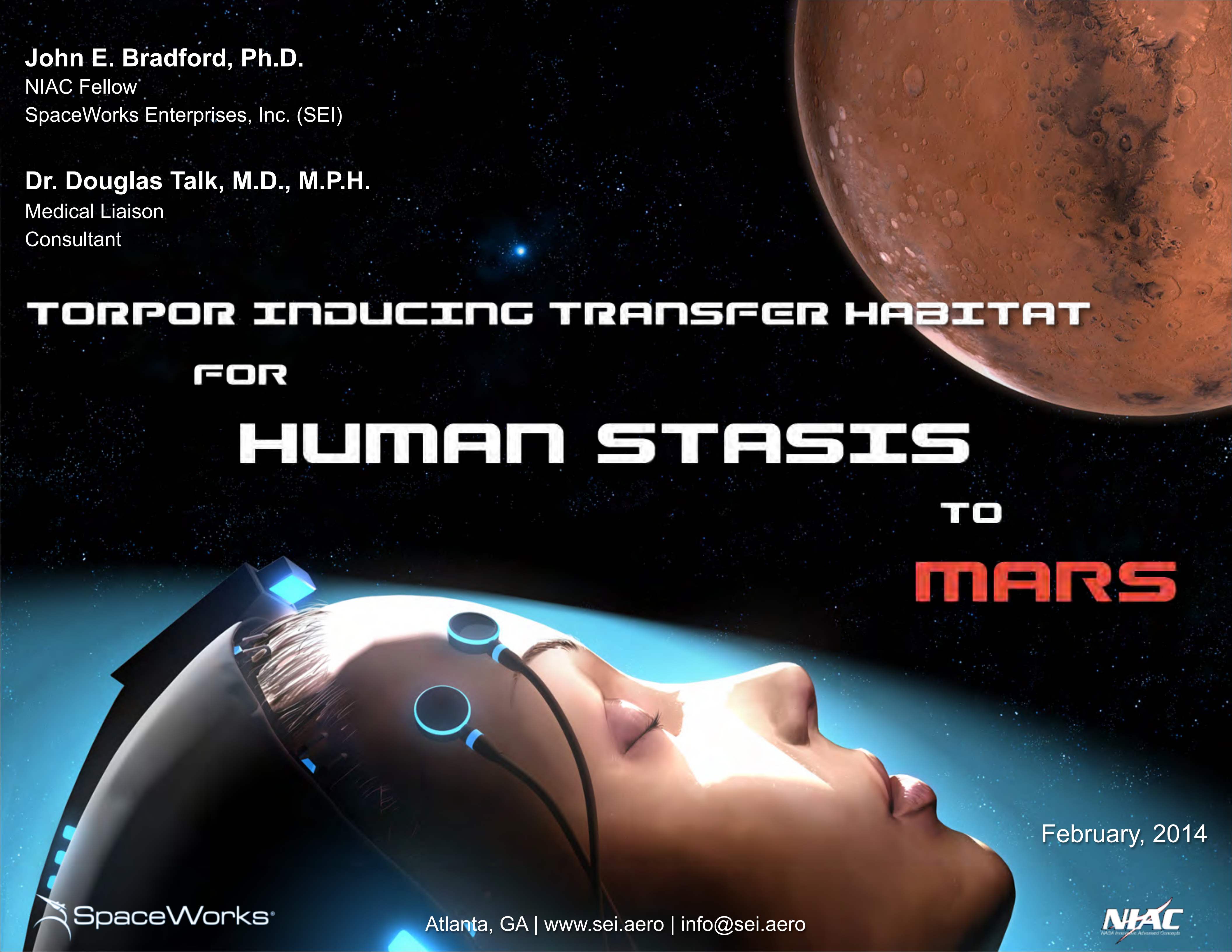

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TORPOR INDUCING TRANSFER HABITAT FOR HUMAN STASIS TO MARS

February, 2014

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SCIENCE FICTION

SOLUTION

Place crew in inactive, low-metabolic Torpor state for mission transfer phases by leveraging evolving medical advances in Therapeutic Hypothermia and Total Parenteral Nutrition.

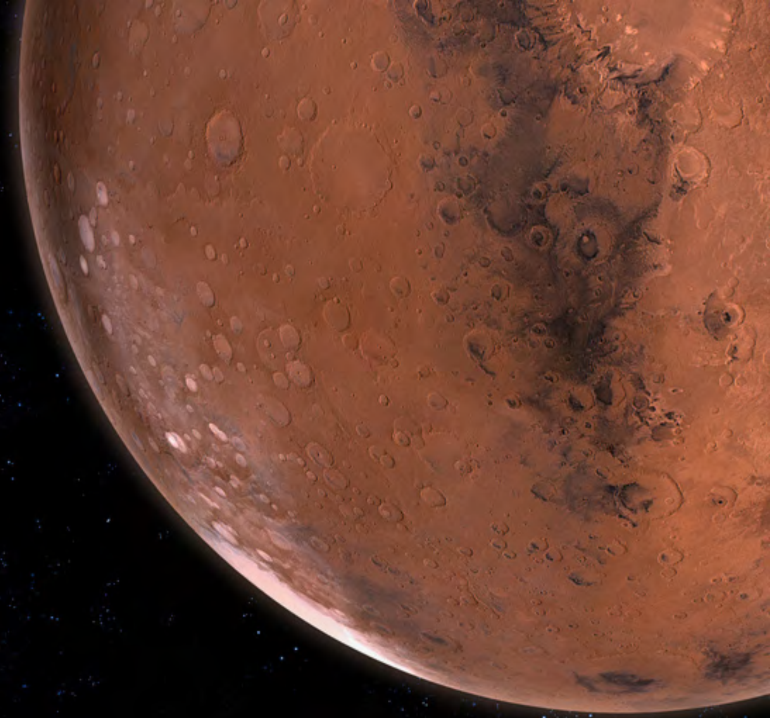
BENEFITS

- Direct benefits include:
  - Reduction in mission consumables due to inactive crew
  - Reduced pressurized volume required for living quarters
  - Eliminate many ancillary crew accommodations (food galley, eating supplies, cooking, exercise equipment, entertainment, etc.)
  - Minimize psychological challenges for crew

- Savings can be used to:
  - Increase mass margins, allowing added subsystem redundancy and improve safety
  - Increase radiation protection/shielding
  - Reduce number of heavy-lift launches and on-orbit assembly operations
  - Expand launch opportunities and mission options

KEY QUESTIONS

- Can current Therapeutic Hypothermia be advanced to point of enabling crew stasis periods of 1-3-6 months?
- Is the combination of Torpor and Total Parenteral Nutrition viable for long-term use?
- Is this approach advantageous at the architecture-level?
- Can this enable a human presence extending beyond Mars?



BACKGROUND

TORPOR/HIBERNATION IN NATURE

Types of Hibernation:

- Obligate Hibernators

  Spontaneously enter hibernation regardless of ambient temperature or access to food. Body temperature drops to environmental temperature and heart/respiration rates slow drastically. Characterized by periods of sleep with periodic arousals where body temperature and heart rate returns to normal levels (e.g. marmots)

- Facultative Hibernators

  Only enter hibernation when either cold stressed, food deprived, or both for survival purposes (e.g. prairie dogs)

- Torpor

  Active metabolic suppression with minimal decrease in body temperature to save energy over winter period (e.g. black bears)

HIBERNATING MAMMALS

Species	Duration [months]	Comment
CARNIVORA		
Black Bear	3 to 5	Minimal body temperature reduction Consumes 25-40% of body mass Nitrogen waste from body is recycled, preventing muscle atrophy
RODENTIA		
Arctic Ground Squirrel	Up to 6	Experiences significant body temperature reductions
Marmot	4.5 to 8.5	Body temperature remains at ambient for days to weeks, followed by a brief return cycle (<24hr) to higher body temperature
Prairie Dog	4 to 5	Can spontaneously awaken to eat on warmer days
Groundhog	Up to 6	Moderate body temperature changes Heart-rate slows to approximately 4 beats per minute.
PRIMATES		
Dwarf Lemur	4 to 5	Can reduce metabolic rate to 2% of “active” rate Only primate known to hibernate

ARTIFICIALLY INDUCING HIBERNATION

Three approaches possible for humans:

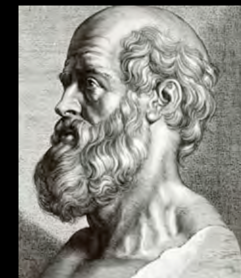
1. **Temperature-based**
   – Lowering of core temperature through either invasive cooling (infusing cooled IV fluids), conductive cooling (through the use of gel pads placed on the body or with evaporative gases in the nasal and oral cavity)

