Defining the Relationship between Biomarkers of Oxidative and Inflammatory Stress and the Risk for Atherosclerosis in Astronauts during and after Long-duration Space Flight (CARDIO OX)

S.M.C. Lee[1], L.C. Ribeiro[1], D.S. Martin[1], S.M. Smith[2], S.R. Zwart[3], S.S. Laurie[1], B.R. Macias[1], and M.B. Stenger[2]

[1]KBRwyle, Houston, TX; [2]NASA Johnson Space Center, Houston, TX; [3]University of Texas Medical Branch, Galveston, TX

Human Research Program Investigators' Workshop

Galveston, TX

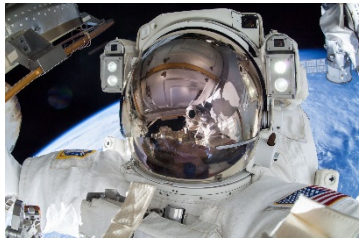
January 2020

Background

Long-duration: 4-6 months

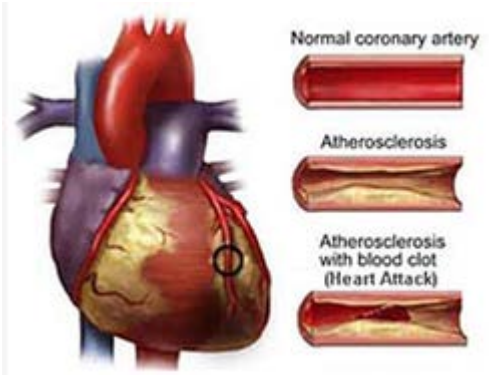
Exploration-class: 1-3 years

Oxidative Stress
Inflammation

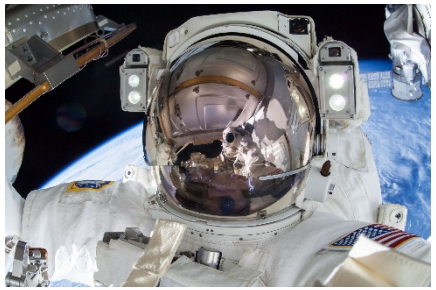


Background

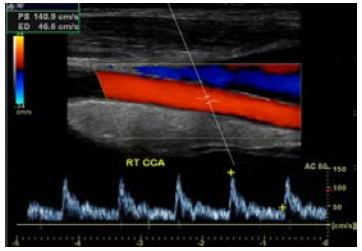
Oxidative Stress
Inflammation



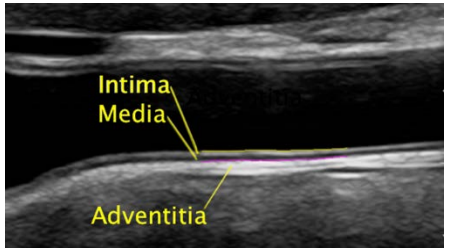
?



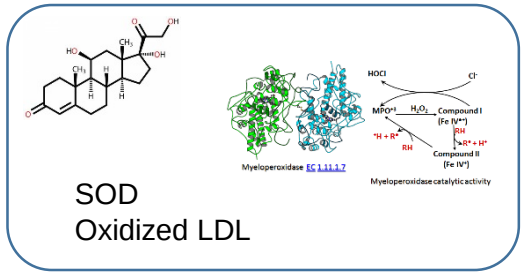
Arterial Function



cIMT



Oxidative and Inflammatory Biomarkers



Purpose and Hypothesis

Purpose:

- To determine if biomarkers of oxidative and inflammatory stress are elevated during and after long-duration spaceflight.
- To determine if vascular structure and function, markers that may predict future atherosclerotic disease, are altered up to 5 years following spaceflight.

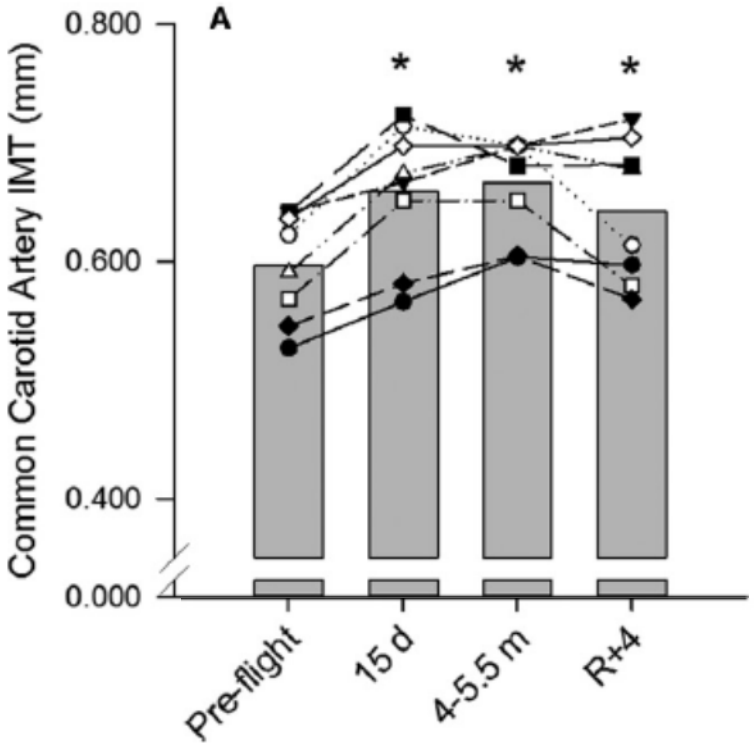
Central hypothesis:

- Biomarkers of oxidative and inflammatory stress will be elevated during long-duration spaceflight and will be related to changes in longer-term vascular structure and function as assessed by carotid intima-media thickness (cIMT) and flow-mediated dilation (FMD).

Carotid and Femoral Artery Intima-Media Thickness During 6 Months of Spaceflight

Philippe Arbeille; Romain Provost; Kathryn Zuj

AEROSPACE MEDICINE AND HUMAN PERFORMANCE Vol. 87, No. 5 May 2016

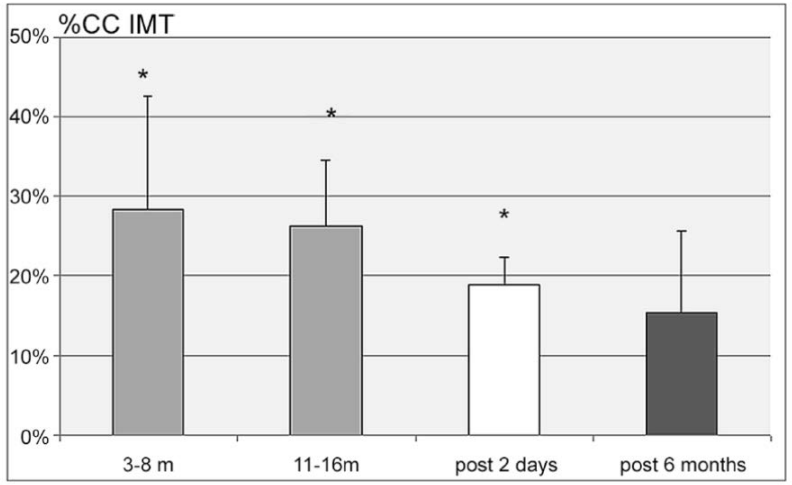


OPEN ACCESS Freely available online PLOS ONE

Adaptation of the Main Peripheral Artery and Vein to Long Term Confinement (MARS 500)

