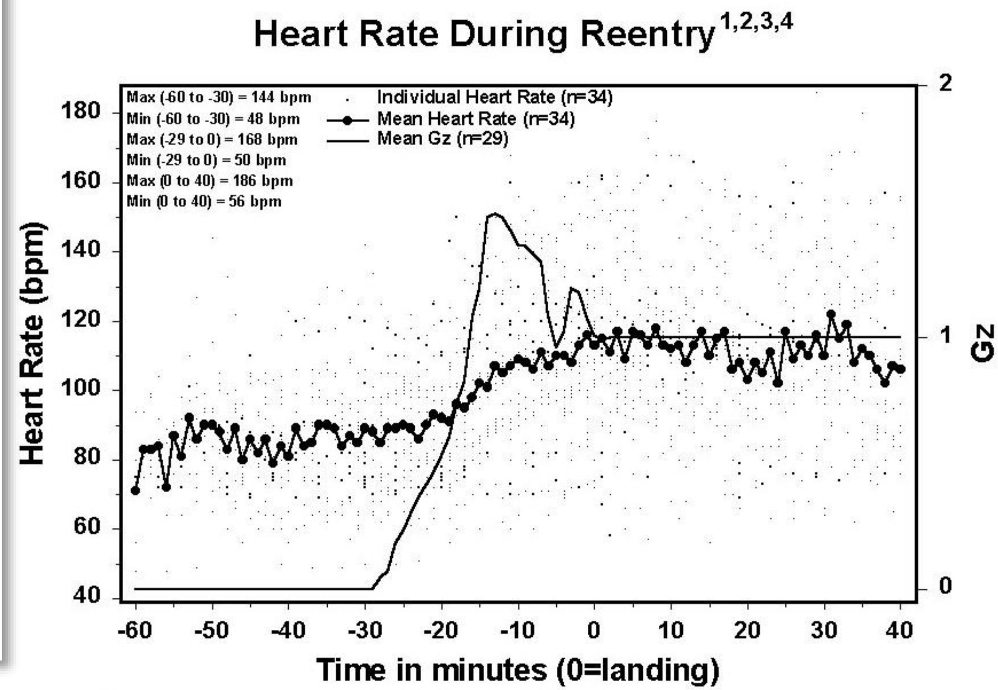


Fig. 34-7. An astronaut's heart rate (—□—), measured via continuous electrocardiographic recording, and acceleration (Gz; ▬▬) are shown for a typical Shuttle re-entry period. A significant tachycardia is observed. Vasovagal episodes occurred just before, and more prominently, just after landing (time 0 = landing). Re-entry is characterized by hypovolemia, depressed baroreflexes, vestibular disturbances, and a significant heat load associated with both the launch-and-entry suits and a warm (35°C–36°C) cabin temperature. Reproduced with permission from Buckey JC Jr, Lane LD, Levine BD, et al. Orthostatic intolerance after space flight. *J Appl Physiol*. 1996;81:16.

NASA Life Sciences Data Archive (http://lsda.jsc.nasa.gov)
Investigators Names: John B. Charles, Michael Bungo, Jay Buckey
Mission (Payload): Shuttle Program
File Name/Inventory ID: meanreentry.jpg



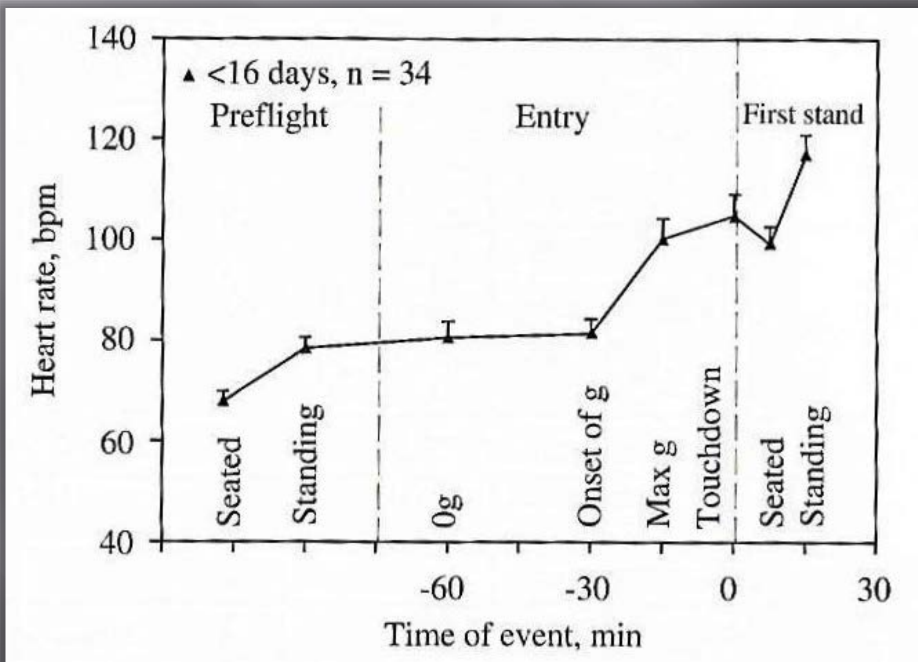
[1] Compiled from data in the Life Sciences Data Archive. Some of these data published in:
Buckey JC, et. al., 1996. J. Appl. Physiol. Vol. 81 (1);
Charles JB, et. al., 1999. NASA SP-534;
Bungo, MW. NASA TM-58240 and TM-58252.

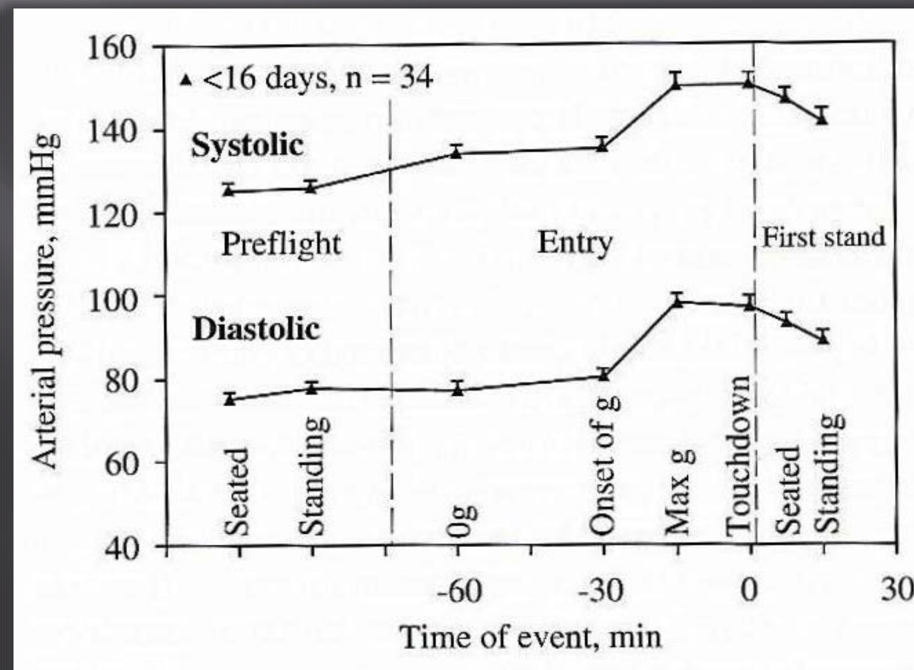
[2] Life Sciences Data Archive does not independently verify results.

[3] Each data point represents an average over a mininum of one minute.

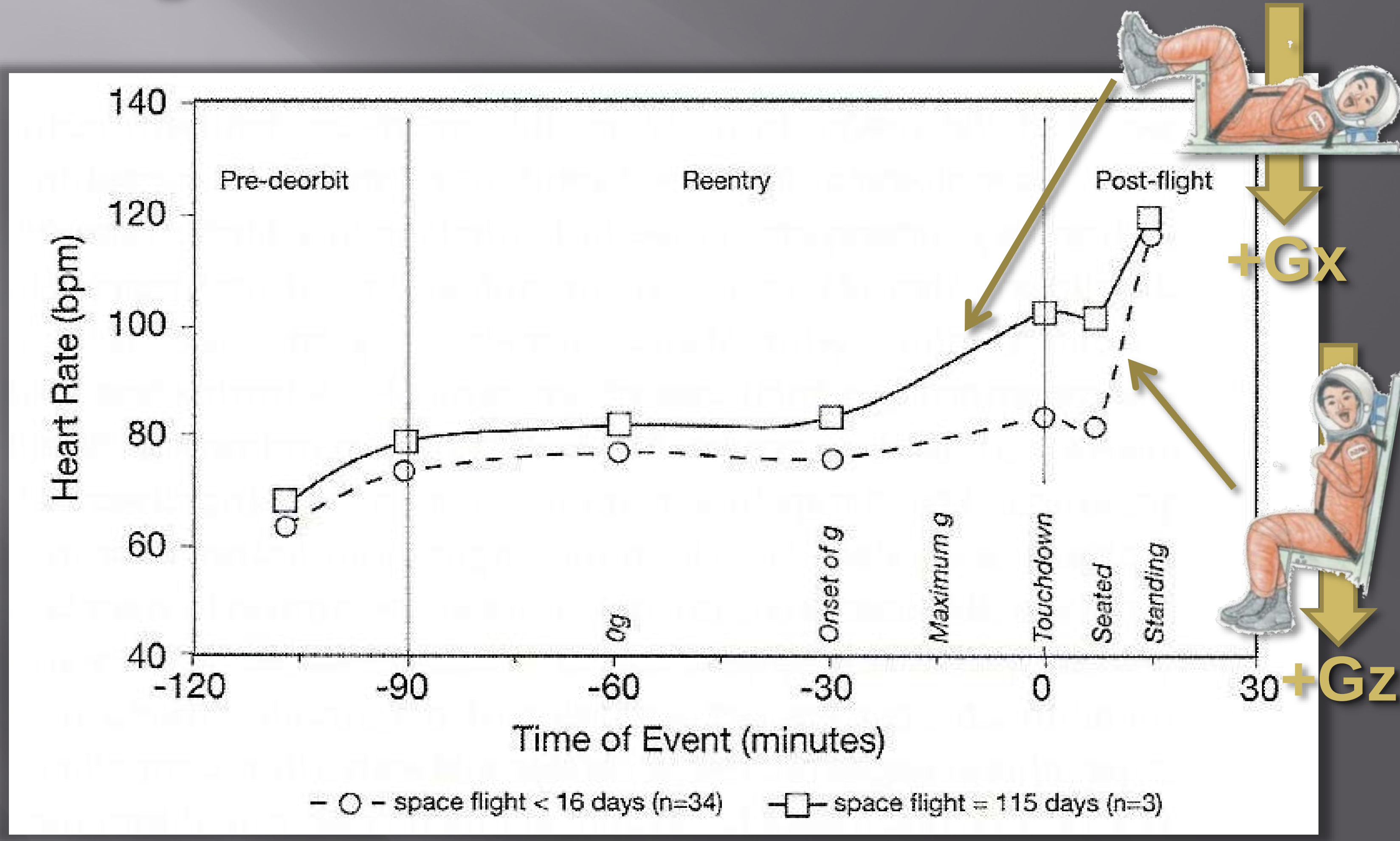
[4] Post-landing heart rates include the middeck stand test if performed.