2. **Chemical/Drug-based**
   – In 2011, Scientists at Univ. Alaska successfully induced hibernation by activating adenosine receptors in arctic ground squirrels
   – Inhaled Hydrogen Sulfide (H2S) shown to induce deep hibernation state within mice by reducing cell demand for oxygen

3. **Brain Synaptic-based**
   – Current research shows significant decreases in the number of dendritic spines along the whole passage of apical dendrites in hibernating creatures

BODY COOLING AS THERAPY

- Historical Views
  - Hypothermia has been applied therapeutically since antiquity
  - The Greek physician Hippocrates, arguably the world's first modern doctor, advocated the packing of wounded soldiers in snow and ice (400 BCE)
  - Napoleonic surgeon Baron Dominique Jean Larrey tested this theory after noting that wounded officers who were kept closer to the fire survived less often than the minimally pampered infantrymen (1810)



- Modern uses: Therapeutic Hypothermia use can be divided into <u>five</u> primary treatment categories:
  1. Neonatal encephalopathy
  2. Cardiac arrest
  3. Ischemic stroke
  4. Traumatic brain or spinal cord injury without fever
  5. Neurogenic fever following brain trauma

HYPOTHERMIA THERAPY MILESTONES

Year	Description
1945	First medical articles concerning use of hypothermia published
1955	Division of Medical Sciences, NRC symposium on the Physiology of Induced Hypothermia, sponsored by U.S. Army, Navy, and Air Force
1980	Animal studies prove that mild hypothermia acts as a general neuro-protectant following a blockage of blood flow to the brain
2002	Two landmark human studies published simultaneously by the New England Journal of Medicine
2003	American Heart Association endorses the use of TH following cardiac arrest
2005	Protocols for use of TH for prenatal infants established
2009	RhinoChill® IntraNasal cooling system enters clinical trials

HUMAN HIBERNATION

- Experiments
  - None beyond short periods involved with Therapeutic Hypothermia (TH)
  - Recent Chinese studies showed evidence of increased benefit from prolonged TH (up to 14-days) without increasing the risk of complication
  - Despite initial results with Hydrogen Sulfide on mice producing a brief hibernation-like/suspended animation state, clinical trials were suspended after subsequent studies did not show this effect occurring in larger animals

- Potential Evidence Supporting Ability and Recovery
  - Mitsutaka Uchikoshi of Japan purportedly survived 24-days without food/water after falling in snow and entering hypothermic state. When found, core temperature had dropped to 22 C (2006)
  - Erika Norby, a one-year old, was revived after her heat stopped beating for over two hours when accident left her exposed to -20 C weather conditions and her core temperature dropped to 17 C (2001)
  - Dr. Anna Bagenholm, at 29 years old, was revived after her heart was stopped for 3 hours after being submerged under ice while skiing. Body temperature dropped to 14 C (1999)

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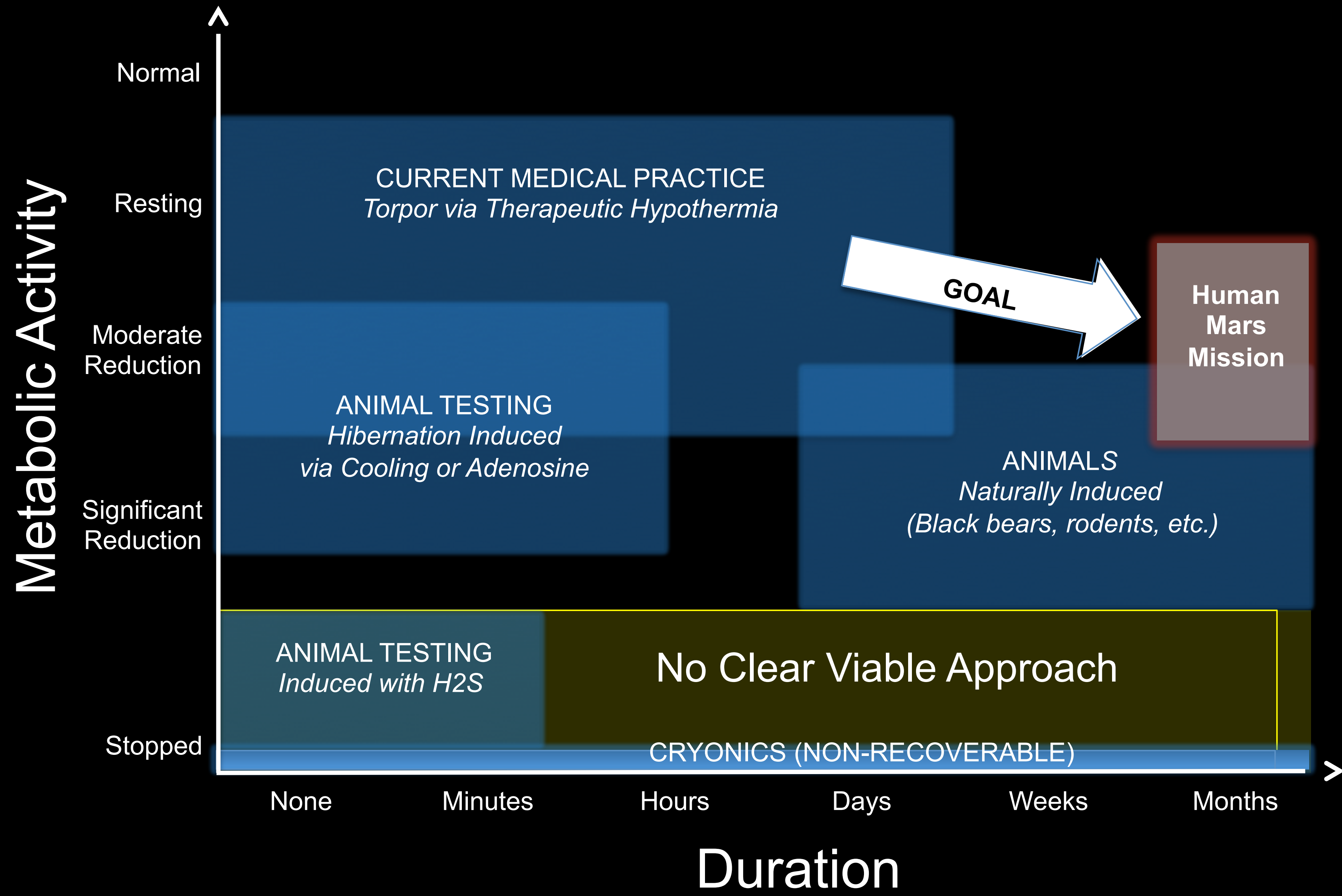
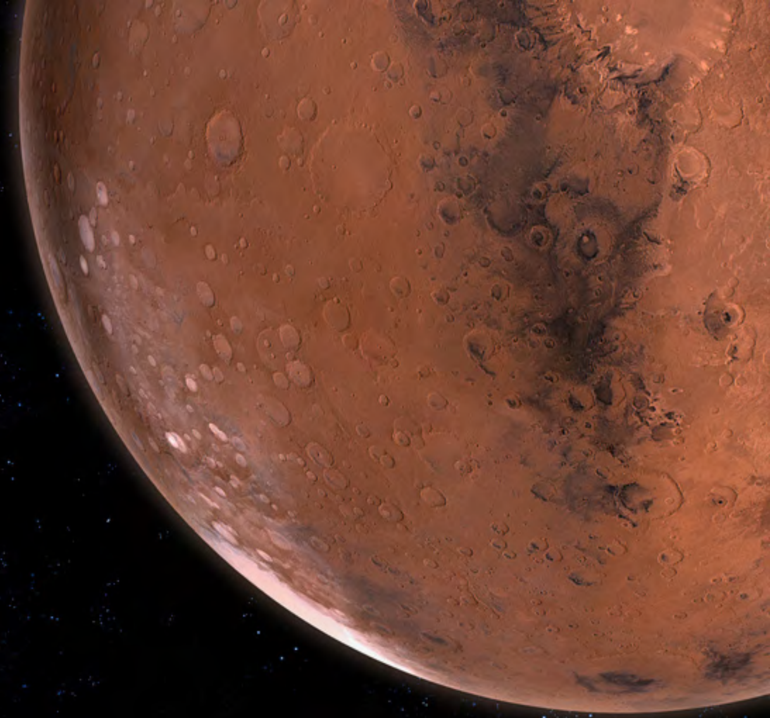
KNOWLEDGE SPECTRUM





CONCEPT MEDICAL PERSPECTIVE

KEY CONCEPTS

Torpor	Reducing human metabolism and inducing a **sleep-like inactive state** for prolonged period of time. Medically accomplished through **therapeutic hypothermia**.
Total Parenteral Nutrition (TPN)	Feeding a person **intravenously by nutritional fluids** delivered via a tunneled central venous catheter or a peripherally inserted central catheter.

