The ICV Study
“Integrated CardioVascular”
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Co-Is: Jim Thomas, MD, Rick Page, MD, Jeff Goldberger, MD, Steve Platts, PhD, Smith Johnston, MD, Doug Hamilton, MD, Jeff Hastings, MD

Cardiac Abnormalities in Rhythm and Diastolic function due to Inactivity, Atrophy and Confinement
UT Southwestern Medical Center
Spacelab Life Sciences - 1

Buckey et al, JAP 1996
Cardiac Atrophy After Spaceflight

LV Mass Continues to Decrease Over 12 Weeks of Bedrest

Left Ventricular Mass (g)

Pre Post

0 140 160 180 200

-1%/week over many studies

Perhonen et al, JAP 2001
Cardiac Atrophy After Spaceflight

Perhonen et al, JAP 2001

Fritsch-Yelle et al, Am J Cardiol 1998

LV Mass Continues to Decrease Over 12 Weeks of Bedrest

~ 1%/week over many studies

Left Ventricular Mass (g)

Perhonen et al, JAP 2001

Fritsch-Yelle et al, Am J Cardiol 1998
2014 Mars Design Reference Mission Scenario (typical)

Flight Profile
- Transit out: 161 days
- Mars surface stay: 573 days
- Return: 154 days

Earth Departure
- Jan. 20, 2014

Mars Departure
- Jan. 24, 2016

Mars Arrival
- June 30, 2014

Earth Arrival
- June 26, 2016
LV Volume Decreases With Tilt Angle But Remains Above Upright On Mars After Landing
Tissue Doppler E' (mean)

Tissue Doppler Velocity Decreases With Tilt Angle

But Is Minimally Affected on Landing Day
Comprehensive Cardiac MRI for LV/RV Structure And Function

Stacked image
For mass and volume

Delayed Enhancement
To detect scar

Tagged image
For untwisting
Comprehensive Cardiac MRI for LV/RV Structure And Function

Stacked image For mass and volume

Delayed Enhancement To detect scar

Tagged image For untwisting
No Change in LV Morphology

LVEDV (ml)

LVESV (ml)

Pre-flight Post-flight

SV (ml)

LVEF (%)

Pre-flight Post-flight
No Change in Left Ventricular Mass

Pre-flight

Post-flight

LV mass (g)

108[90-134]

109[98-145]
No Change in RV Morphology
No Change in Right Ventricular Mass

RV mass (g)

Pre-flight
Post-flight
One Astronaut (very fit before flight)

Pre-flight:
- LVEDV: 165mL
- LV Mass: 178 g

Post-flight #2:
- LVEDV: 168 mL
- LV Mass: 176 g

LV Untwisting Velocity: \(-41.5\) deg/sec

Myocardial Tagging

Post-flight:
- LVEDV: 149 mL
- LV Mass: 158 g

LV Untwisting Velocity: \(-46.5\) deg/sec
Another Astronaut (less fit)

LV mass 74 gm
LVEDV  78 ml

Peak untwist -51 deg/sec

Pre-flight

Structural Imaging

Myocardial Tagging

LV mass 87 gm
LVEDV  90 ml

Peak untwist -46 deg/sec

Post-flight
Cardiac Mass
Is Determined by Cardiac Work

\[ SW = SV \times BP \]

\[ CW = SW \times HR \]

\[ CW/\text{Day} = \Sigma SW_i \]
Heart Rate

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<thead>
<tr>
<th>Time (s)</th>
<th>HR (BPM)</th>
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<td>90</td>
<td>57</td>
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Stroke Volume

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During evening (stable blood pressure)

During exercise

During sleep
During day time (stable blood pressure)

During exercise

During night time (sleep)
**Pre-Flight**

- Walk to Building S4
- Robotic Training
- Drink Coffee
- Walk a Dog

**Elliptical Machine (Exercise)**

**Cardiac Work (mmHg*ml)**

**Sleep**

**Red: Information from Flight Diary**
Change in LV Mass with Spaceflight Is Proportional to Changes in Volume Work

\[ y = 0.56x + 4.1 \]

\[ R^2 = 0.644 \]
POTS: young women whose hearts are “two sizes too small”
Presence of Delayed Enhancement In Patients Identifies High Risk For Ventricular Arrhythmias