Heart rate during re-entry and postflight orthostasis and ambulation





Heart rate during re-entry and postflight orthostasis and ambulation



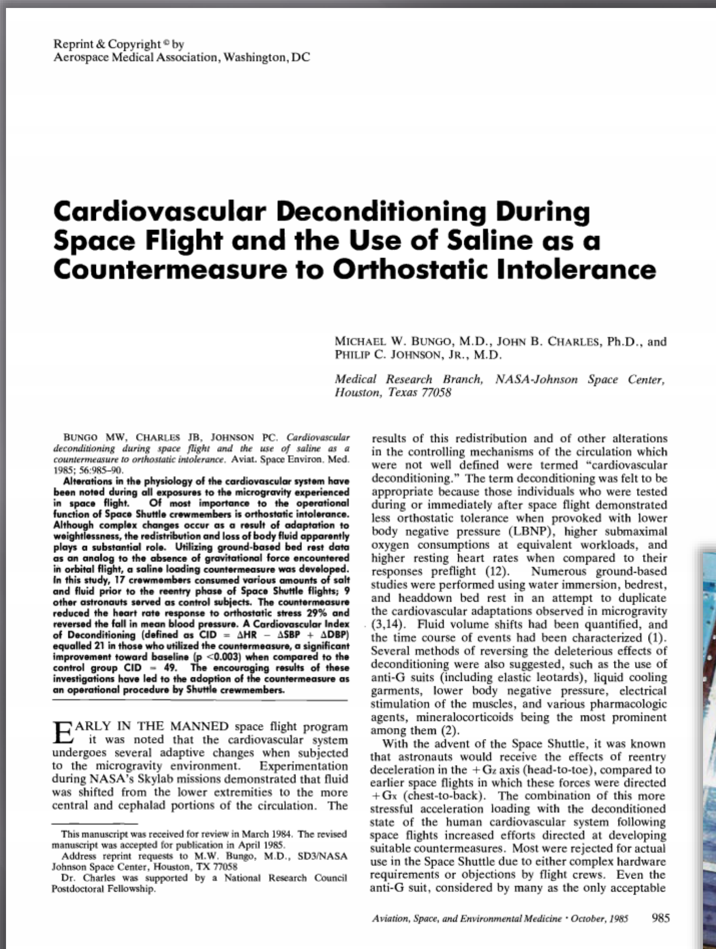
Combined Countermeasure

Oral Fluid Loading during Lower Body Negative Pressure

Background

- Need for effective OI countermeasures due to upright piloted landings of Space Shuttle
- "Combined countermeasure" 4-hr LBNP + oral saline fluid loading more effective than fluid loading alone (Hyatt *et al.*, 1977)
  - 2-hr treatment shown <u>not</u> effective
- LBNP + fluid loading selected as Spacelab study (Johnson, 1978), in-flight medical investigation (Charles, 1989)
- NASA adopted fluid loading alone at end of mission as interim OI countermeasure for Shuttle crews (1984)

Countermeasure for decreased plasma volume: oral rehydration



Cardiovascular Deconditioning During Space Flight and the Use of Saline as a Countermeasure to Orthostatic Intolerance

MICHAEL W. BUNGO, M.D., JOHN B. CHARLES, Ph.D., and PHILIP C. JOHNSON, JR., M.D.

Medical Research Branch, NASA-Johnson Space Center, Houston, Texas 77058

BUNGO MW, CHARLES JB, JOHNSON PC. *Cardiovascular deconditioning during space flight and the use of saline as a countermeasure to orthostatic intolerance.* Aviat. Space Environ. Med. 1985; 56:985–90.

Alterations in the physiology of the cardiovascular system have been noted during all exposures to the microgravity experienced in space flight. Of most importance to the operational function of Space Shuttle crewmembers is orthostatic intolerance. Although complex changes occur as a result of adaptation to weightlessness, the redistribution and loss of body fluid apparently plays a substantial role. Utilizing ground-based bed rest data as an analog to the absence of gravitational force encountered in orbital flight, a saline loading countermeasure was developed. In this study, 17 crewmembers consumed various amounts of salt and fluid prior to the reentry phase of Space Shuttle flights; 9 other astronauts served as control subjects. The countermeasure reduced the heart rate response to orthostatic stress 29% and reversed the fall in mean blood pressure. A Cardiovascular Index of Deconditioning (defined as CID = ΔHR − ΔSBP + ΔDBP) equalled 21 in those who utilized the countermeasure, a significant improvement toward baseline (p <0.003) when compared to the control group CID = 49. The encouraging results of these investigations have led to the adoption of the countermeasure as an operational procedure by Shuttle crewmembers.

EARLY IN THE MANNED space flight program it was noted that the cardiovascular system undergoes several adaptive changes when subjected to the microgravity environment. Experimentation during NASA's Skylab missions demonstrated that fluid was shifted from the lower extremities to the more central and cephalad portions of the circulation. The results of this redistribution and of other alterations in the controlling mechanisms of the circulation which were not well defined were termed "cardiovascular deconditioning." The term deconditioning was felt to be appropriate because those individuals who were tested during or immediately after space flight demonstrated less orthostatic tolerance when provoked with lower body negative pressure (LBNP), higher submaximal oxygen consumptions at equivalent workloads, and higher resting heart rates when compared to their responses preflight (12). Numerous ground-based studies were performed using water immersion, bedrest, and headdown bed rest in an attempt to duplicate the cardiovascular adaptations observed in microgravity (3,14). Fluid volume shifts had been quantified, and the time course of events had been characterized (1). Several methods of reversing the deleterious effects of deconditioning were also suggested, such as the use of anti-G suits (including elastic leotards), liquid cooling garments, lower body negative pressure, electrical stimulation of the muscles, and various pharmacologic agents, mineralocorticoids being the most prominent among them (2).

With the advent of the Space Shuttle, it was known that astronauts would receive the effects of reentry deceleration in the $+G_z$ axis (head-to-toe), compared to earlier space flights in which these forces were directed $+G_x$ (chest-to-back). The combination of this more stressful acceleration loading with the deconditioned state of the human cardiovascular system following space flights increased efforts directed at developing suitable countermeasures. Most were rejected for actual use in the Space Shuttle due to either complex hardware requirements or objections by flight crews. Even the anti-G suit, considered by many as the only acceptable

This manuscript was received for review in March 1984. The revised manuscript was accepted for publication in April 1985.

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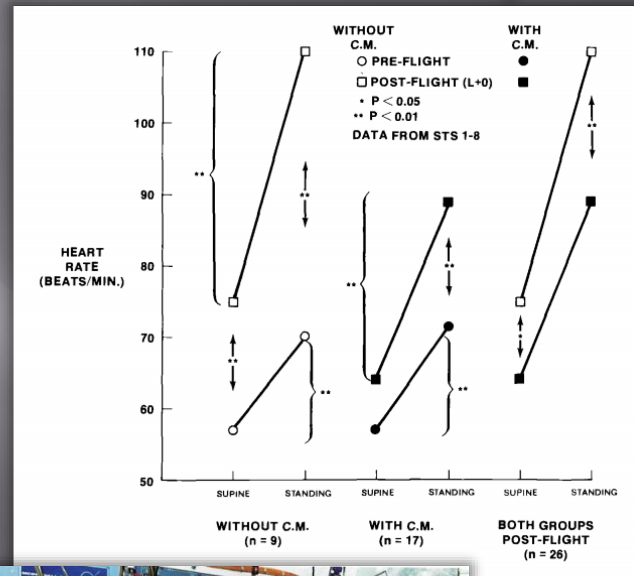
Dr. Charles was supported by a National Research Council Postdoctoral Fellowship.