THERAPEUTIC HYPOTHERMIA

- Therapeutic Hypothermia (TH) is a medical treatment that **lowers a patient's body temperature** in order to help reduce the risk of ischemic injury to tissue following a period of insufficient blood flow.

- Initial use started in 1980's, but since 2003 has become a **staple of Critical Care** for newborn infants suffering from fetal hypoxia and for adults suffering from head trauma, neurological injuries, stroke and cardiac arrest.

- Benefits of hypothermic therapy have been **well proven and are inexpensive to implement and use**. Standard protocols exist in most major medical centers throughout the world.

TH IN WIDESPREAD USE

N.Y. Times (2013) - Michael Schumacher at critical stage in treatment for head injury. Doctors treating ex-F1 champion are keeping him in an induced, hypothermic comatose state to cool his brain and reduce swelling

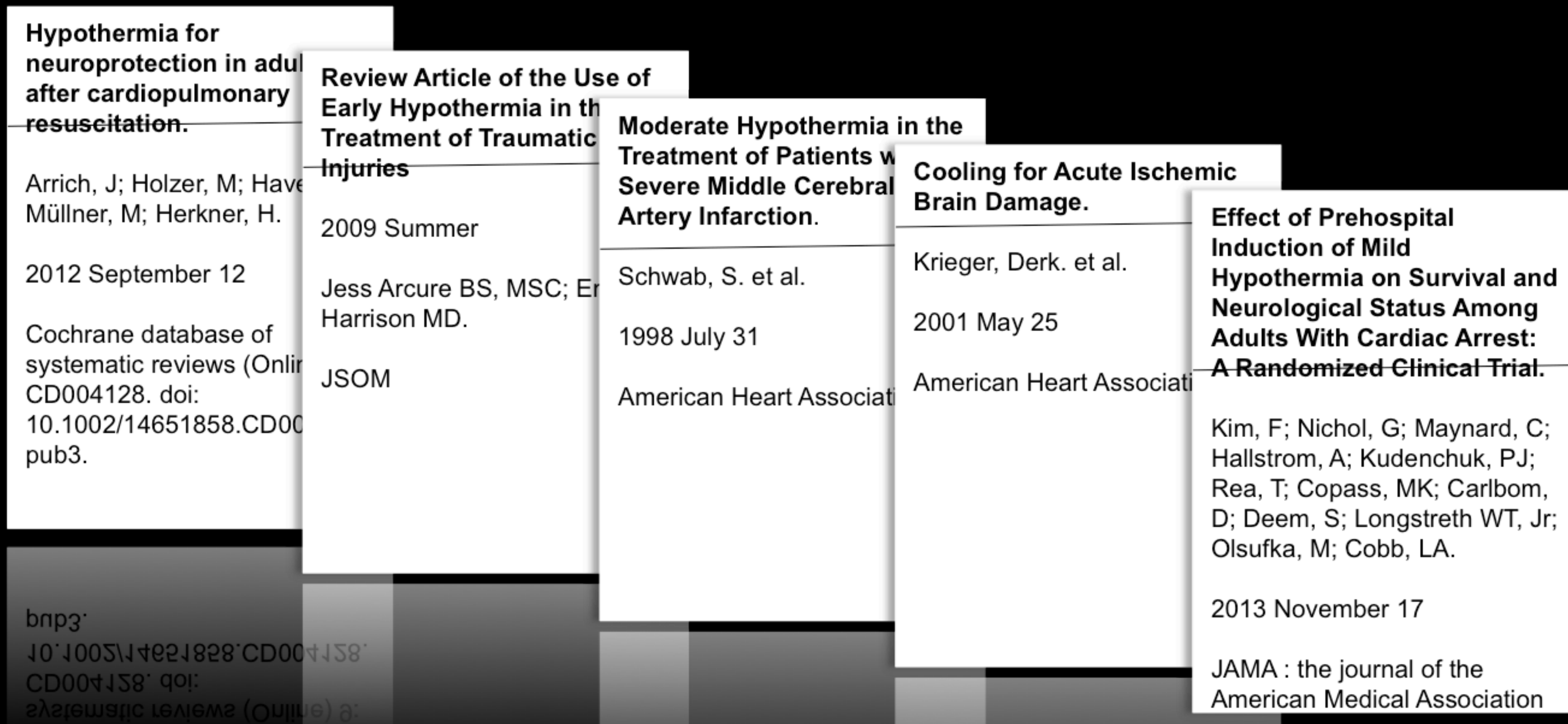
Boston Globe (2013) – Small Lily Harvey's life saved five times by staff at Southampton General Hospital's PICU by keeping her in hypothermic state

Los Angeles Times (2013) - Burbank marathoner thanks medical pros who saved him after finish-line heart attack

Associated Press (2013) - 28-Year-Old Cardiac Arrest Survivor Meets EMS Personnel Who Helped Save Him

Associated Press (2013) - Brave toddler born with major heart complications defies odds to take part in 10k walk in aid of hospital that saved her

TH KNOWLEDGE BASE



- Sydenham E, Roberts I, Alderson P. Hypothermia for traumatic head injury. Cochrane Database of Systematic Reviews 2009, Issue 2. Art. No.: CD001048. doi:10.1002/14651858.CD001048.pub4.
- Kammersgaard, L.P. et al. "Admission Body Temperature Predicts Long-Term Mortality After Acute Stroke http://stroke.ahajournals.org/cgi/content/abstract/33/7/1759." American Heart Association. March 12, 2002, pg. 1759-1762.
- Ginsberg, Myron et al. "Combating Hyperthermia in Acute Stroke." American Association. November 10, 1997, pg. 529-534.
- Polderman, Kees. "Induced hypothermia and fever control for prevention and treatment of neurological injuries." Lancet. 2008; 371: 1955–69.
- Schwab, Stefan et al. "Feasibility and Safety of Moderate Hypothermia After Massive Hemisphere Infarction." American Heart Association. June 4, 2001, pg. 2033-2035.
- Holzer, Michael et al. "Efficacy and Safety of Endovascular Cooling After Cardiac Arrest." Stroke. 37:000-000. July 2006.
- Clumpner M, Mobley J. Raising the dead: Prehospital hypothermia for cardiac arrest patients may improve neurological outcome and survival to discharge. EMS 37(9): 52-60, Sep 2008.
- Harris et al 2012 Systematic review of head cooling in adults after traumatic brain injury and stroke. Health Technology Assessment 16(45):1-175, Appendix VII Non-invasive head cooling devices and methods. Full text at: http://www.hta.ac.uk/1777
- Jacobs et al 2007 Cooling for newborns with hypoxic ischaemic encephalopathy. Cochrane Database of Systematic Reviews 2007, Issue 4. Art. No.: CD003311. DOI: 10.1002/14651858.CD003311.pub2.
- Holzer, Michael. "Mild Hypothermia to Improve the Neurologic Outcome After Cardiac Arrest." New England Journal of Medicine. (2002) Vol. 346, No. 8.
- Hypothermia After Cardiac Arrest: An Advisory Statement by the Advanced Life Support Task Force of the International Liaison Committee on Resuscitation - Nolan et ...
- Etc…

MOTIVATION

- Despite decades of technology advancements, the feasibility and affordability of a manned mission to Mars continues to be extremely challenging…

- Human crew and associated support items are a major driver on Mars mission mass, required number of launches, and complexity

“Anytime you introduce humans, it’s an order of magnitude or two more challenging”

– Dr. Bobby Braun, former NASA Chief Technologist

- What if we could minimize the crew “footprint” on the architecture? How could this be achieved? What would be the potential impact?

CURRENT PROCEDURE FOR TH

=

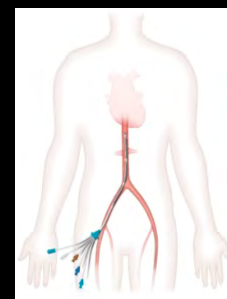
	Cooling	Rewarming
Target Temperature	89° to 93° F	97° to 98° F
Rate of Change	1° F per hour	1° to 4° F per hour
Time Required	6 hours	2 to 8 hours

- Patients are cooled to a mild hypothermic state (defined as a core temperature between 32 to 34°C / 89 to 93°F)
- Various cooling approaches exist, but there is no evidence demonstrating the superiority of any one cooling method over another
- Shivering is commonly suppressed with a continuous infusion of propofol and fentanyl, with or without intermittent treatment with benzodiazepines (e.g. midazolam)

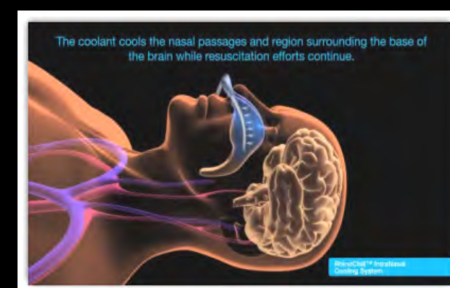
BODY THERMAL MANAGEMENT

There are three possible mechanisms for thermal management of crew.