Philippe Arbeille[1]*, Romain Provost[1], Nicole Vincent[2], Andre Aubert[3]

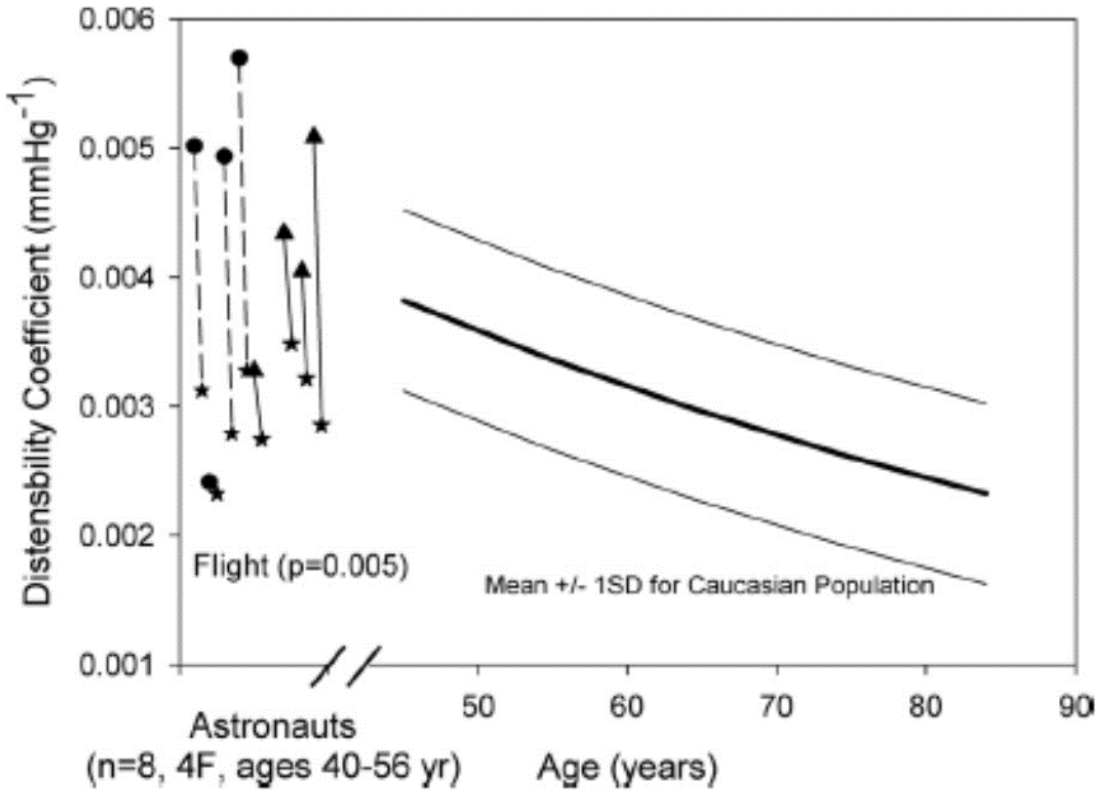
1 Medicine Physiologie Spatiale (UMPS-CERCOM) University Hospital Trousseau, Tours, France, 2 CRIP Laboratoire d'informatique, Faculte de Medecine, Paris V, France, 3 University Hospital Gasthuisberg, O&N Lab. of Experimental Cardiology, KU Leuven, Leuven, Belgium



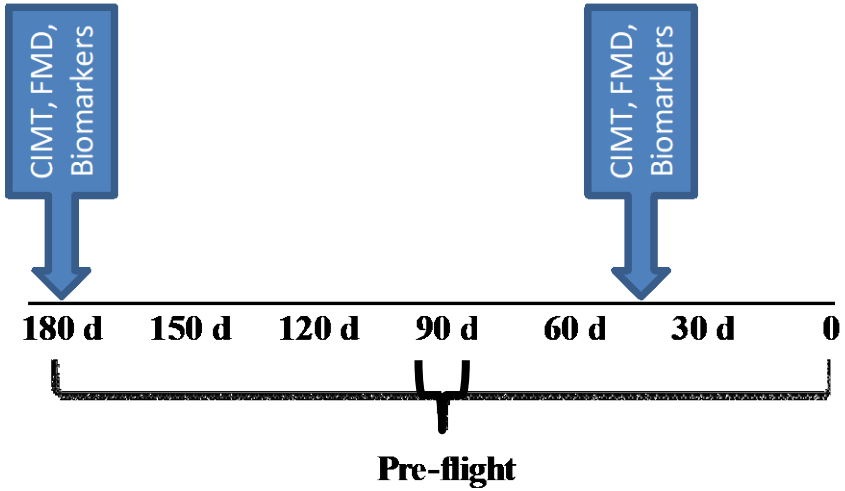
Increased postflight carotid artery stiffness and inflight insulin resistance resulting from 6-mo spaceflight in male and female astronauts

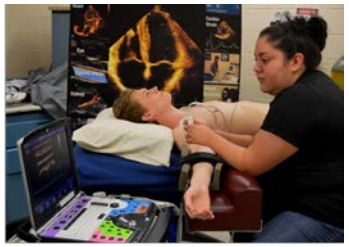
Richard L. Hughson,[1] Andrew D. Robertson,[1] Philippe Arbeille,[2] J. Kevin Shoemaker,[3] James W. E. Rush,[4] Katelyn S. Fraser,[1] and Danielle K. Greaves[1]

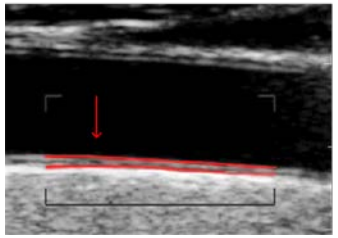
[1]Schlegel-University of Waterloo Research Institute for Aging, Waterloo, Ontario, Canada; [2]Unite Medecine Physiologie Spatiale, CERCOM, EFMP, CHU Trousseau, Tours, France; [3]School of Kinesiology and Department of Physiology and Pharmacology, University of Western Ontario, London, Ontario, Canada; and [4]Faculty of Applied Health Sciences, University of Waterloo, Waterloo, Ontario