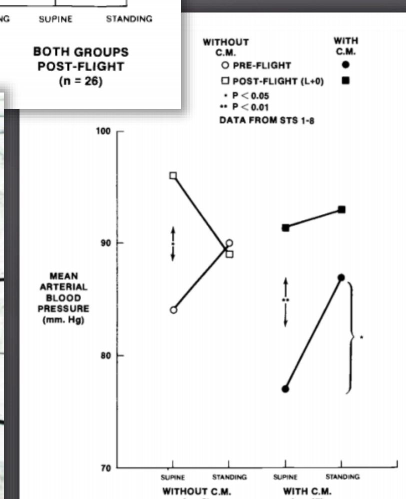
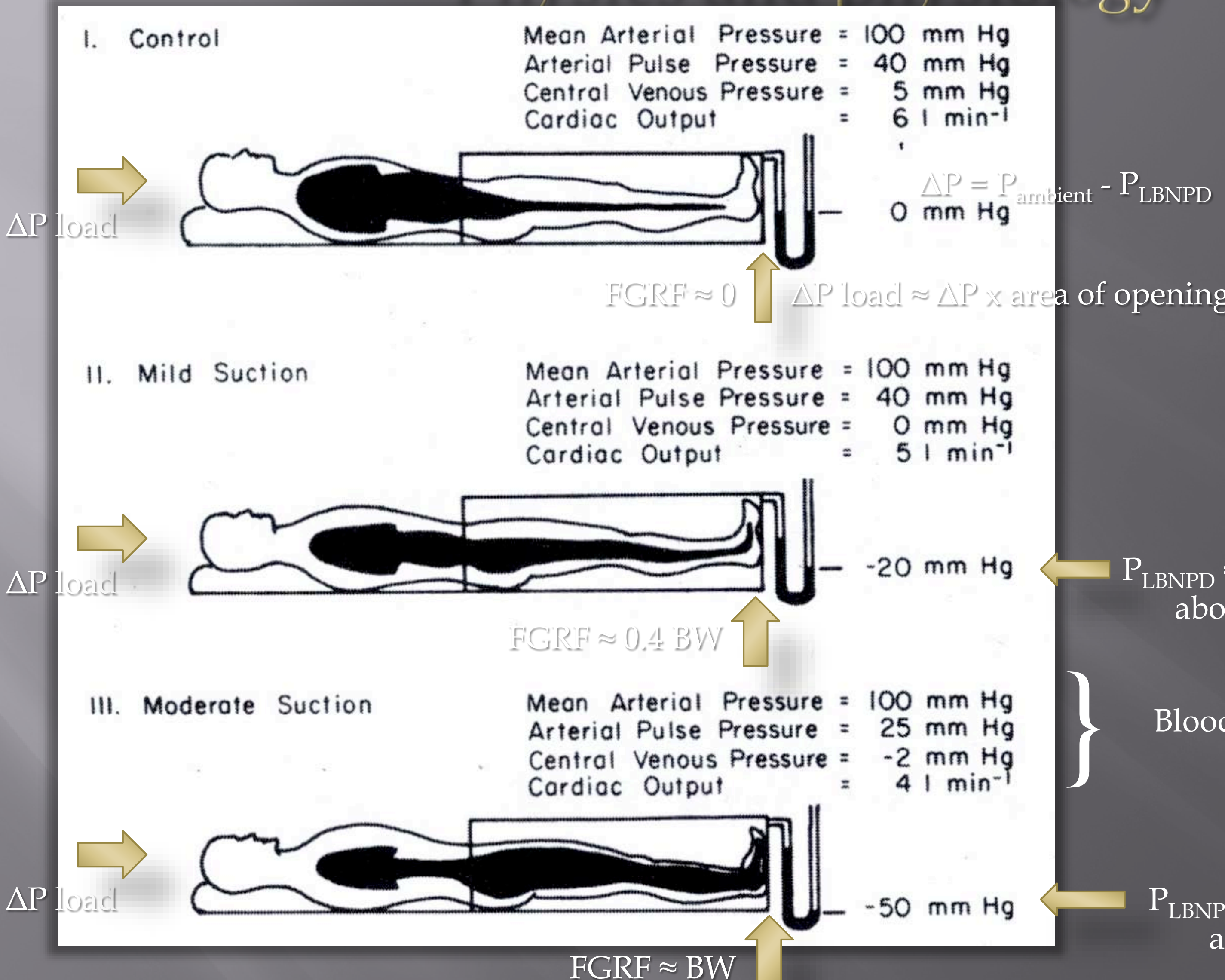


Fig. 2. Responses of mean blood pressure to orthostasis pre- and post-spaceflight, with or without counter measure.

Lower Body Negative Pressure (LBNP) Physics and physiology



P_{LBNPD} ≈ 230 m (770 ft) above sea level

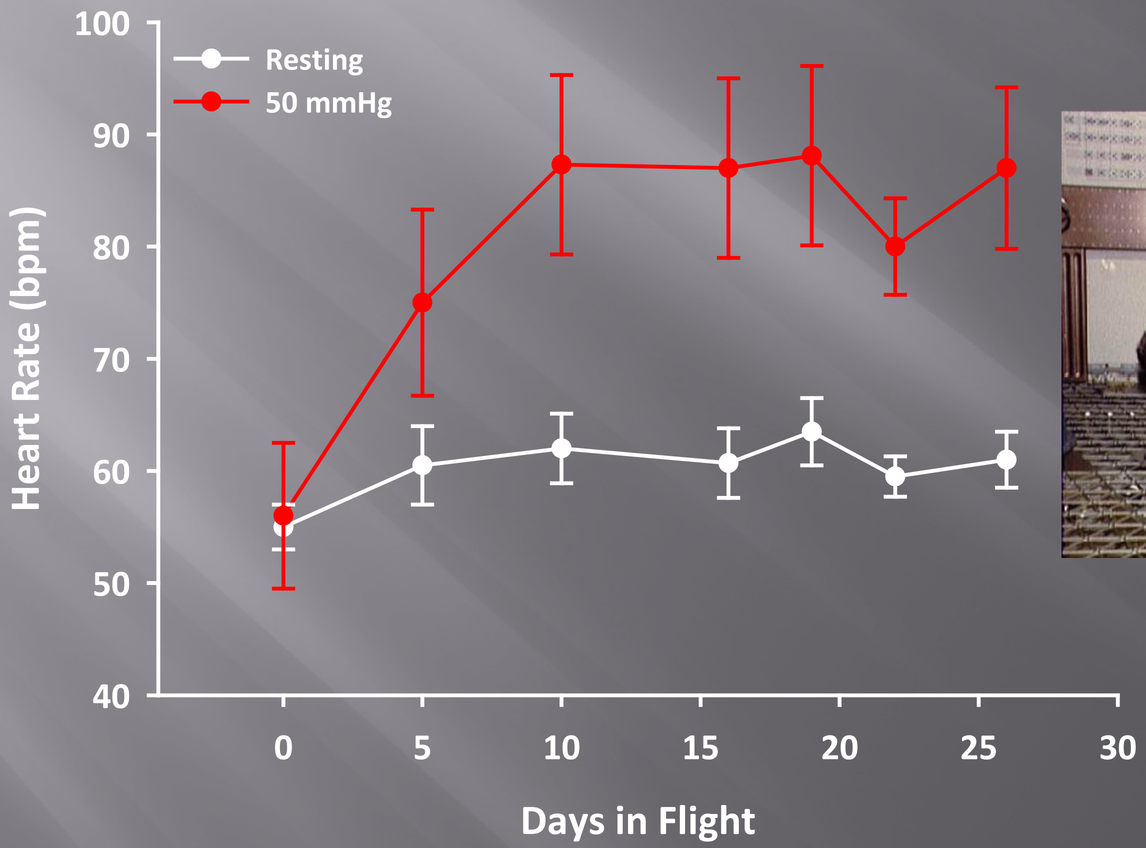
Blood volume shift ≈ 0.6 ℓ
f(ΔP, time @ ΔP)

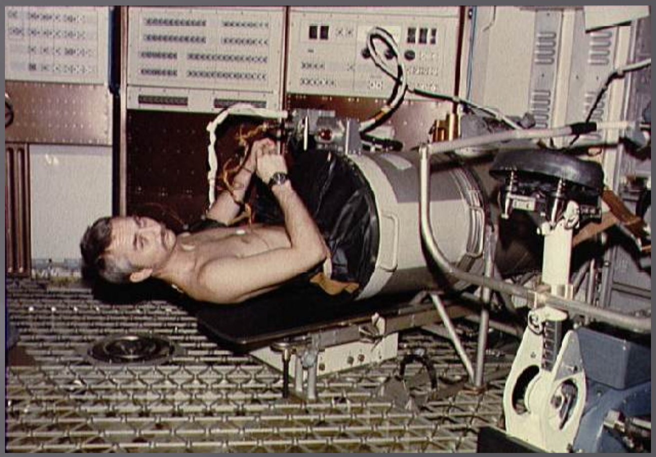
P_{LBNPD} ≈ 600 m (1970 ft) above sea level

"LBNP … provides a non-gravity dependent way to shift fluid from the upper to lower body." Buckey, 2006.

Sources: Rowell, 1986; Buckey, 2006; Smith, 1990.

HR Response to LBNP in Spaceflight: Skylab (1973-1974)



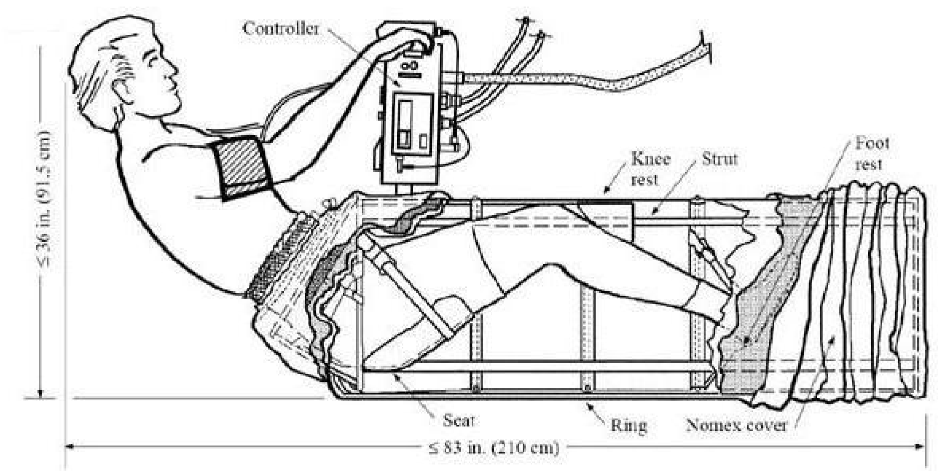


Objectives

1. Determine efficacy of combined fluid loading and sustained LBNP countermeasure to reverse OI during space flight and to assess length of time countermeasure would be effective during space flight
2. Determine whether countermeasure can be successfully employed 24 h prior to landing to prevent OI during stand test after landing
3. Assess rate of development of OI during short-duration space flight using more frequent LBNP tests than Skylab