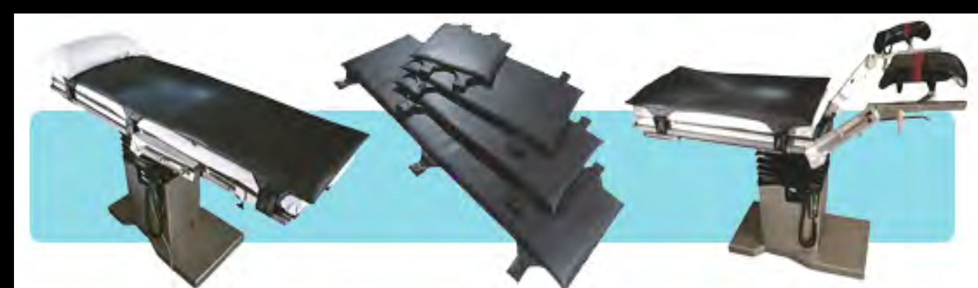
1. Invasive – e.g. CoolGard 3000R™ with IcyT catheter by ZOLL Medical.



2. Non-invasive – e.g. RhinoChill System ™



3. Passive Cooling with rewarming – e.g. KOALA System ™

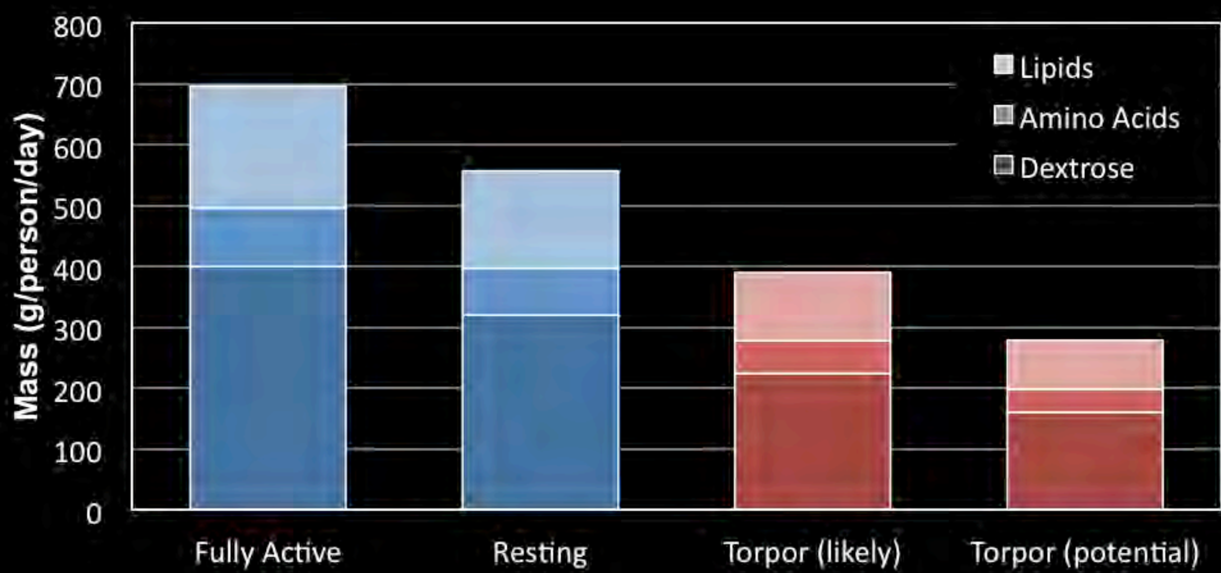


All are low mass, low power, and easily automated.

TOTAL PARENTERAL NUTRITION

TPN is the feeding of a person **intravenously** by a mixture containing lipids, amino acids, dextrose, electrolytes, vitamins, and trace elements; **all essential nutrients** for human body to function

- Delivered via a tunneled central venous catheter or a peripherally inserted central catheter (PICC)
- Administered through pump or gravity IV, usually given at around 50 ml hour with supplemental maintenance fluids
- Bypasses the usual process of eating and digestion; digestive tract is inactive



* Note dosage does not include maintenance fluids

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POTENTIAL MEDICAL CHALLENGES

Issue	Initiator	Solution/Comment
TORPOR-SPECIFIC		
Thromboembolism (Blood Clotting)	Prolonged sleep status and indwelling IVs	Periodic heparin flushes to dissolve clots, Clotting is generally reduced in TH state, Minimize IV access
Bleeding	Decrease in coagulation factor activity	Not a significant concern outside of trauma May decrease risk of thromboembolism
Infection	Temperature reduction in white blood cell activity	Minimize IV access, improved sterile techniques, use of tunneled catheters and antibiotic-infused catheters
Electrolyte Imbalances	Decreased cellular metabolism	Close monitoring and IV stabilization with TPN
Fatty Liver and Liver Failure	Long term TPN usage	Can alternate source of lipids to reduce risk
Other Complications (hypo/ hyper glycemia, bile stasis, etc.)	TPN and reduced metabolic rate	Augment TPN with insulin, exogenous CCK, etc. Avoid abrupt termination of TPN
GENERAL CREWED SPACEFLIGHT		
Bone Demineralization and Density Loss	Prolonged zero-G environment	Pharmaceuticals (e.g. bisphosphonates) Artificially-induced gravity
Muscle Atrophy	Disuse	Automated physical therapy tools Neuromuscular electrical stimulation (NMES)

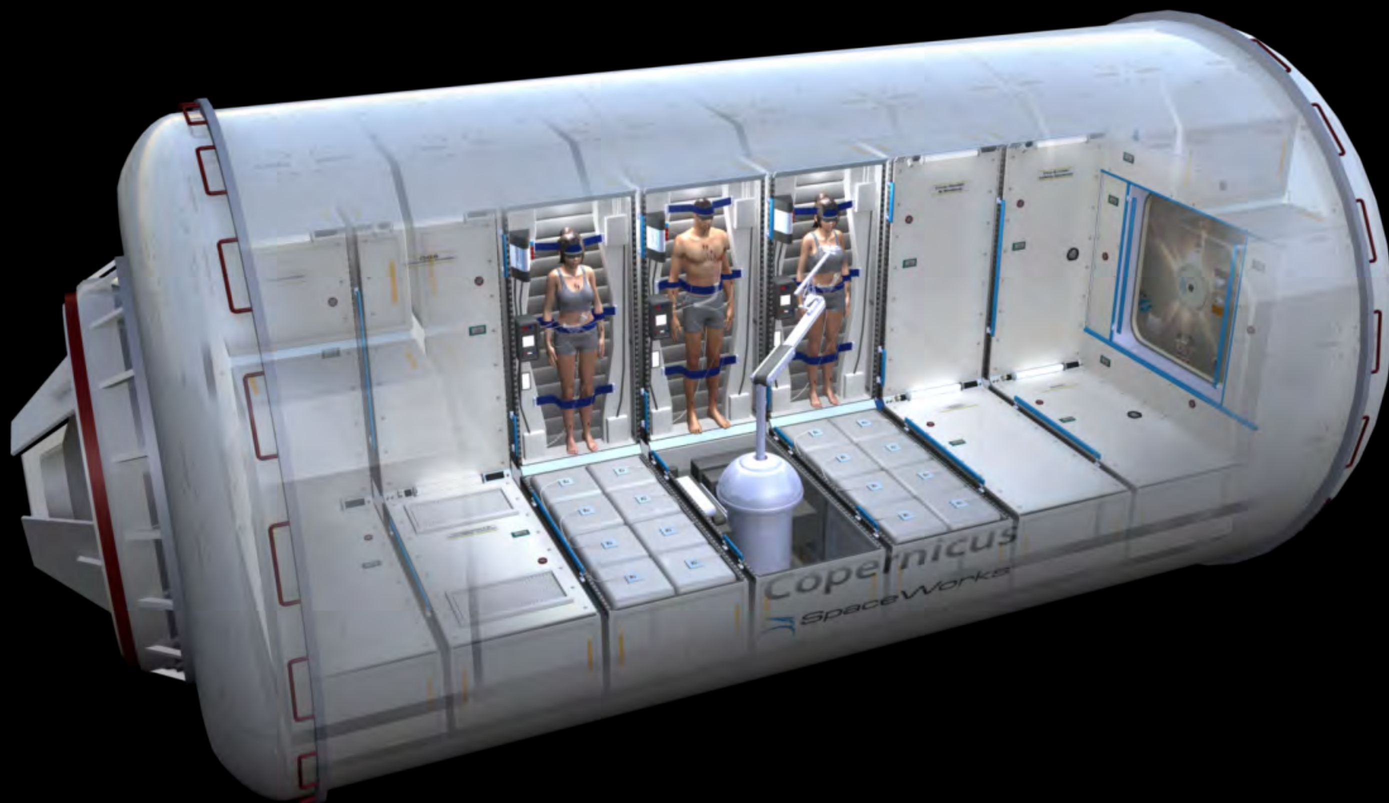
MEDICAL QUESTIONS

- What is the best technique for obtaining hypothermic state?
- Are there any long-term torpor and TPN affects on crew health?
- How does long-term torpor affect crew functional abilities?
- What are the protocols during emergency warming/wake scenarios? Can this process be accelerated?