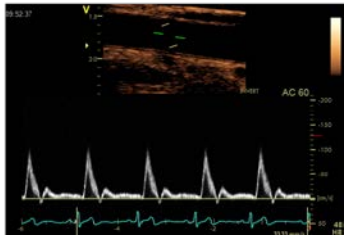


Study Timeline

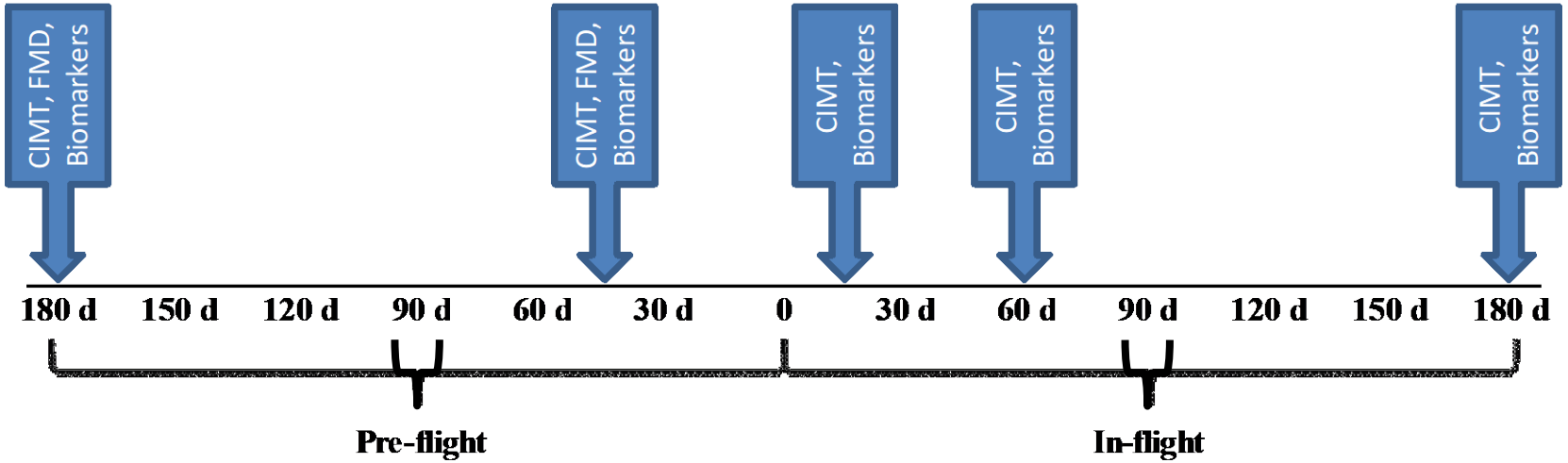


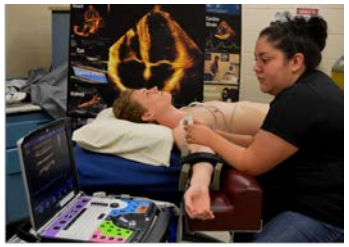


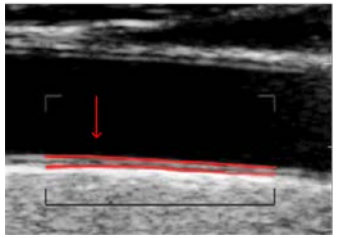


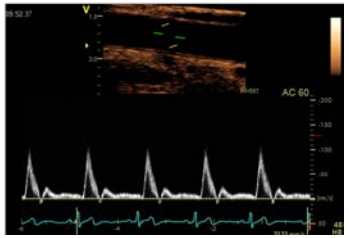


Study Timeline

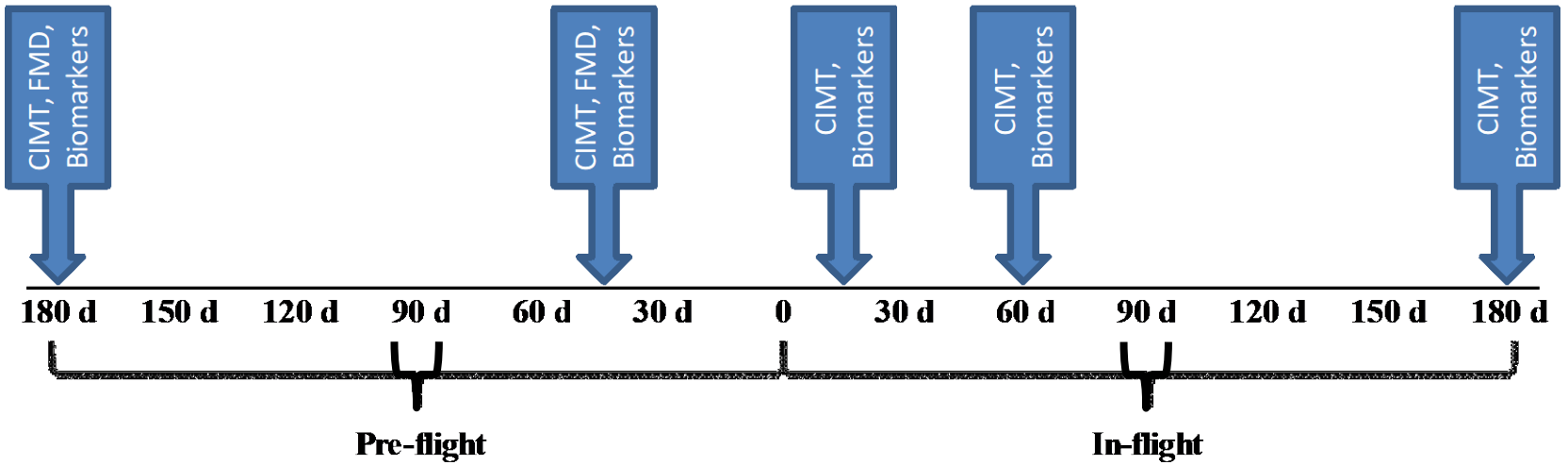


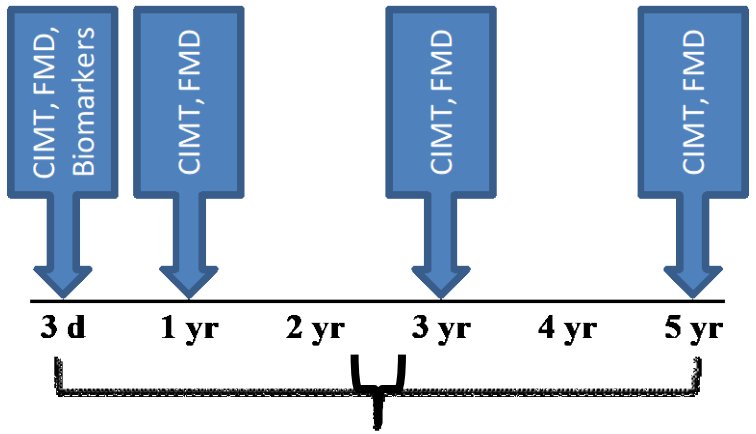






Study Timeline





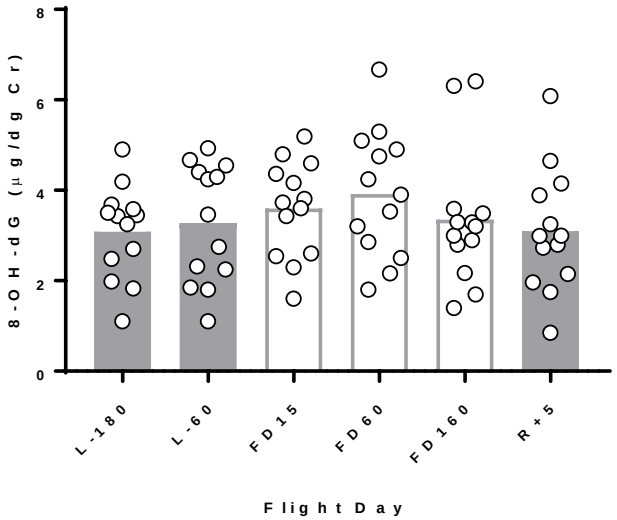
Subjects (3F, 10M)