Methods

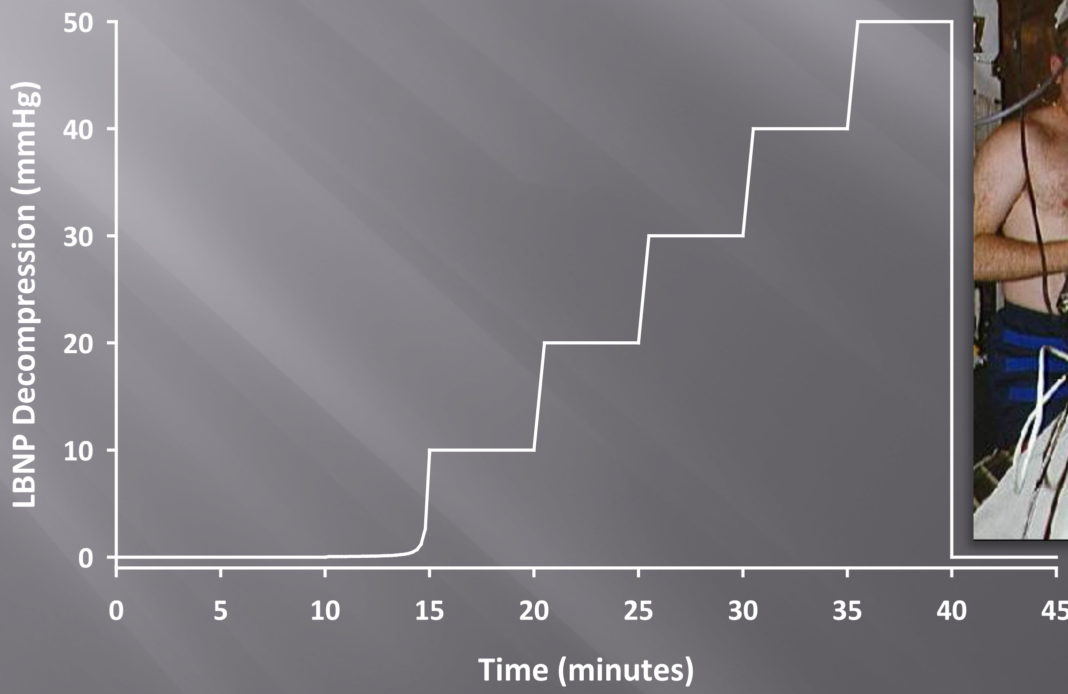
- 18 astronauts (15 men, 3 women) volunteered
  - Data combined from two separate but related studies (DSO 478 & 623)
  - Analyses based on subsets with necessary characteristics
- Space Shuttle flights of 6-14 days
- Collapsible LBNP device used as both testing and countermeasure modality

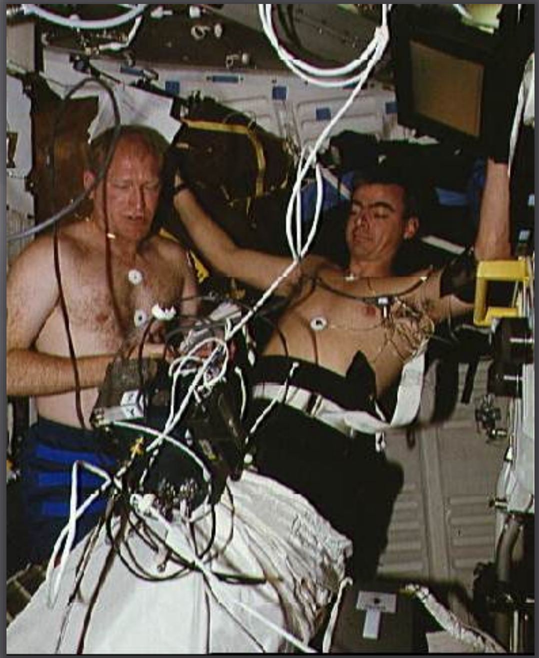


Schematic of the Lower Body Negative Pressure (LBNP) device

Development of OI

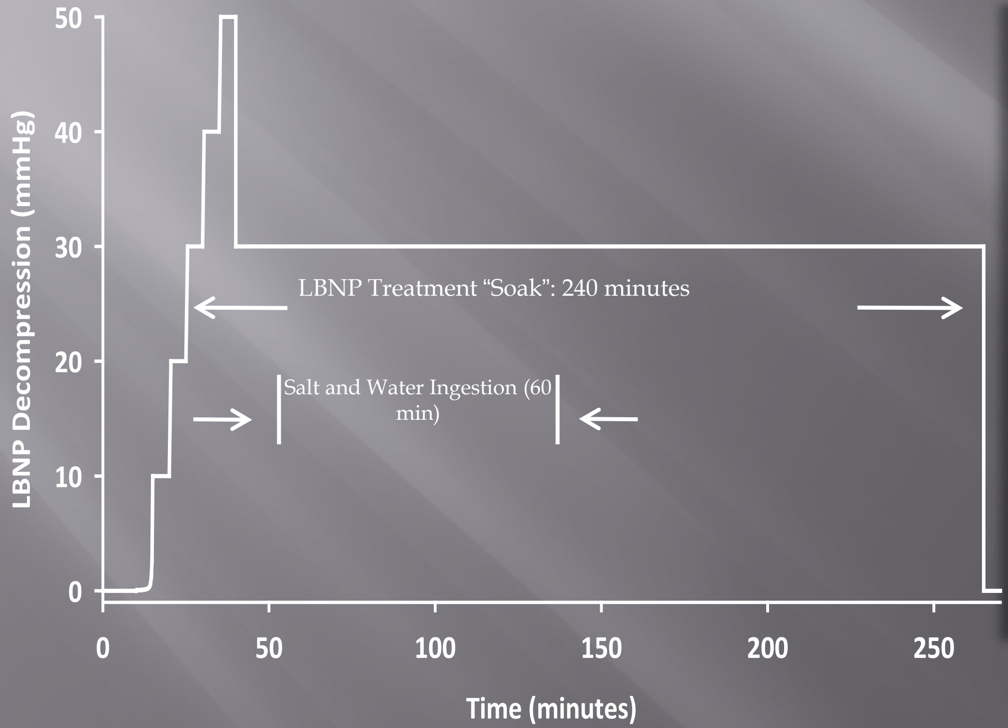
- LBNP "ramp" tests at ~3-day intervals to document progressive loss of orthostatic tolerance (n=13)
  - 5-min stages of 10 mmHg decompression to 50 mmHg
- No countermeasure prior to these ramp tests



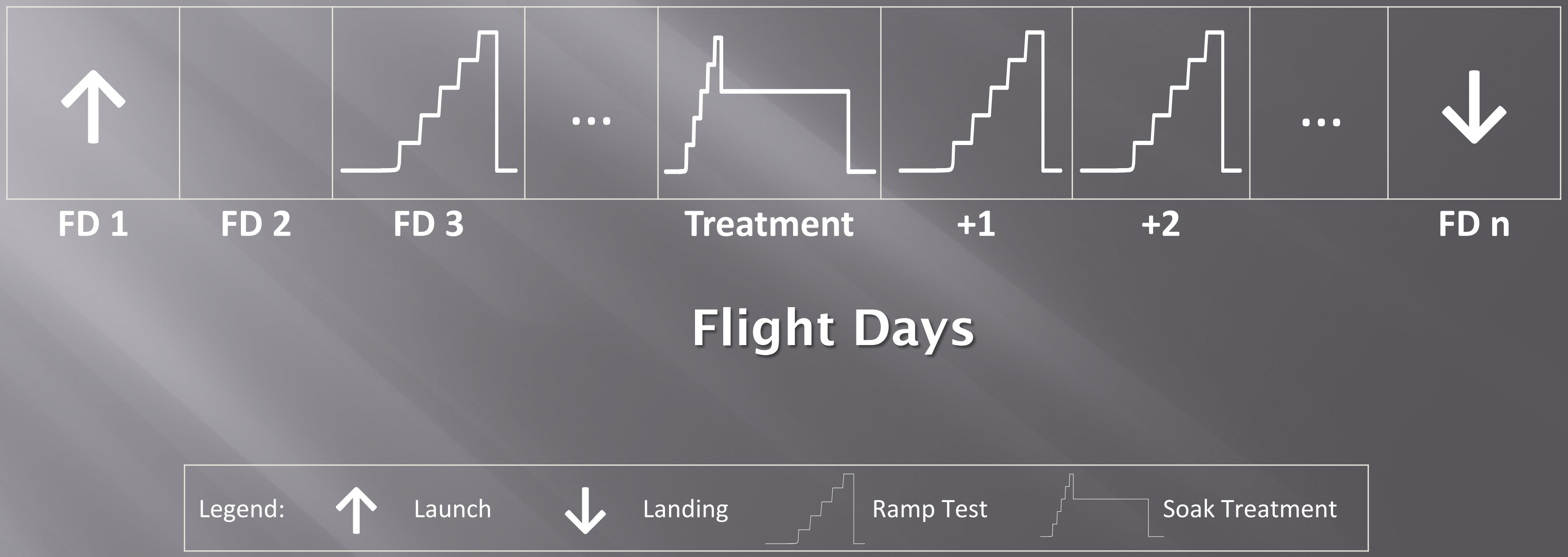


In-flight Countermeasure

- Ingested ~1 ℓ water or artificially-sweetened fruit beverage and ~8 gm salt during 4-h LBNP "soak" treatment (n=8)
- Compared pre-flight heart rate (HR) and blood pressure (BP) responses to prior LBNP ramp test to in-flight responses to ramp tests one and two days after 4-h LBNP soak treatment