CREW HABITAT

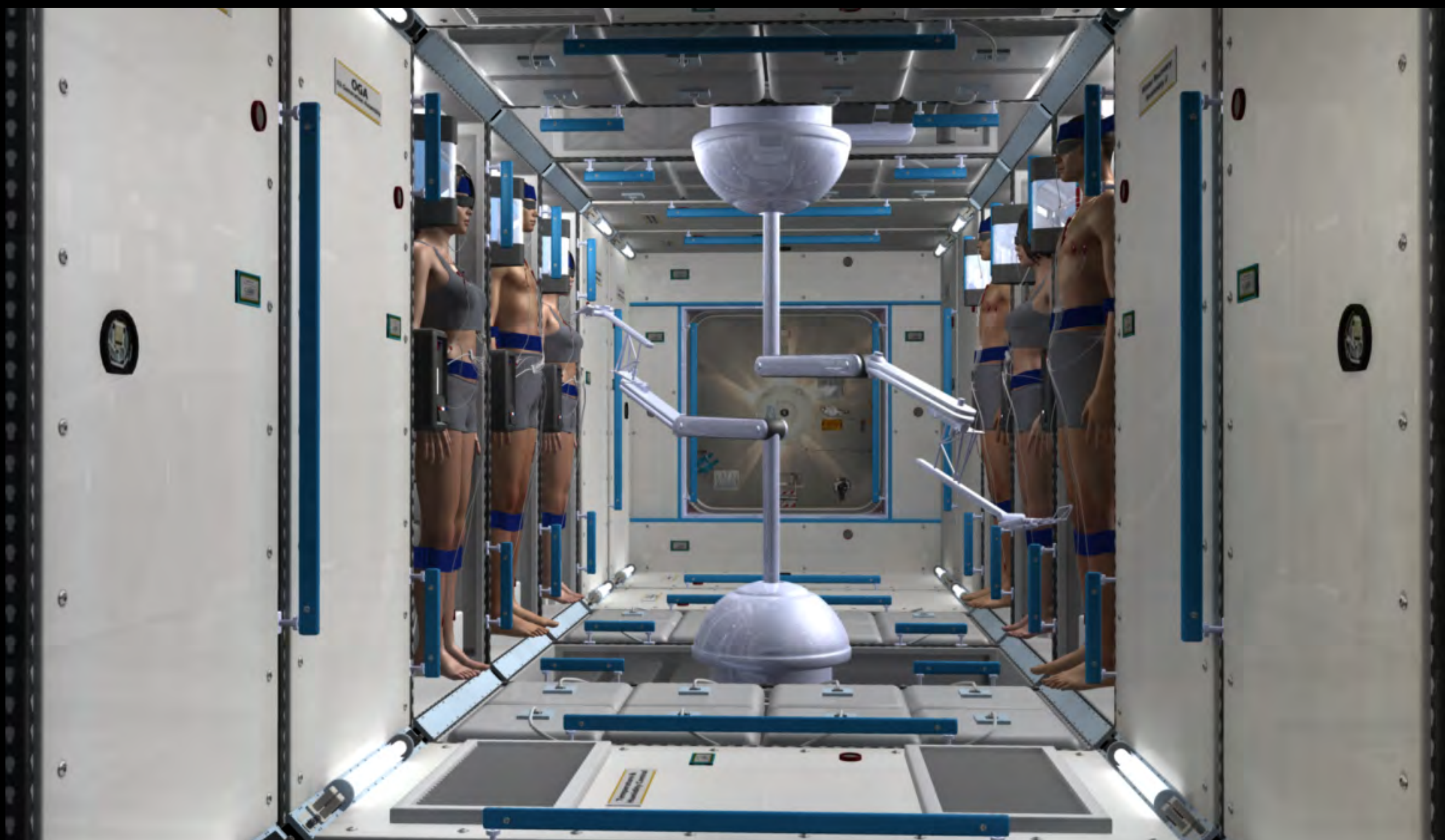
OVERVIEW

- Baseline “zero-G” habitat design evolved from ISS crew modules
- Closed-loop oxygen production and water recovery
- Supports 6 crew for in-space mission segments
  - Carries TPN solution for 180-day out/return mission + 500-day aborted surface mission contingency
- Two end-hatches provide access to Earth Return Vehicle (ERV) and docking port
  - Provide additional livable volume in event of an emergency/“awake” crew



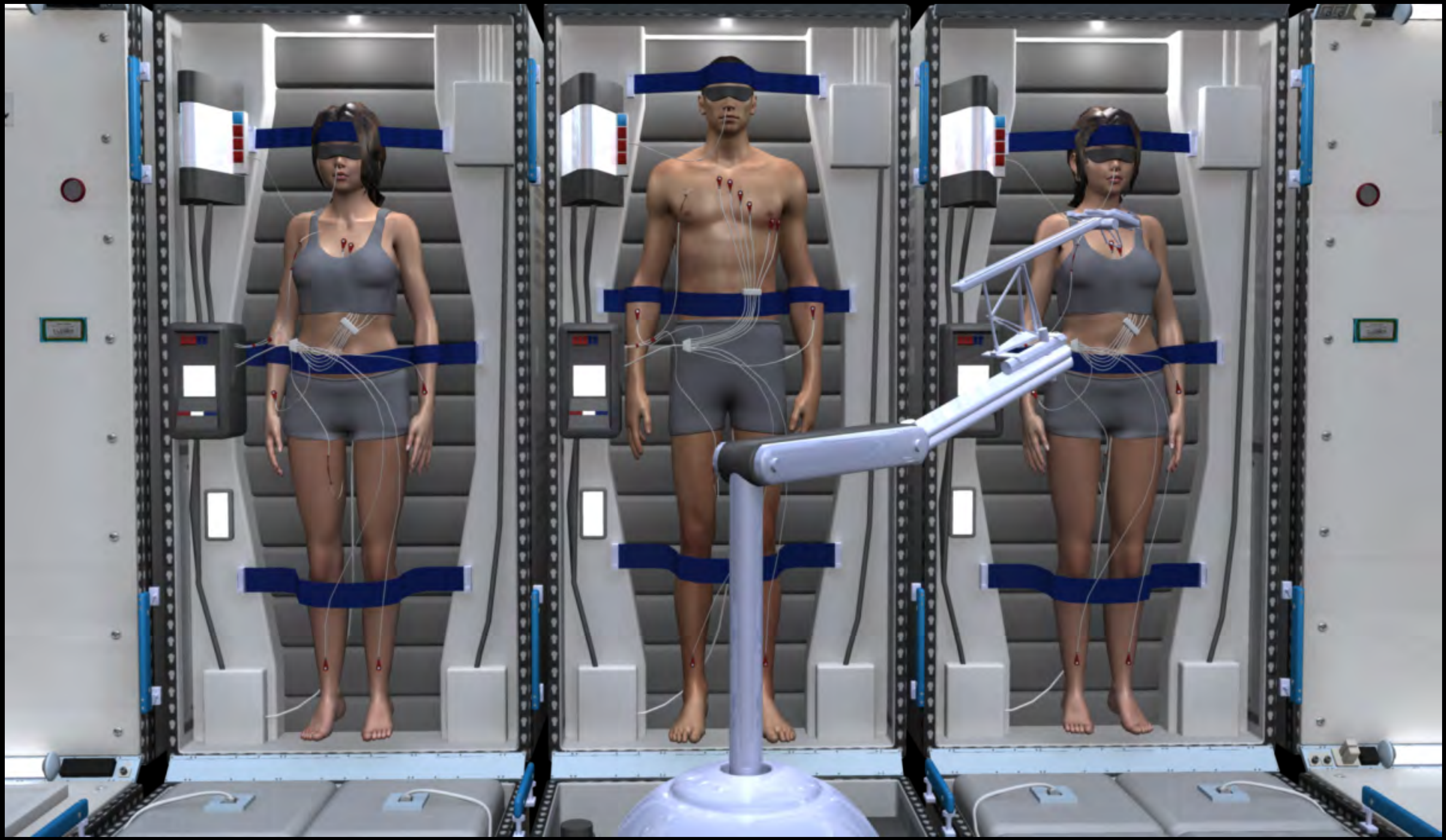
INTERIOR

- Robotic Manipulator Arms used to manage, manipulate crew as needed
- Supports Neuromuscular Electrical Stimulation (NMES) for muscle activation to prevent muscular atrophy
  - Very low level electrical impulse administered to key muscle groups