Adabag, A. S. et al. J Am Coll Cardiol 2008;51:1369-1374
No Focal Delayed Enhancement After Spaceflight
T1 Mapping with MOLLI sequence

PRE-FLIGHT

T1 pre-contrast: 1172 ms

POST-FLIGHT

T1 pre-contrast: 1168ms

T1 post-contrast: 444 ms

T1 post-contrast:494 ms

Lots of Arrhythmias Observed – Both Pre And During Spaceflight
No Consistent Changes in Ventricular Ectopy
No Consistent Changes in Supraventricular Ectopy
The Heart’s Electrical Activity Coordinates the Heart Beat

Depolarization

- $I_{Na}$
- $I_{Ca}$
- $I_{to}$

Repolarization

- $I_{kr}$
- $I_{ks}$

Inward Current

Outward Current

QRS

ST

T wave

-80mV
Raw ECG

Signal-averaged ECG

Collaboration with Jeff Goldberger, MD and Jason Ng PhD from Northwestern
12-lead ECG

Inverse Dower Transform

Frank-lead ECG

Filtered and amplified Frank-lead

40 Hz Bidirectional Highpass Filter

ECG Magnitude
QRSd: QRS duration (late potentials: >114 ms)
RMS = Root-mean-square voltage in last 40 ms (late potentials: <20uV)
LAS = Low-amplitude (<40 µV) signal duration in terminal QRS
(late potentials: >38 ms)
Signal-Averaged ECG Subject H

Pre1

FD14

FD30

FD75

FD135

R-15

Time (ms)

Amplitude (uV)

fQRSd = 66 ms
RMS = 105.1038 uV
LAS = 17 ms

fQRSd = 68 ms
RMS = 125.2844 uV
LAS = 16 ms

fQRSd = 66 ms
RMS = 115.7917 uV
LAS = 16 ms

fQRSd = 96 ms
RMS = 23.173 uV
LAS = 30 ms

fQRSd = 101 ms
RMS = 21.0425 uV
LAS = 33 ms

fQRSd = 67 ms
RMS = 125.849 uV
LAS = 15 ms

fQRSd = 96 ms
RMS = 23.173 uV
LAS = 30 ms
No Clear Trends for Changes in SAECG Measures of Conduction
TW Alternans
Astronaut B
Lead V5 (MMA)
Slight Increase in Resting TWA in Any Lead But Not Changed in V5 (most clinical data)
Summary Conclusions from ICV

1). Given current training programs, and ground based interventions, cardiac morphology (right and left ventricular mass and volume) and function (EF and untwisting) are preserved after 6 months of spaceflight.

When landing on Mars after a 6 month flight, cardio-vascular function is highly likely to be sufficient to allow exploration activities, and there is little risk of orthostatic intolerance;

2). This cardiac adaptation to long duration spaceflight depends on the relative change in cardiac work between pre-flight and post-flight levels;
Summary Conclusions from ICV

3). In some individuals, a subtle change in cardiac ultrastructure may occur, that is suggestive of myocardial fibrosis. Whether this is an idiosyncratic response in a rare astronaut (e.g., subclinical myocarditis), or a more common direct response to the hemodynamics of spaceflight (pregnancy analogy) is unknown.

4). In general, long duration spaceflight does not appear to increase the risk for cardiac arrhythmias, and there are no microgravity specific changes in electrophysiology.

* However, there may be some astronauts who acquire a risk for potentially serious arrhythmias (and their secondary manifestations), either as a result of an infection, or an atypical response to microgravity.
So Many People To Thank!

1). The amazing technical support from the JSC Cardiovascular lab: Chris Ribreiro, David Martin, Stuart Lee, Mike Stenger and the rest of their team;

2). Outstanding project support from our Wylie team: Kelly Norwood, Matt Roper, Gwen Sandoz, Cathy Modica, et al;

3). Extraordinary flight surgeons; Doug Hamilton, Smith Johnston, and all the individual astronaut flight surgeons;

4). NASA Science Management: Peter Norsk, John Charles, Clarence Sams, Chuck Sawin, Victor Schneider and many others;

5). Many colleagues who helped with data analysis: Jason Ng, Jamie Kowal, James Daniels, Shuaib Abdullah, Shigeki Shibata, Qi Fu.