Generic In-flight Test & Countermeasure Schedule

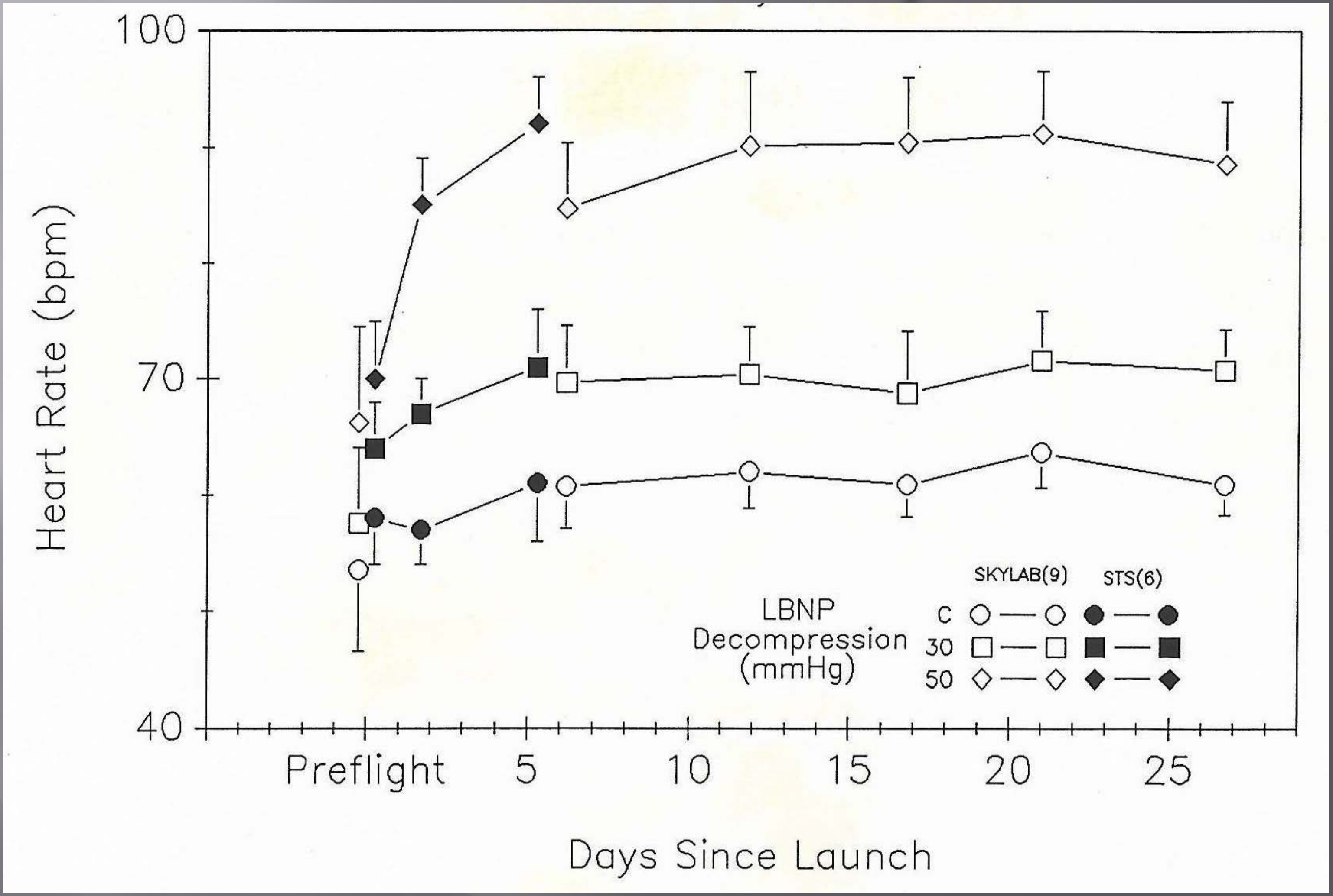


Actual In-flight Test Schedule

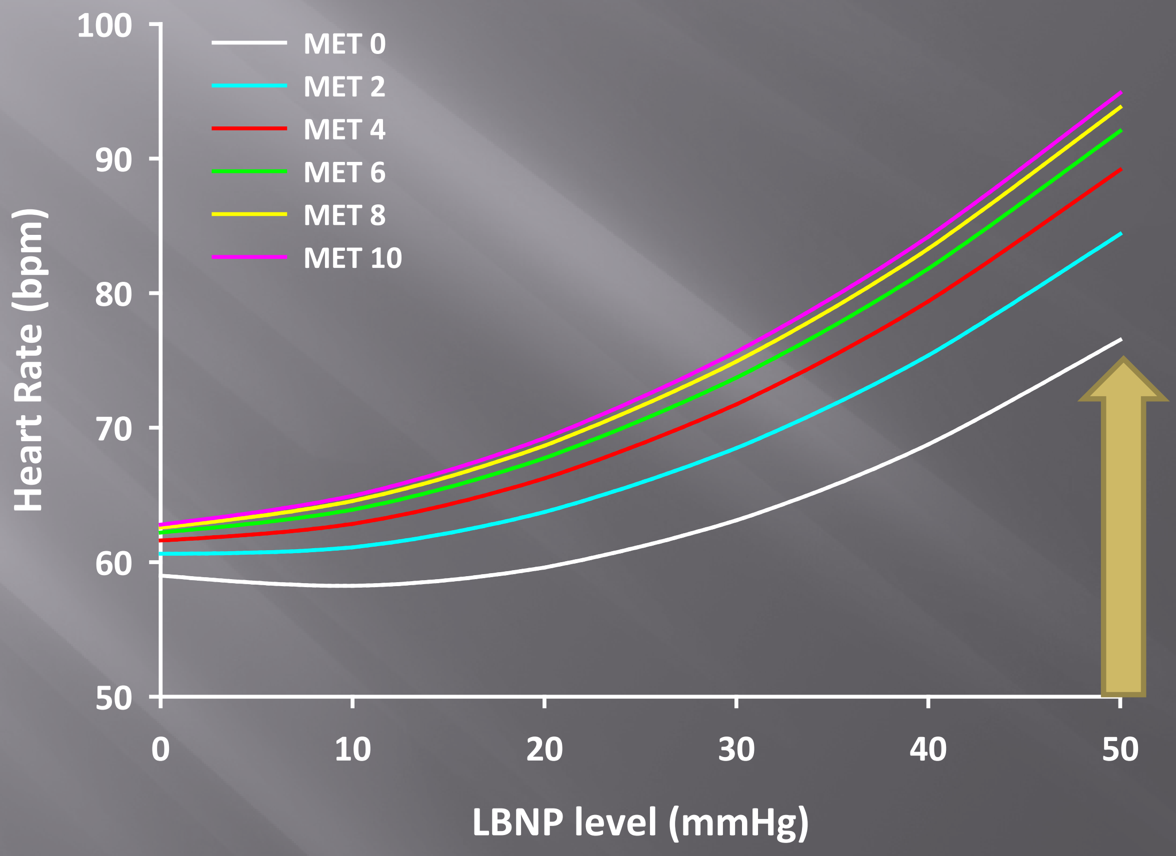
Flight Duration (days)	FD 1	FD 2	FD 3	FD 4	FD 5	FD 6	FD 7	FD 8	FD 9	FD 10	FD 11	FD 12	FD 13	R+0
8.9			R			S	R	R						
8.9		R				S	R	R						
7.0		R			R									R
7.0		R			R	S								R
7.0			R		R									
7.0		R		R			R							
13.8			R		R					S	R	R		R
13.8		R		R					S	R	R			R
7.9				S	R	R								R
7.9					S	R	R							R
9.9		R			S	R	R							
9.9		R				S	R	R						R
9.9				R			R							
14.0			R			R								
14.0			R		R				R		R		S	
14.0		R		R			R				R		S	
14.0		R		R			R				R			
14.8			R	R				R		R			S	
14.8			R		R			R		R			S	

Crewmembers participated in LBNP ramp test (R) and soak treatment (S) sessions based on availability in flight. Shaded squares indicate end of mission (R+0, landing day)

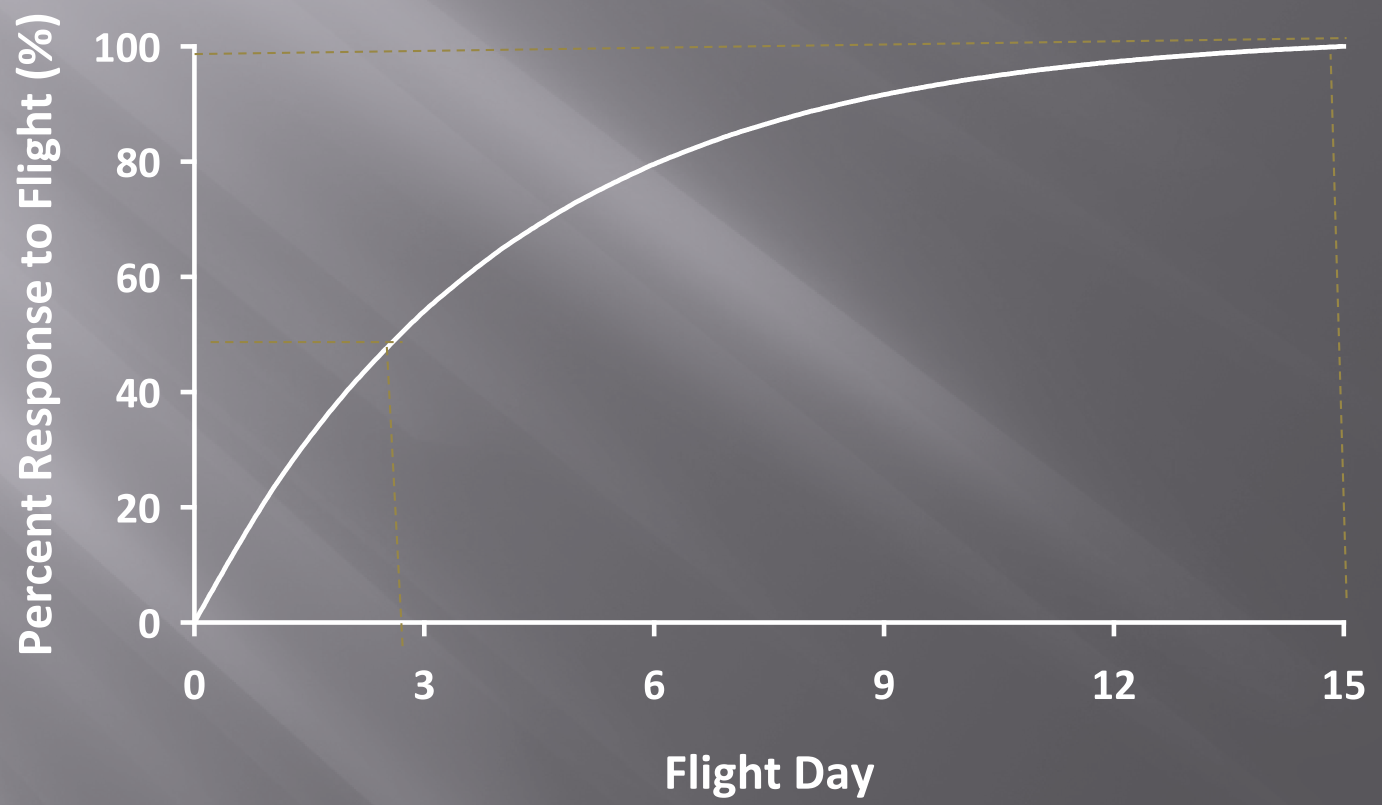
Heart rate response to LBNP: Shuttle and Skylab