CREW ACCOMMODATIONS

- Crew nutrition provided through automated administration of TPN with active monitoring and feedback
- Body thermal control maintained with redundant cooling (intranasal) and warming (conduction/convection) systems



CREW SUPPORT SYSTEMS

Thermal pads (warming)

TPN administered via tunneled central venous catheter in chest

Alternate tunneled central venous catheter for TPN administration in inner thigh

Thermal management system inserted through nasal cavity (cooling)

Sensor leads across body

Urine collection assembly and drain line

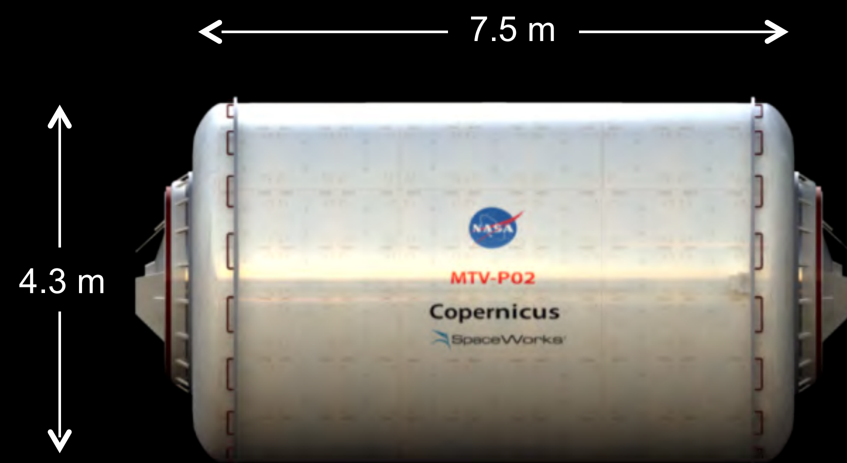
Human model assets credit: http://tf3dm.com/ and http://www.turbosquid.com/

SIZE COMPARISON

Reference Habitat (NASA DRA 5.0)

Total Pressurized Volume : 475 m^3
Habitable Volume : 380 m^3
Mass with Consumables : 41.3 t
Power Required : 50 kW

Torpor Stasis Habitat

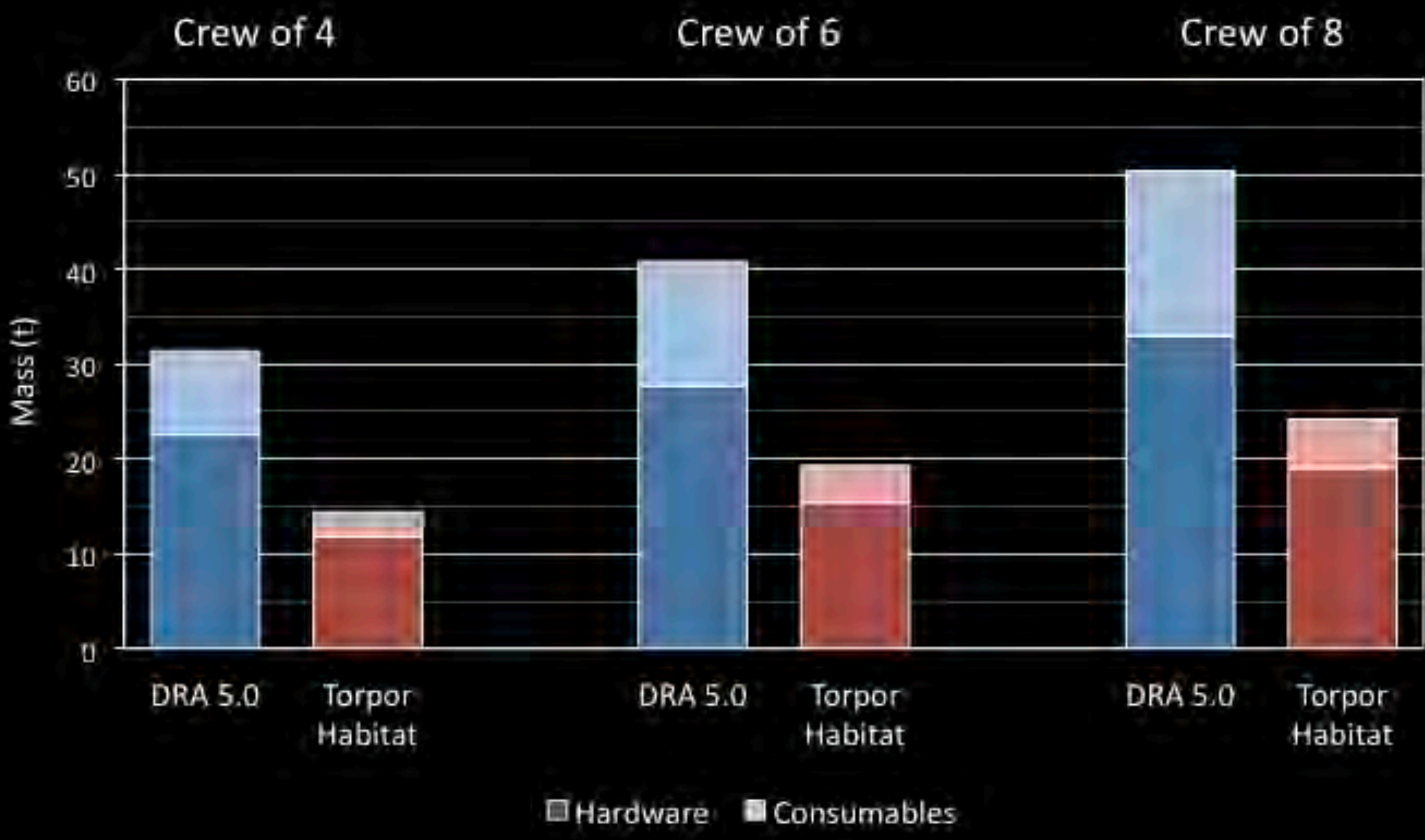


Total Pressurized Volume : 105 m^3
Habitable Volume : 40 m^3
Mass with Consumables : 19.8 t
Power Required : 30 kW

MASS COMPARISON

ITEM	DRA 5.0 Reference (kg)	Zero-G Stasis Habitat (kg)	Delta (%)
Structure	2,080	1,170	*-44%*
Crew Accommodations	3,960	1,400	*-65%*
Environmental Control & Life Support	3,850	2,410	*-37%*
Thermal Management System	1,210	750	*-38%*
Power System	6,240	3,420	*-45%*
Avionics	280	280	-
EVA Systems	840	840	-
Mass Growth Allowance (30%)	4,690	2,660	*-43%*
Additional Spares	4,550	2,500	*-45%*
Crew	560	560	-
Total Transit Habitat Mass	**28,260**	**15,990**	*-43%*
Food (Return + Outbound Trip)	5,480	1,620	*-70%*
Food (Contingency)	7,600	2,250	*-70%*
Total Consumables Mass	**13,080**	**3,870**	*-70%*
TOTAL MASS IN LEO	**41,330**	**19,860**	*-52%*