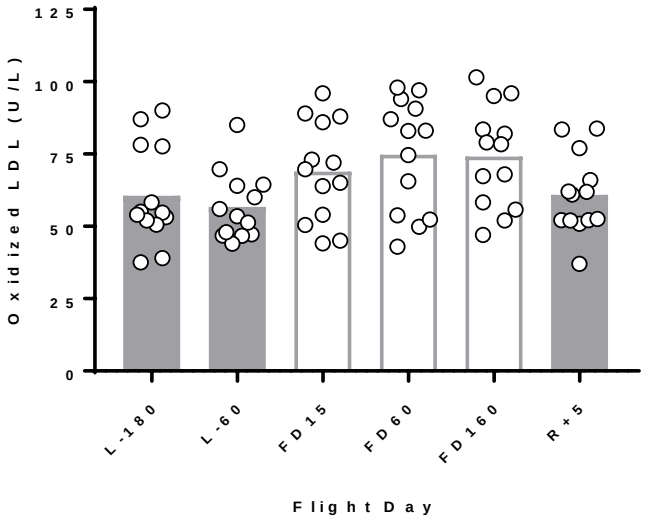
	Mean ± SD	Range
Age (yr)	46 ± 8	38 - 58
Height (cm)	176 ± 7	165 - 185
Weight (kg)	79.0 ± 11.3	62.2 - 94.6
VO_2peak (L/min)	3.25 ± 0.58	2.17 - 4.02
VO_2peak (mL/kg/min)	41.5 ± 4.8	32.0 - 47.4
Flight Duration (days)	189 ± 61	126 - 340

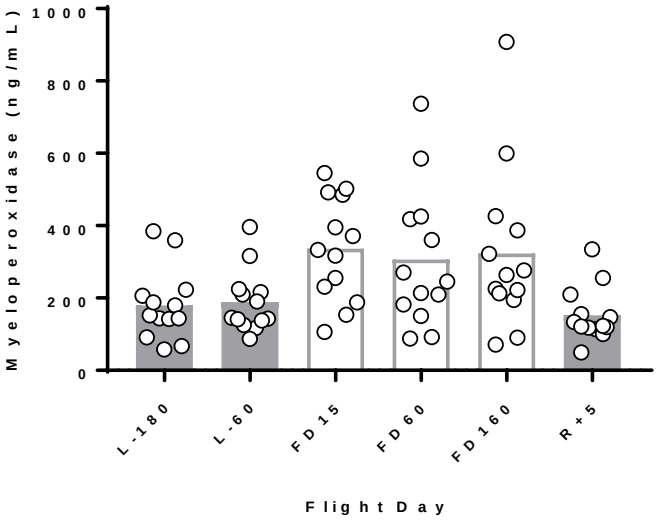
Urine and Blood Biomarkers

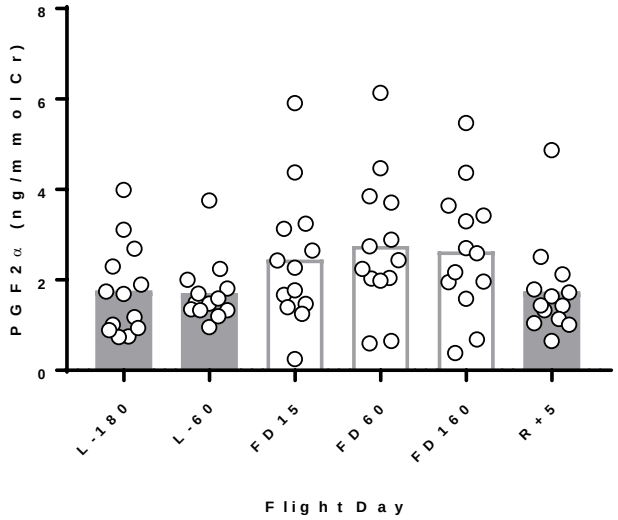
Oxidative Markers	Inflammatory Markers
8-hydroxy 2 deoxyguanosine (8-OH2dG)	Cortisol
8-iso-prostaglandin F2α (PGF2α)	Fibrinogen
Glutathione (oxidized and reduced)	Cytokines (TNF-α, IL-6, etc)
Superoxide dismutase (SOD)	hsC-reactive protein
Glutathione peroxidase	Total B2 microglobulin
Malondialdehyde	Neopterin
Myeloperoxidase	Lipoprotein-associated phospholipase (Lp-PLA2)
Oxidized LDL	