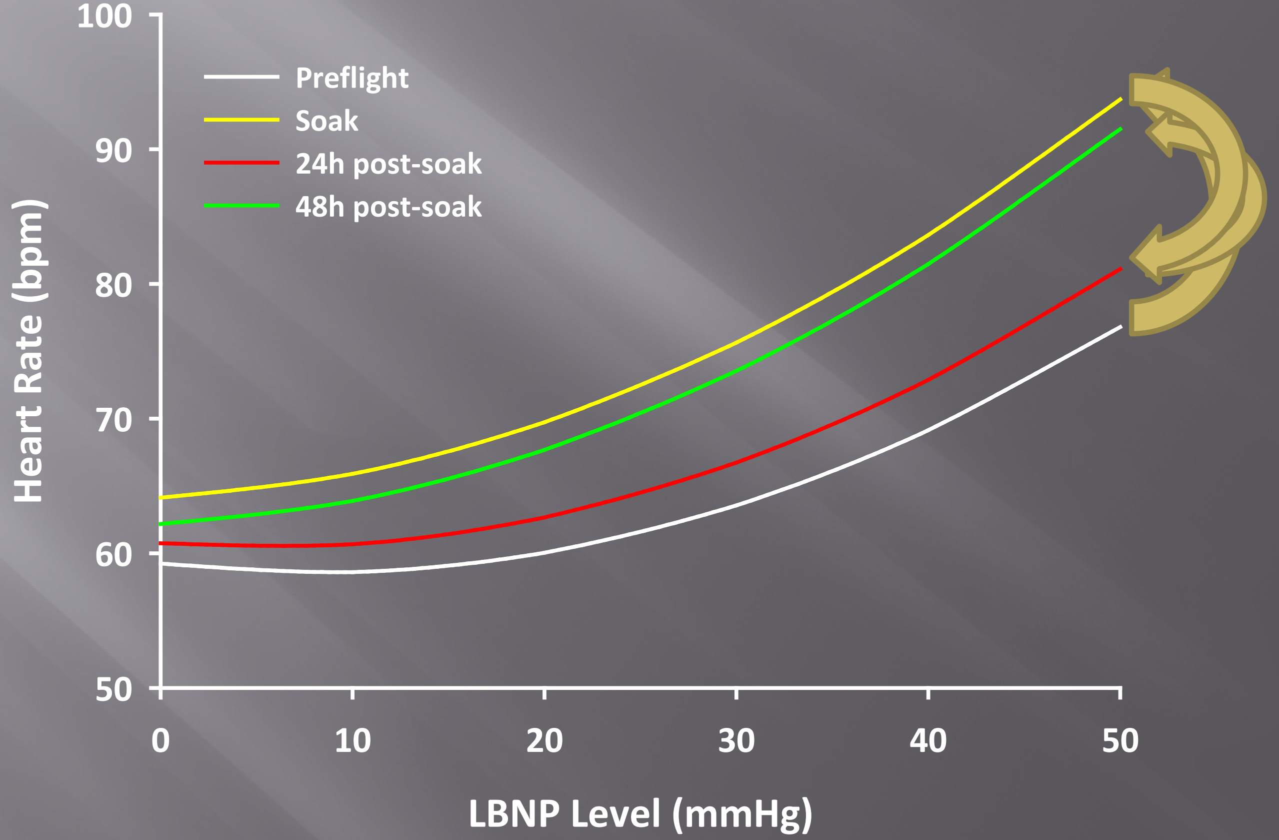
Modeled HR Response to LBNP During Space Shuttle Missions



Modeled HR Response to -50 mmHg LBNP across Flight Days



Modeled HR During Ramp Test Before and After Soak Countermeasure



Post-flight OI assessment

- All crewmembers used NASA's operational fluid-loading protocol before de-orbit and wore AGS during re-entry and landing
- Countermeasure subjects performed LBNP soak within 24 hours of landing (n=5)
- Stand test results were compared to cohort of subjects from STS flights of similar duration (n=7)
  - 5/5 treatment subjects completed 5-minute post-flight stand test
  - 5/7 untreated cohort subjects completed it
  - No between-group differences in HR and BP responses to standing post-flight

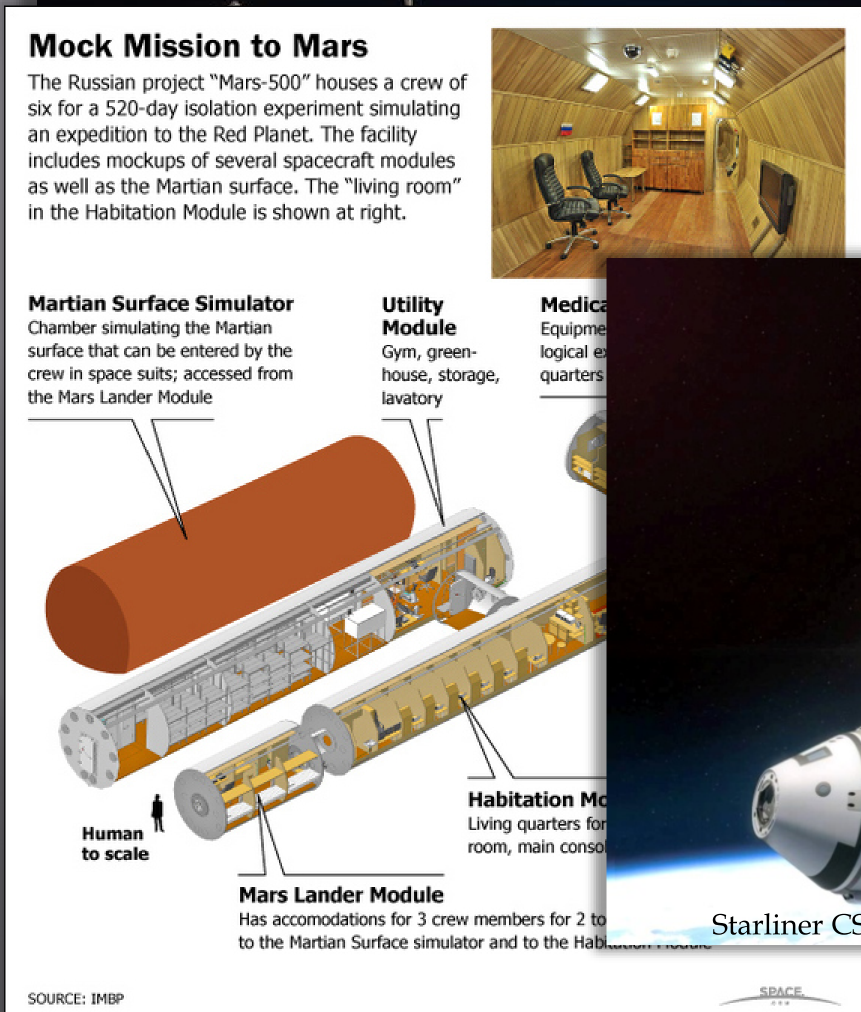
Combined Countermeasure constraints

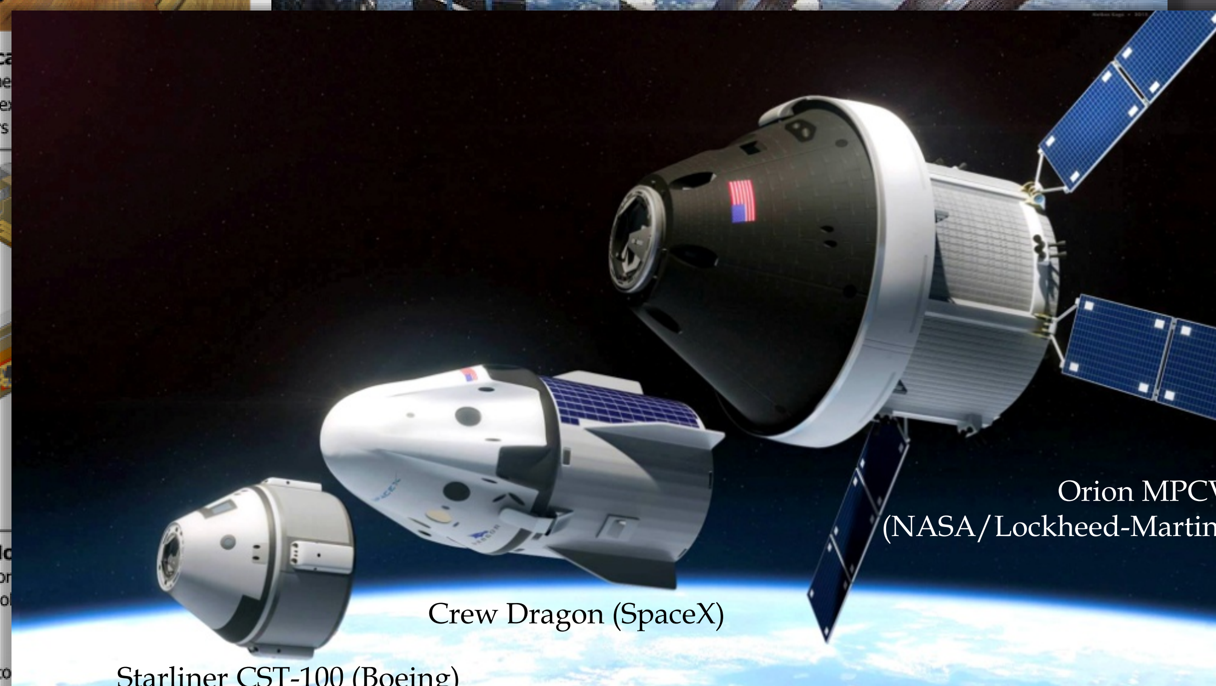
- 4-hr LBNP plus fluid loading proved too cumbersome for short Shuttle missions
  - Unacceptable constraint for 4 hr during busy pre-landing preps
    - Abbreviated 2-hr treatment previously shown to be ineffective
  - Too much time required for treating entire crew: 4 hours x 7 astronauts within 16-hour duty day
    - Multiple LBNPDs?
    - Triage, prioritize pilots?
    - Incidence of presyncope is ~20% following short-duration missions
    - “Treatment is worse than the disease”