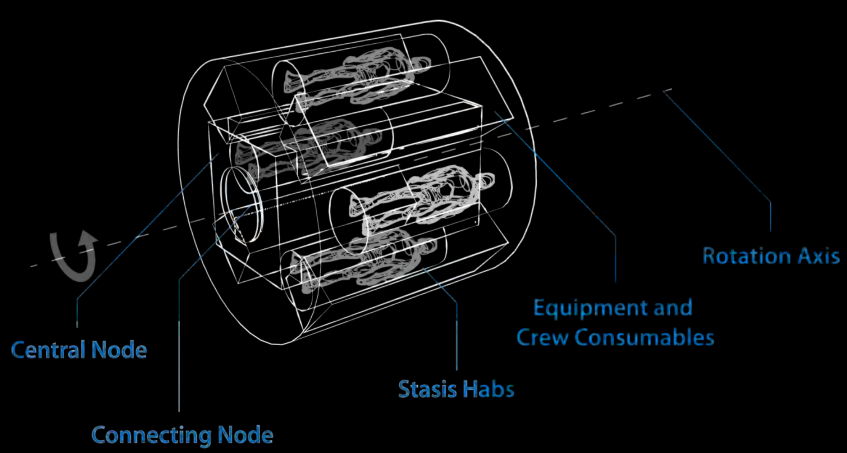
CREW SIZE COMPARISON



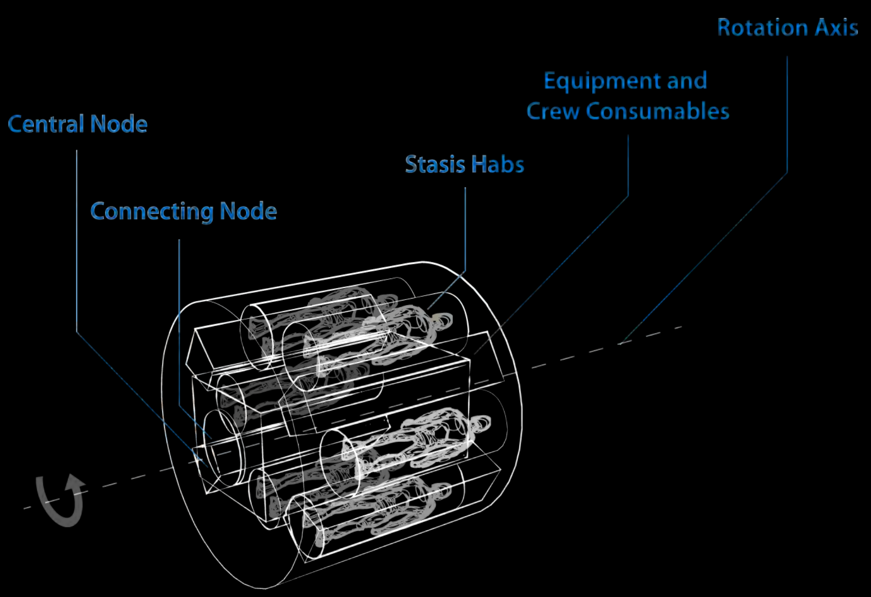
Torpor System Permits Crew Size Growth of Over 2X !

ARTIFICIALLY-GRAVITY HAB DESIGN

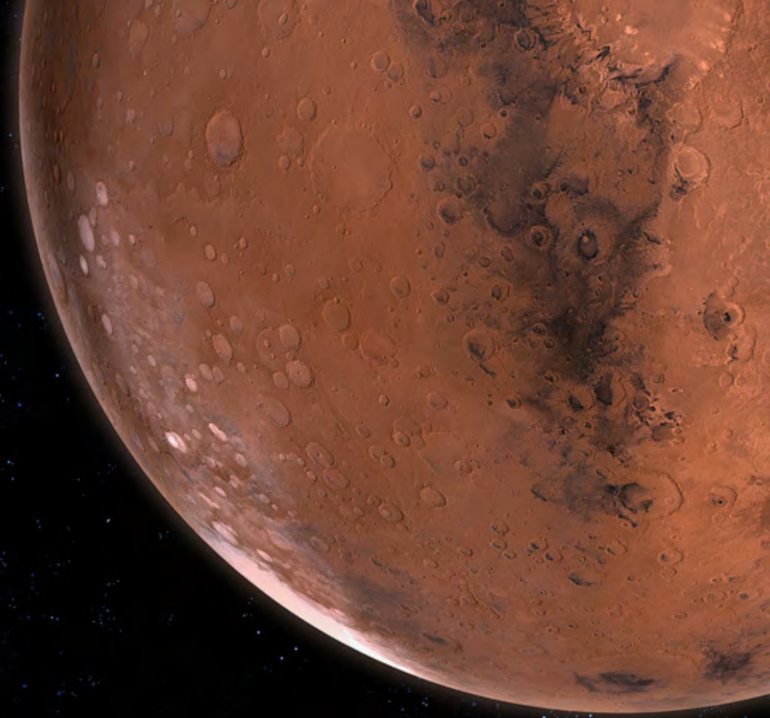
- For the Mars DRA 5.0, the baseline habitat approach is to provide a zero-gravity environment for the crew
- Performance assessment of habitats designed to support an induced gravity environment is currently underway



4-Crew

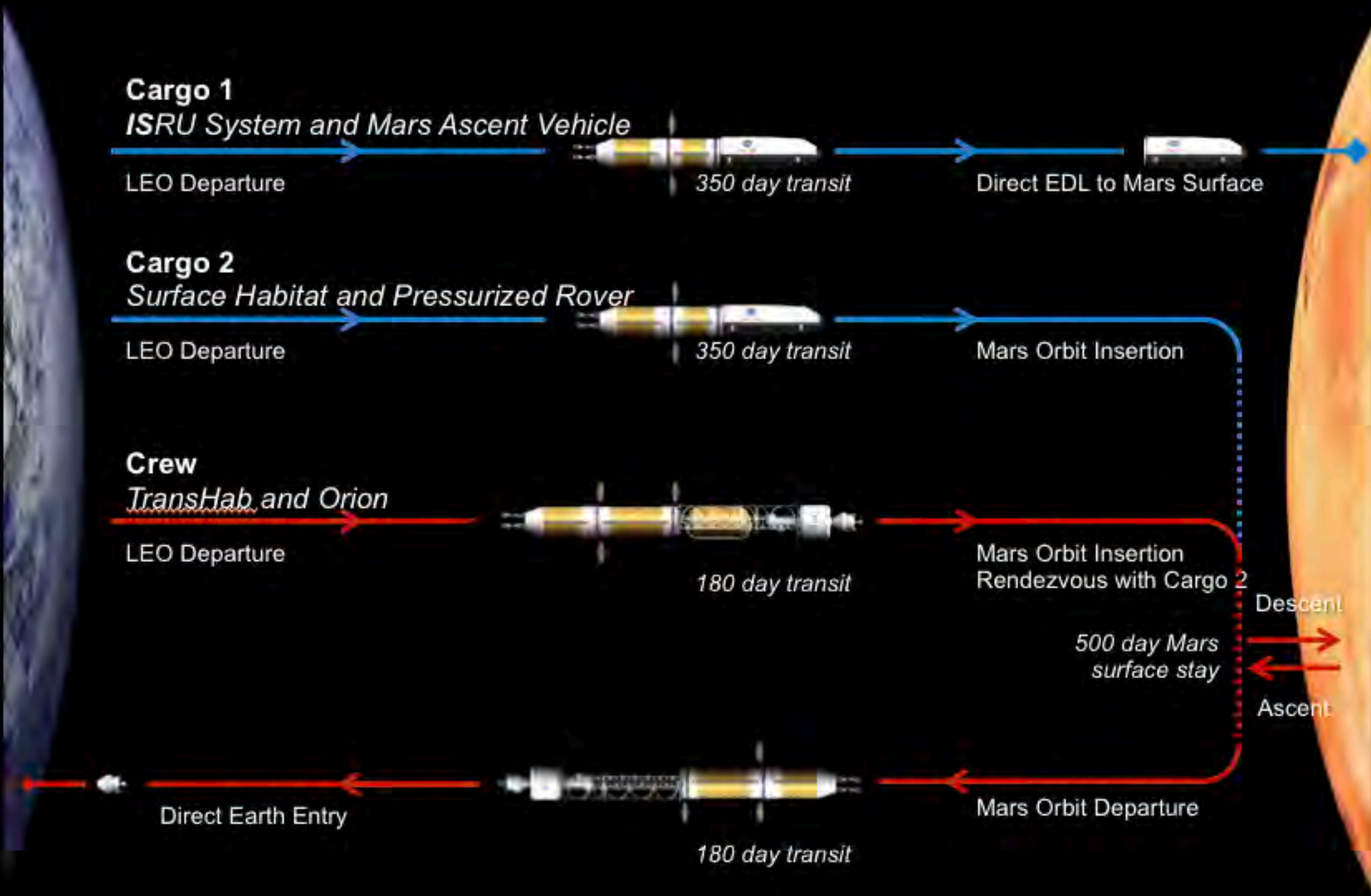


6-Crew



MARS MISSION ARCHITECTURE

NASA MARS DRA 5.0



MISSION MODELING

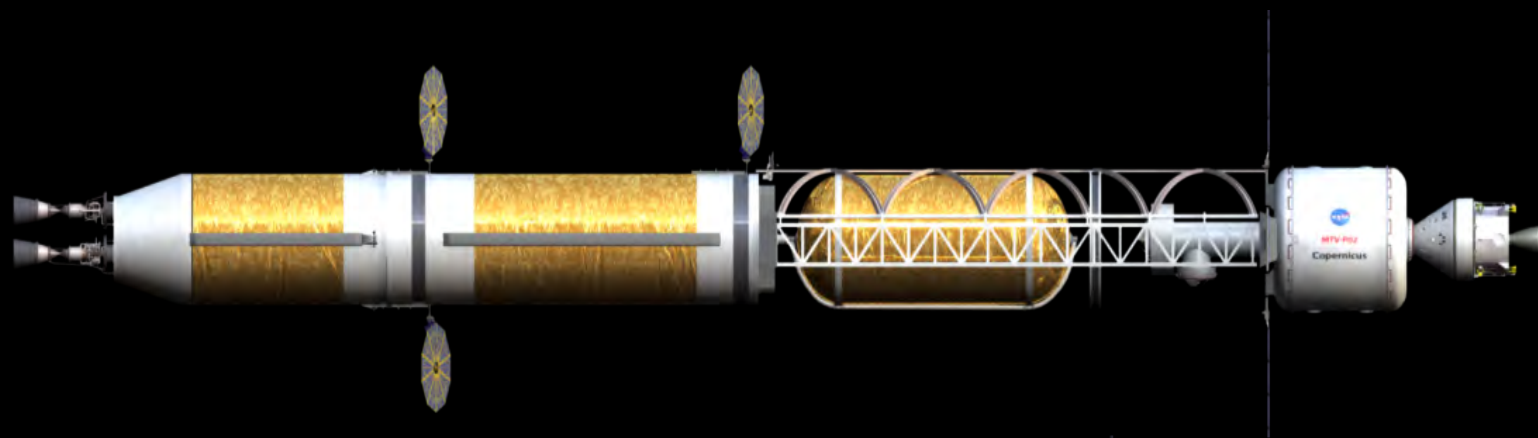
- Based on DRA 5.0 final reports, an end-to-end mission model was constructed to replicate the study results assuming the same ground rules, technologies, margins, and mission performance (i.e. delta-Vs).