Biomarkers of Oxidative Stress

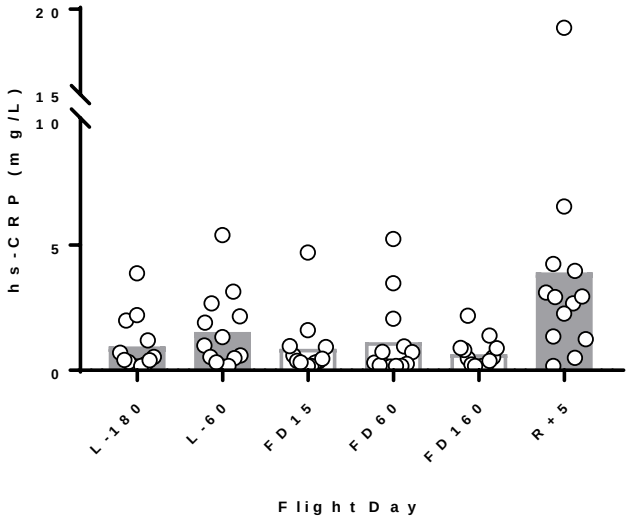


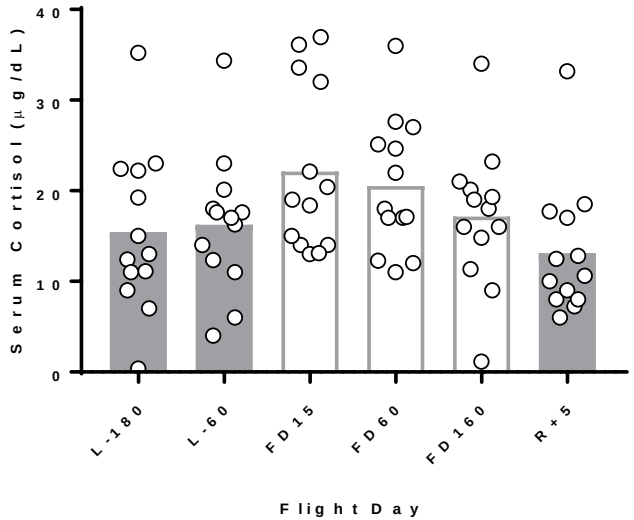


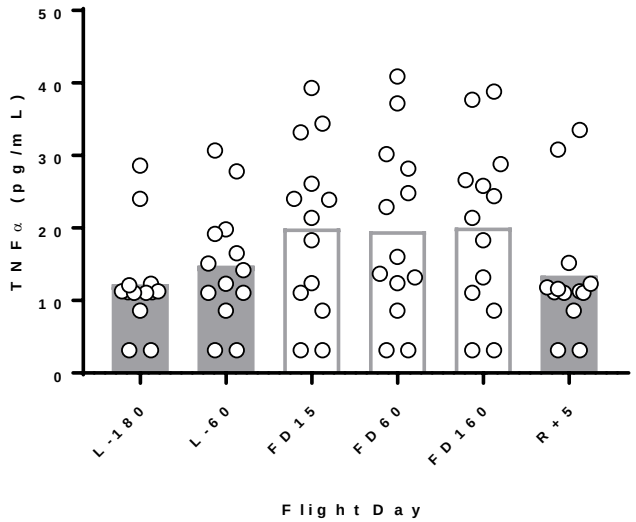


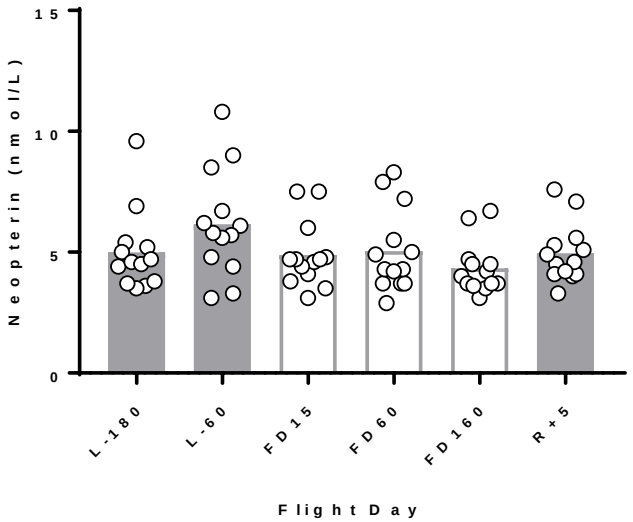


Biomarkers of Inflammation

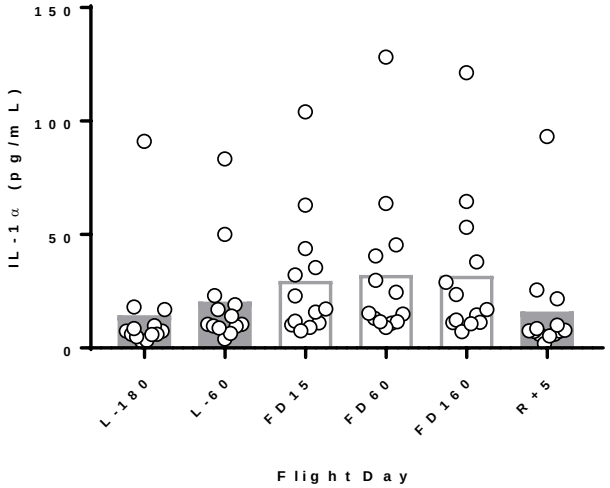


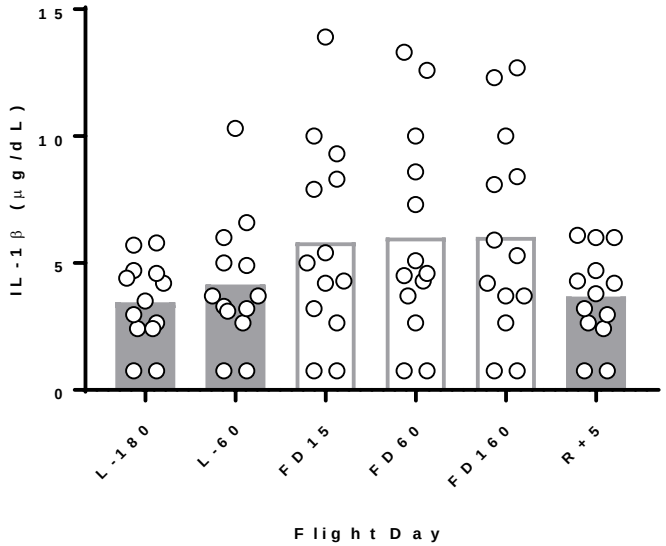


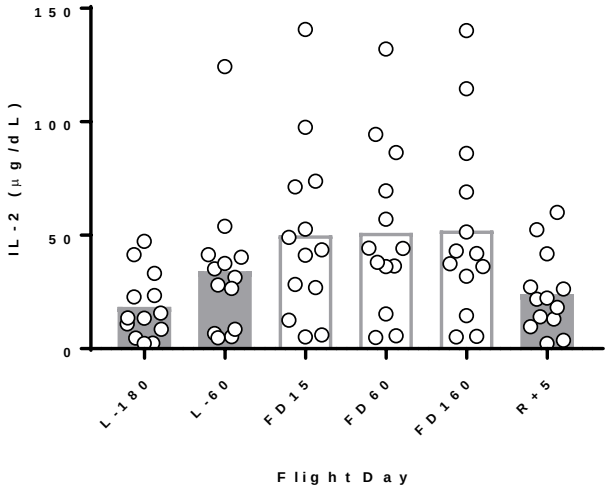


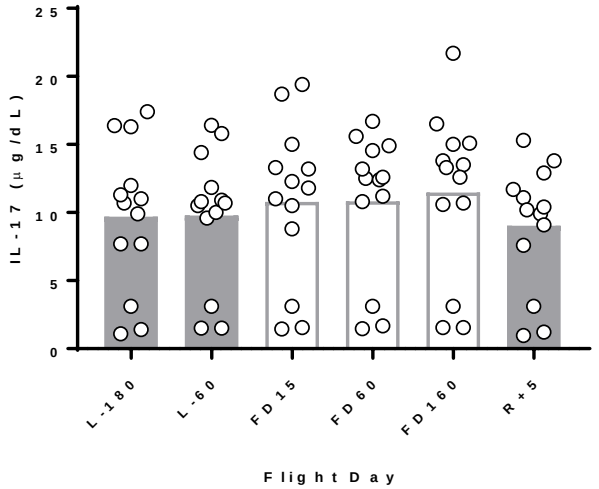


Cytokines

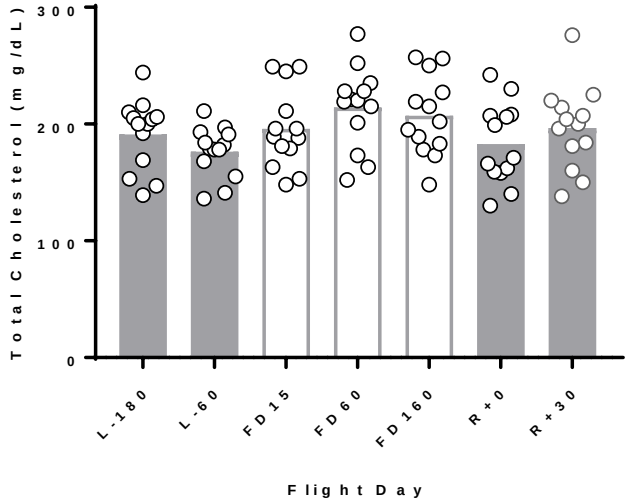

IL-1α (pg/mL)
150
100
50
0
L-180
L-60
FD15
FD60
FD160
R+5
Flight Day

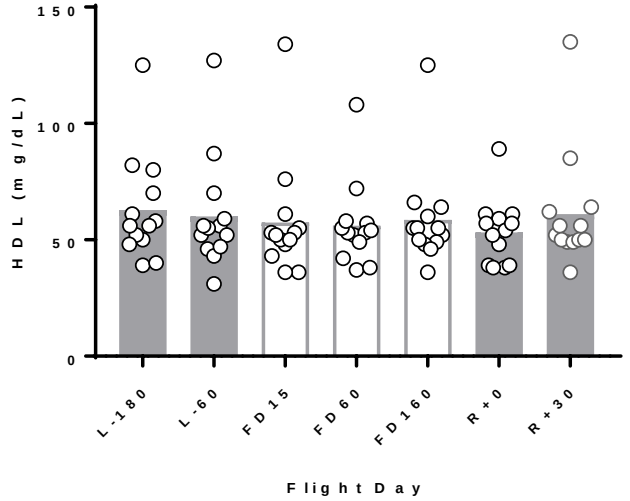