Combined Countermeasure alternatives

- Multiple other operational countermeasures to OI already available:
  - Oral fluid loading
  - Recumbent seating
  - Lower body compression garments
  - Cooling garments
  - Mission design not requiring early sustained orthostasis

Preparation for Future Space Exploration





time.com/meet-the-twins-unlocking-the-secrets-of-space/

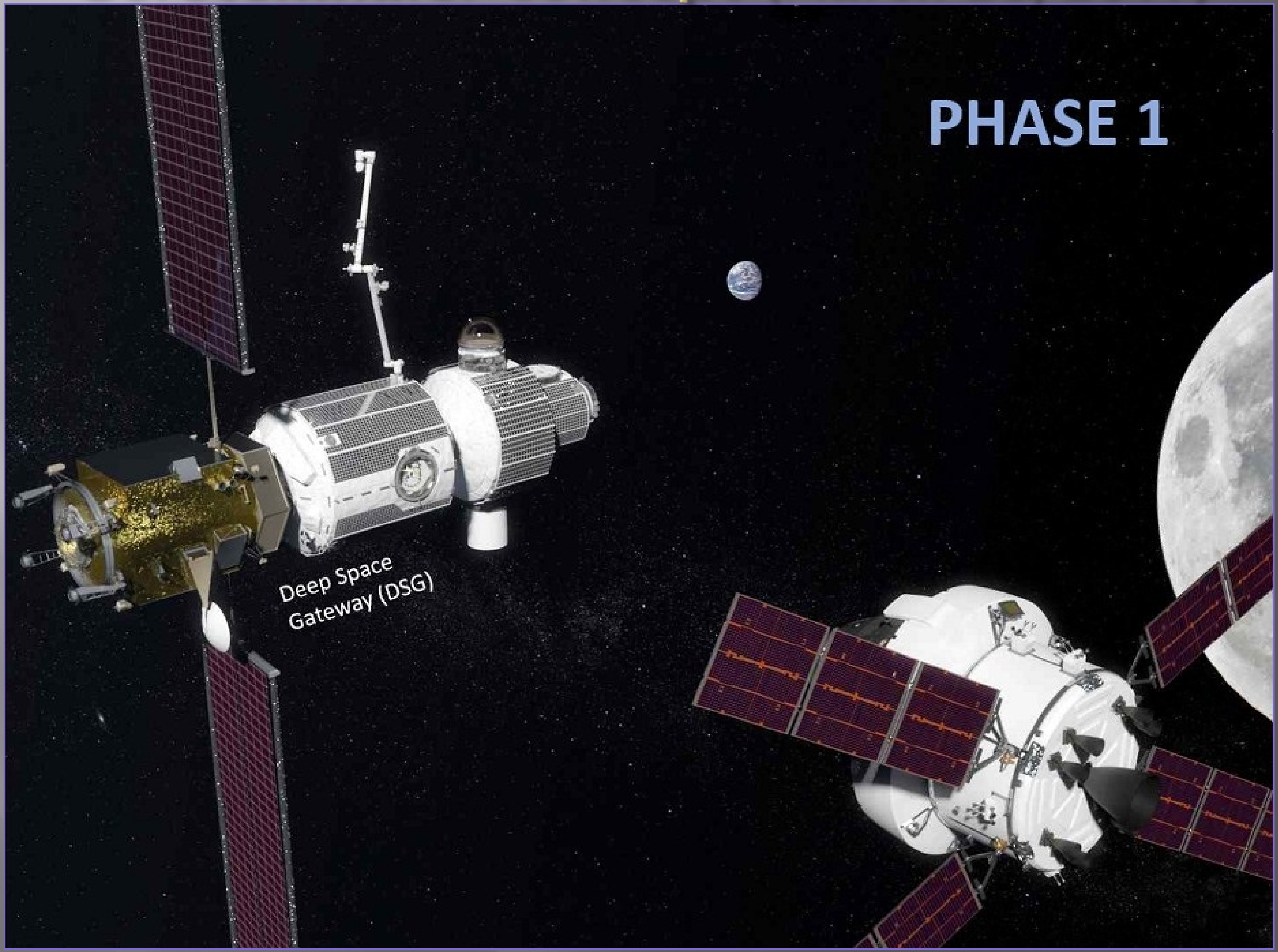

340 days in space
(close enough for government work)

Current research

FIELD TEST

FLUID SHIFTS

After ISS
Gerstenmaier concept (March 28, 2017)

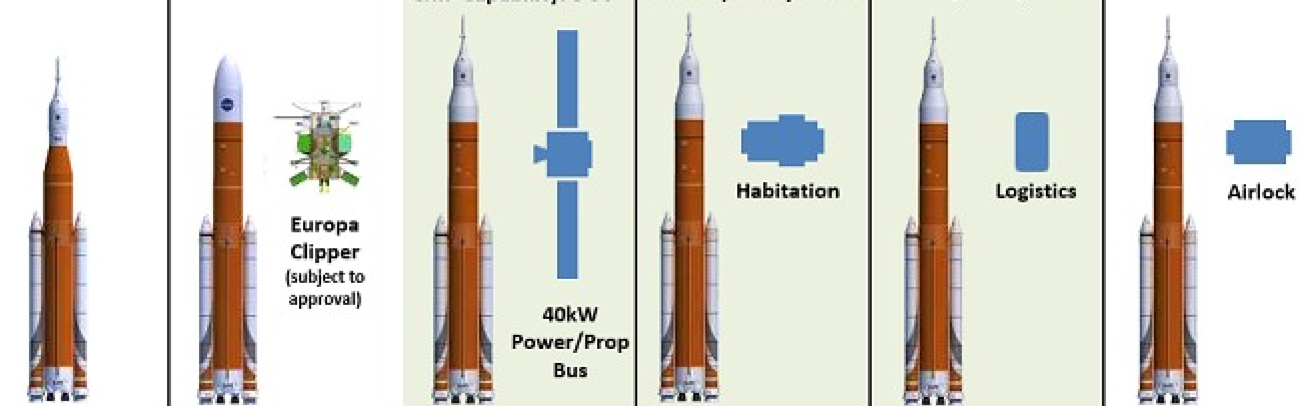


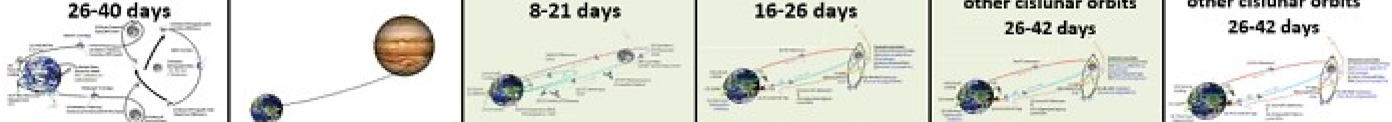
https://arstechnica.com/science/2017/03/for-the-first-time-nasa-has-begun-detailing-its-deep-space-exploration-plans/.

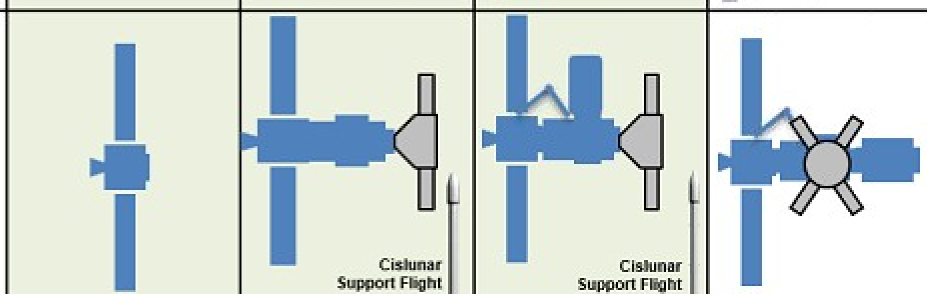
Phase 1 Plan

Establishing deep-space leadership and preparing for Deep Space Transport development

		Deep Space Gateway Buildup			
EM-1	Europa Clipper	EM-2	EM-3	EM-4	EM-5
2018 - 2025					2026
SLS Block 1 Crew: 0	SLS Block 1B Cargo Europa Clipper (subject to approval)	SLS Block 1B Crew: 4 CMP Capability: 8-9T 40kW Power/Prop Bus	SLS Block 1B Crew: 4 CMP Capability: 10mT Habitation	SLS Block 1B Crew: 4 CMP Capability: 10mT Logistics	SLS Block 1B Crew: 4 CPL Capability: 10mT Airlock
Distant Retrograde Orbit (DRO) 26-40 days	Jupiter Direct	Multi-TLI Lunar Free Return 8-21 days	Near Rectilinear Halo Orbit (NRHO) 16-26 days	NRHO, w/ ability to translate to/from other cislunar orbits 26-42 days	NRHO, w/ ability to translate to/from other cislunar orbits 26-42 days
Gateway (blue) Configuration (Orion in grey)			Cislunar Support Flight	Cislunar Support Flight	







These essential Gateway elements can support multiple U.S. and international partner objectives in Phase 1 and beyond

Known Parameters:

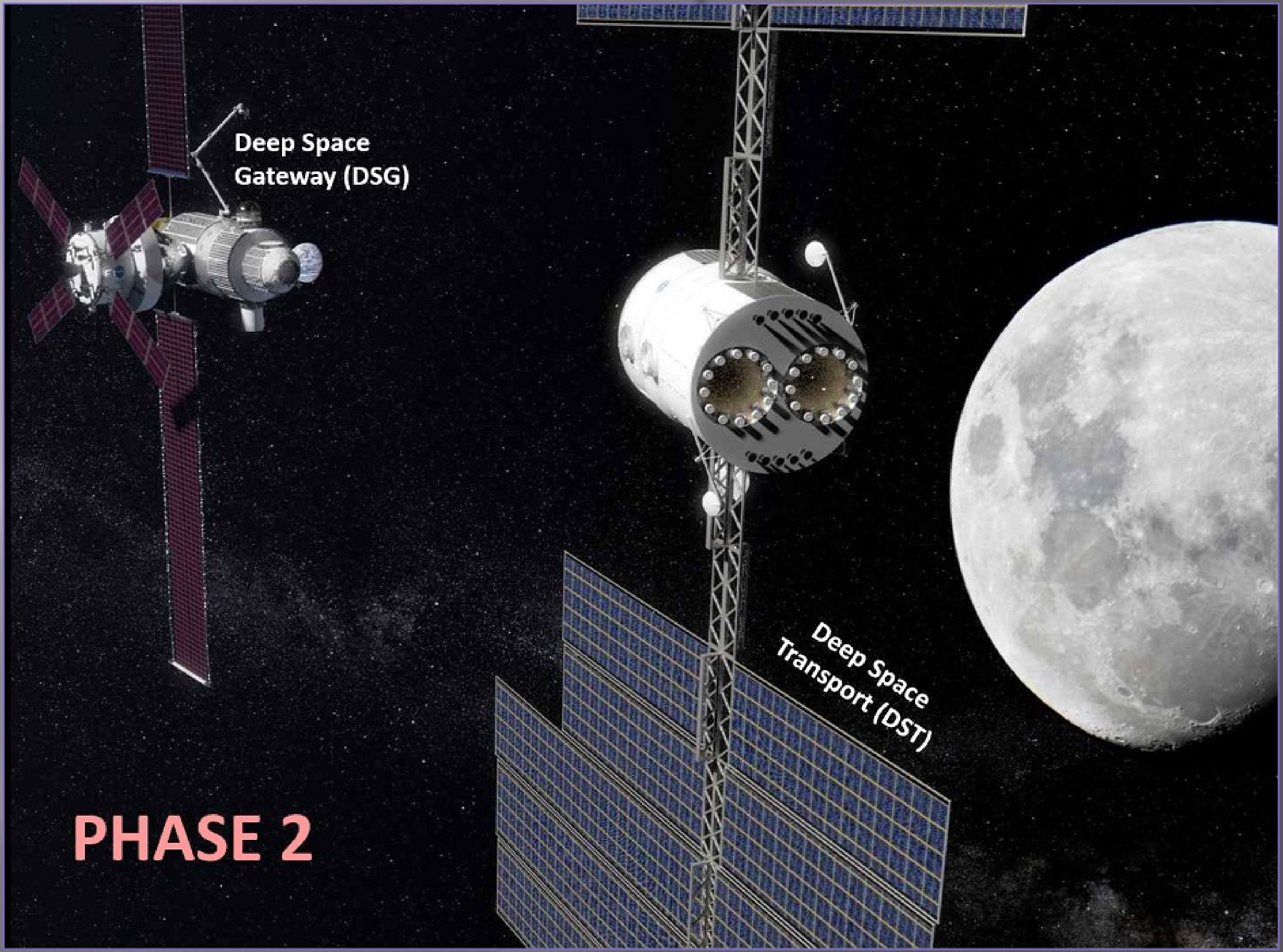
- Gateway to architecture supports Phase 2 and beyond activities
- International and U.S. commercial development of elements and systems
- Gateway will translate uncrewed between cislunar orbits
- Ability to support science objectives in cislunar space

Open Opportunities:

- Order of logistics flights and logistics providers
- Use of logistics modules for available volume
- Ability to support lunar surface missions

After ISS

Gerstenmaier concept (March 28, 2017)



https://arstechnica.com/science/2017/03/for-the-first-time-nasa-has-begun-detailing-its-deep-space-exploration-plans/.

(PLANNING REFERENCE) Phase 2 and Phase 3

Looking ahead to the shakedown cruise and the first crewed missions to Mars

Transport Delivery		Transport Shakedown		Mars Transit	
EM-6	EM-7	EM-8	EM-9	EM-10	EM-11
2027		2028 / 2029		2030+	
SLS Block 1B Cargo P/L Capability: 41t TLI	SLS Block 1B Crew: 4 CMP Capability: 10t	SLS Block 1B Cargo P/L Capability: 41t TLI	SLS Block 2 Crew: 4 CMP Capability: 13+t	SLS Block 2 Cargo P/L Capability: 45t TLI	SLS Block 2 Crew: 4 CMP Capability: 13+t
Deep Space Transport	Logistics	DST Logistics & Refueling	Logistics	DST Logistics & Refueling	Logistics
DST checkout in NRHO 191-221 days Cislunar Support Flight		DSG: continued operations in cislunar space DST: shakedown in cislunar space with return to DSG in NRHO 300-400 days Cislunar Support Flight		DSG: continued operations in cislunar space DST: Mars transit and return to DSG in NRHO Cislunar Support Flight	

Reusable Deep Space Transport supports repeated crewed missions to the Mars vicinity

Known Parameters:

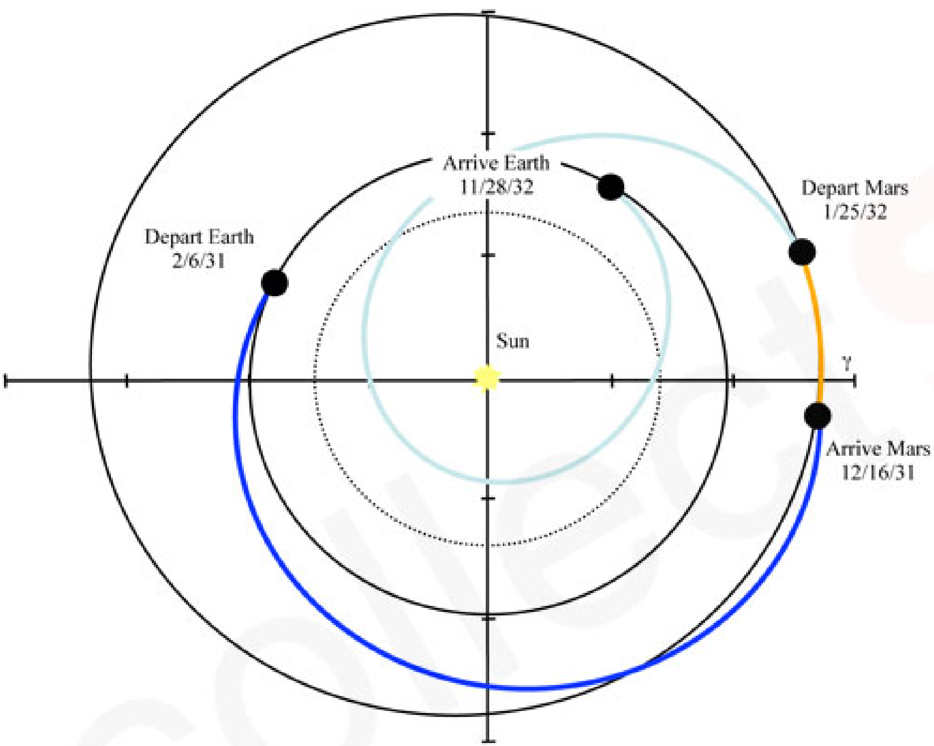
- DST launch on one SLS cargo flight
- DST shakedown cruise by 2029
- DST supported by a mix of logistics flights for both shakedown and transit
- Ability to support science objectives in cislunar space

Open Opportunities:

- Order of logistics flights and logistics providers
- Shakedown cruise vehicle configuration and destination/s
- Ability to support lunar surface missions

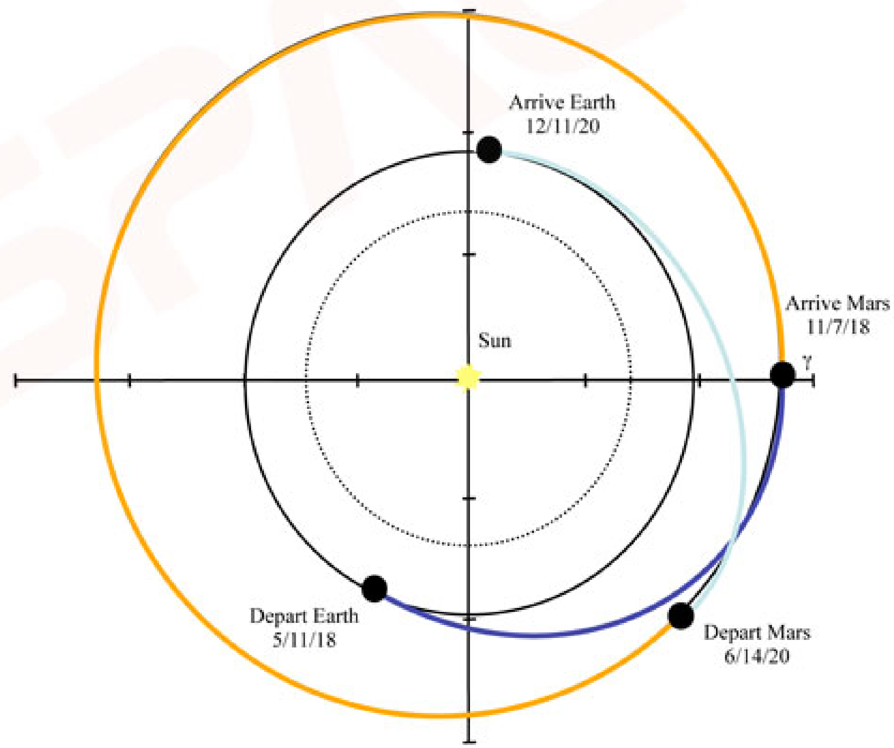
Human Mars Mission Classes

"Short-Stay" ("Opposition-Class")



MISSION TIMES	
Outbound	313 days
Stay	40 days
Return	308 days
Total Mission	661 days

"Long-Stay" ("Conjunction-Class")



MISSION TIMES	
Outbound	180 days
Stay	545 days
Return	180 days
Total Mission	905 days

Final thoughts

- Space exploration has epitomized complex activities resulting in dramatic success for generation or more
- Progress in space exploration requires concerted efforts of many dedicated people over long periods of time to implement many complex activities
- Every step forward comprises multitude of smaller steps in technical and programmatic domains
- Success depends on ability to coordinate people in accomplishing common important goal
- University of Kentucky experience was foundation for long and rewarding career in space life sciences research and management