- DRA 5.0 TransHab element was then replaced with the torpor-inducing habitat design (both zero-G systems), and the entire crew transfer stage was resized with the lower mass habitat

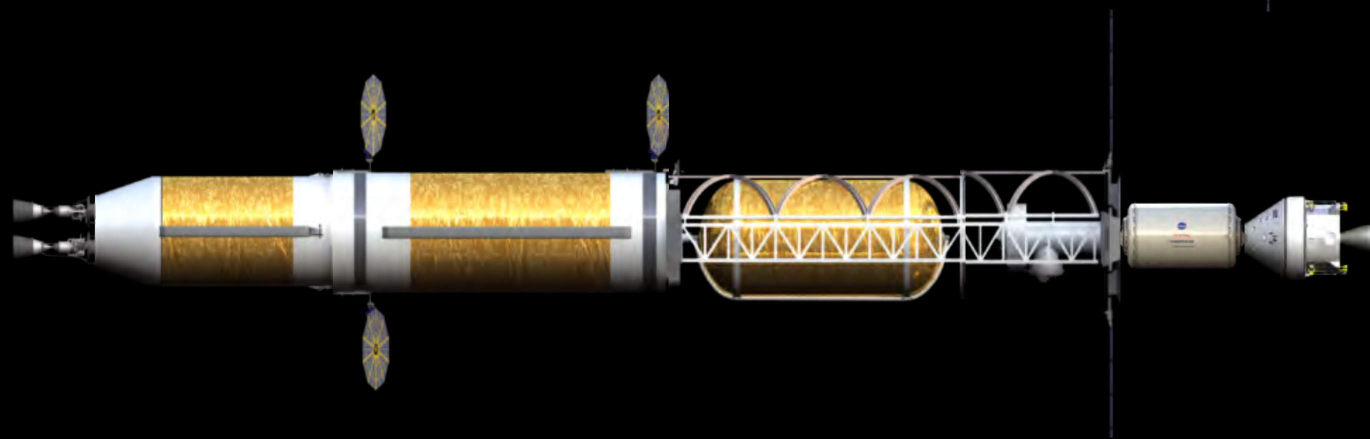
- For comparison, both the baseline NTR-powered transfer stage as well as the all-chemical LOX/LH2-powered transfer stage were evaluated

NTR SYSTEM COMPARISON

DRA 5.0
Reference
Crewed MTV
IMLEO : 356 t
Length : 97 m



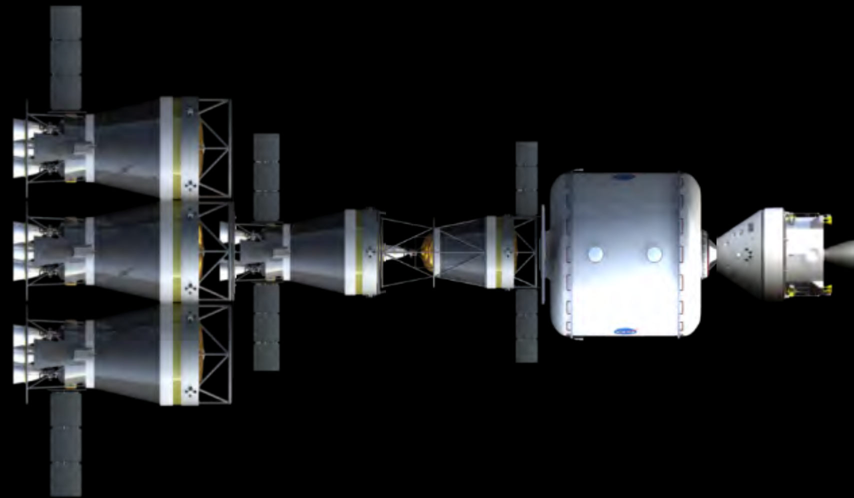
Torpor-Enabled
Crewed MTV
IMLEO : 271 t
Length : 85 m



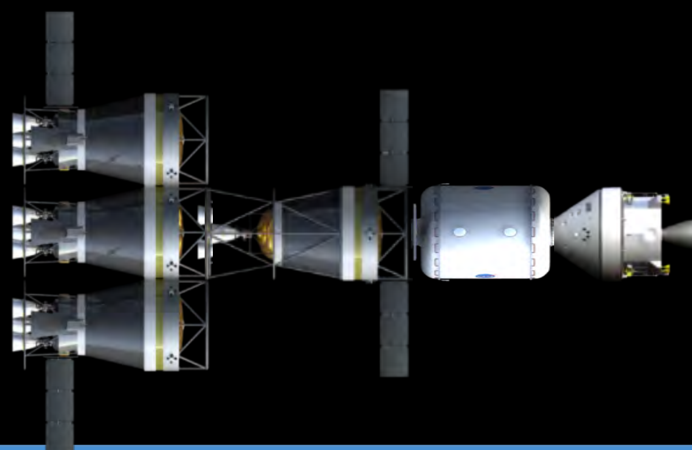
IMLEO Savings of over <u>85 t</u> for NTR-Powered System!
Equivalent mass requires Isp increase of >200 s on NTR

CHEMICAL SYSTEM COMPARISON

DRA 5.0
Reference
Crewed MTV
IMLEO : 486 t
Length : 76 m



Torpor-Enabled
Crewed MTV
IMLEO : 335 t
Length : 57 m



IMLEO Savings of over <u>150 t</u> for Chemical-Powered System.
Elimination of Entire Stage and Reduction of Engine Count.
Chemical architecture IMLEO lower than non-Torpor NTR-based system!

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SYNOPSIS

SUMMARY

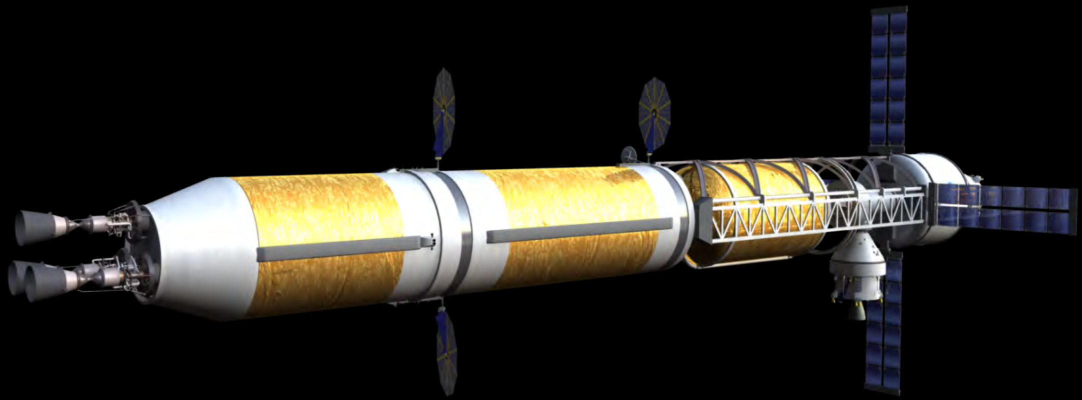
- Our approach is based on extending current medical practices and avoids the intractable challenges often associated with cell metabolic cessation through cryogenic freezing, etc.

- TH is a proven treatment for traumatic injuries, but it has not been applied for non-critical care purposes
  - While a number of animal studies are on-going on temperature and drug-inducement, they have yet to examine impact of prolonged TH treatments

- Multi-faceted concept that introduces wide-ranging questions that span medicine, physiology, psychology, and aerospace system design
  - Team is working to identify the key questions and challenges in these areas

CONCLUSIONS

- To date, have found **no "show-stoppers"**, although more research and review is still required
- Results indicate **substantial mass reduction** and potential for significant architecture improvements for even conservative system design
- Discussions with medical personnel continue to be encouraging



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