IL-1β (µg/dL)
15
10
5
0
L-180
L-60
FD15
FD60
FD160
R+5
Flight Day

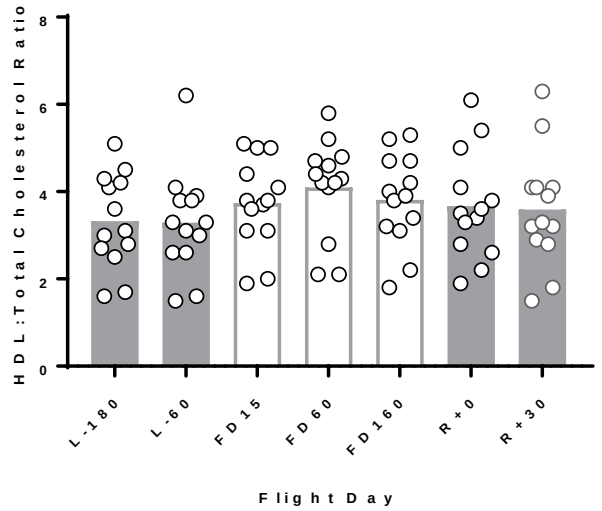

IL-2 (µg/dL)
150
100
50
0
L-180
L-60
FD15
FD60
FD160
R+5
Flight Day

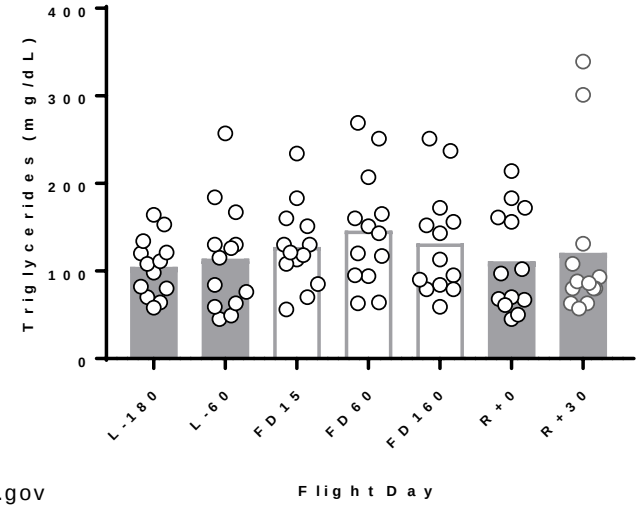

IL-17 (µg/dL)
25
20
15
10
5
0
L-180
L-60
FD15
FD60
FD160
R+5
Flight Day

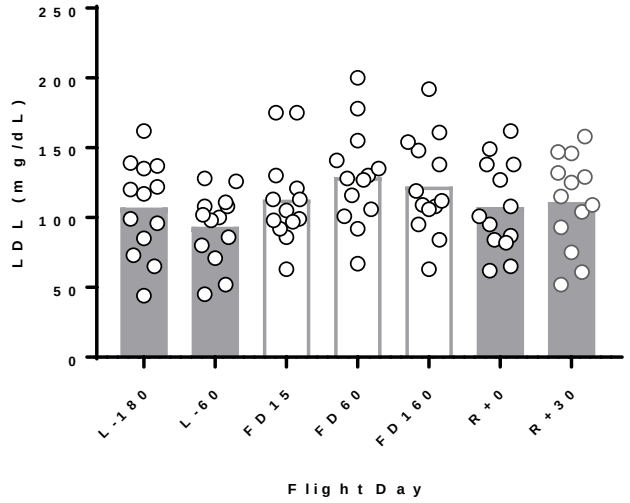
Lipid Profile

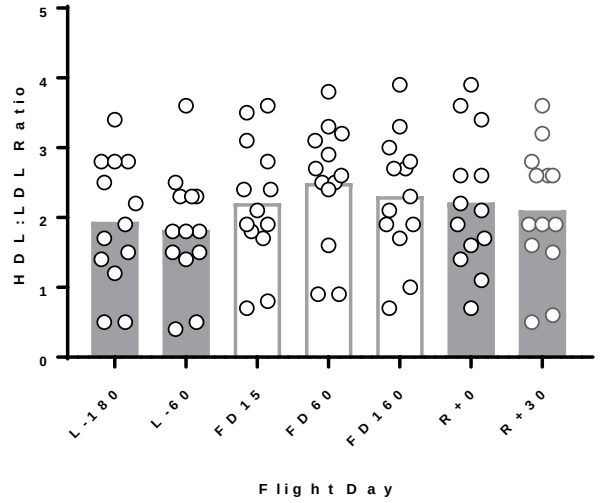




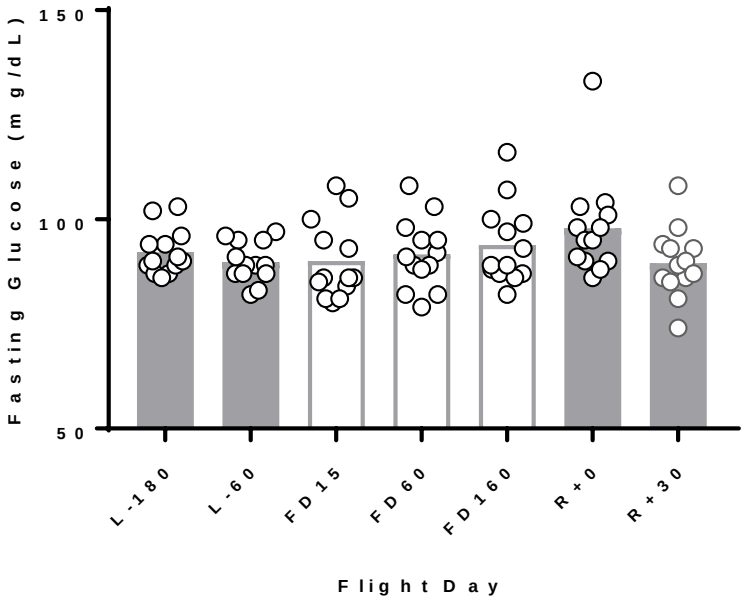


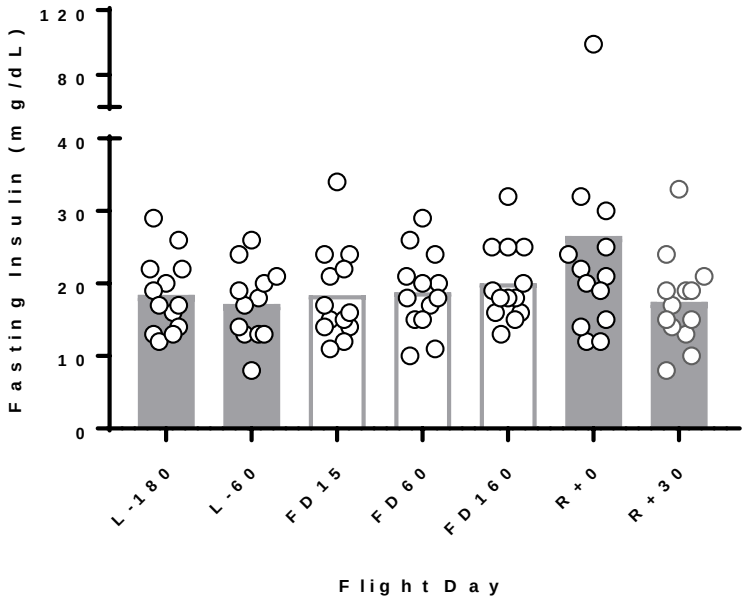


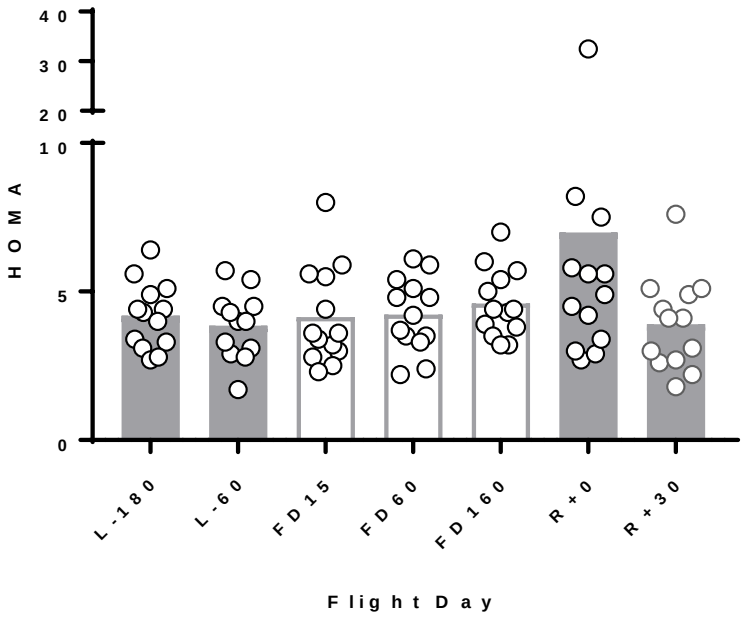




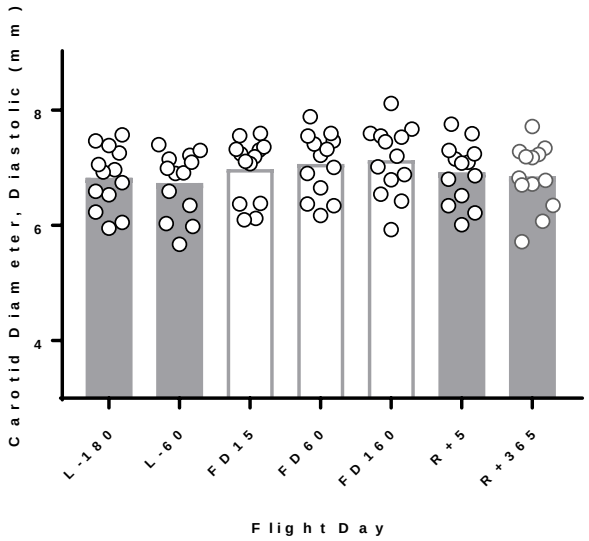
Insulin Resistance

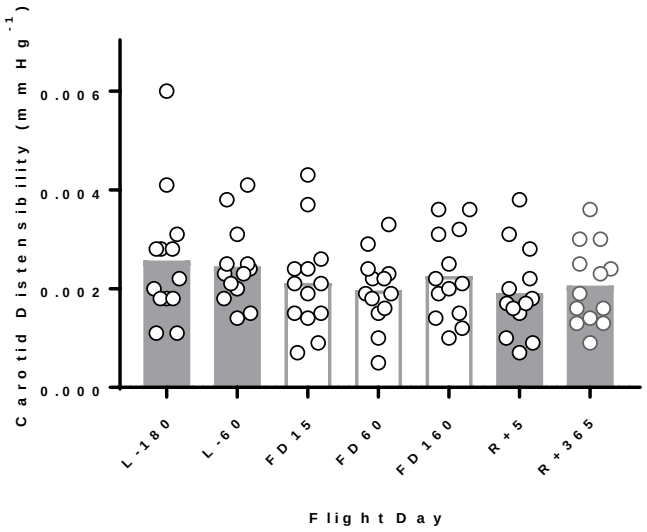


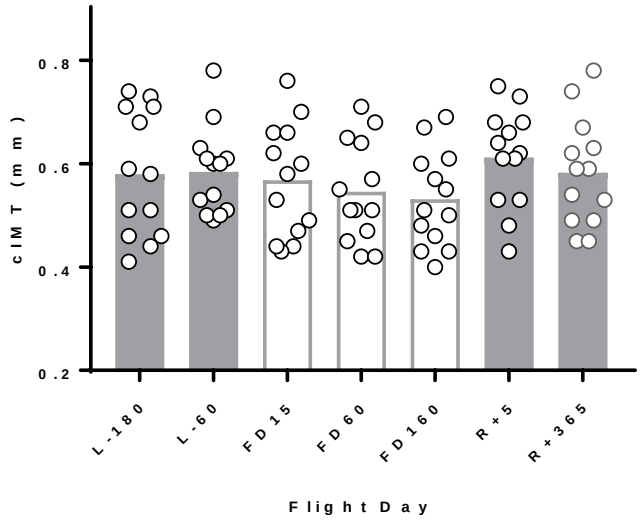


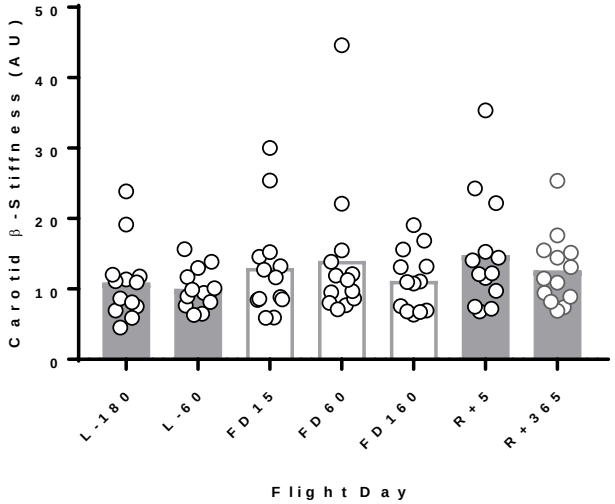


Carotid Artery Structure and Function





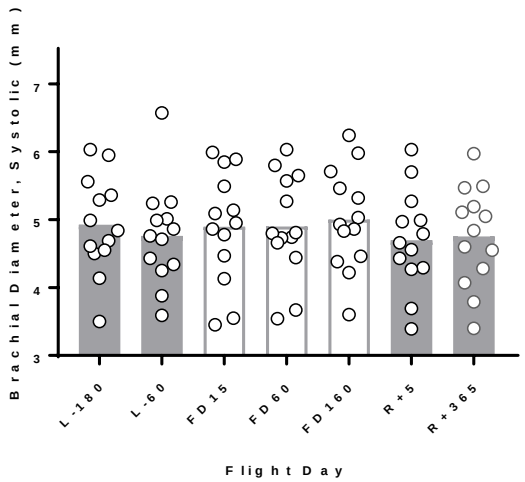


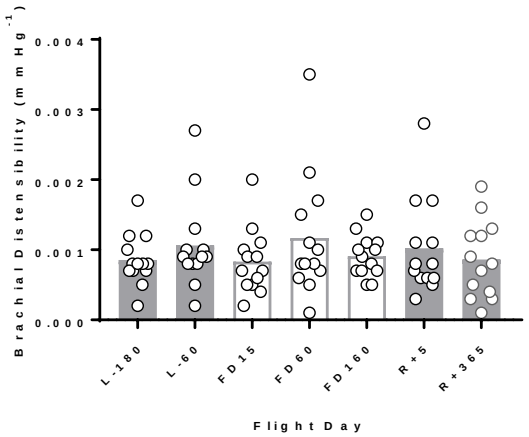


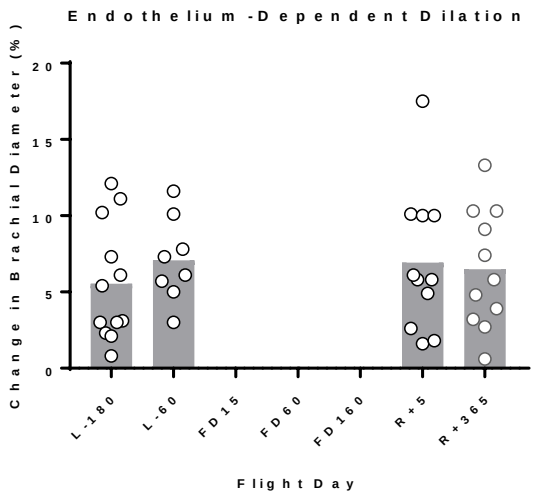
Relation of Biomarkers to Carotid Structure and Function

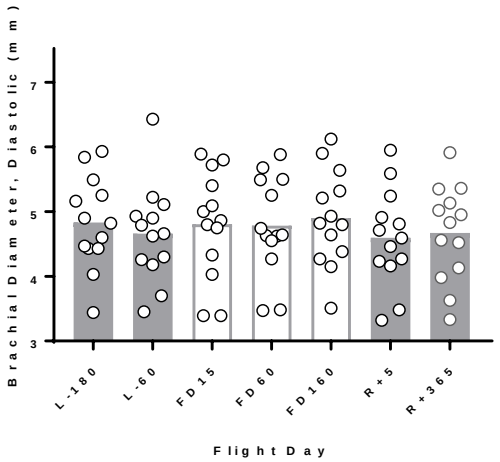
		D	95% CI	P_{inc}
cIMT	Systolic Blood Pressure	-0.16	-0.32 , 0.00	0.42
	Total Cholesterol	-0.14	-0.29 , 0.02	0.43
	LDL	-0.07	-0.22 , 0.07	0.46
	hs-CRP	**0.28**	0.13 , 0.43	0.64
	Oxidized LDL	-0.22	-0.37 , -0.06	0.39
Intima-Media Area	Systolic Blood Pressure	-0.09	-0.23 , 0.04	0.45
	Total Cholesterol	-0.08	-0.24 , 0.07	0.46
	LDL	-0.03	-0.16 , 0.10	0.48
	hs-CRP	**0.25**	0.11 , 0.40	0.63
	Oxidized LDL	-0.10	-0.25 , 0.04	0.45
Carotid Distensibility	Systolic Blood Pressure	-0.21	-0.42 , 0.00	0.40
	Total Cholesterol	0.02	-0.16 , 0.20	0.51
	LDL	-0.05	-0.26 , 0.16	0.48
	hs-CRP	-0.17	-0.36 , 0.02	0.42
	Oxidized LDL	-0.01	-0.30 , 0.28	0.49

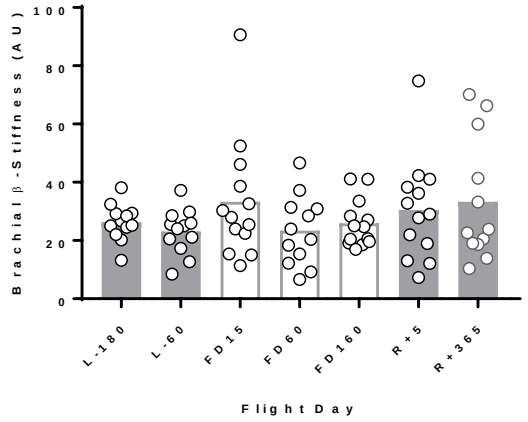
Brachial Artery Structure and Function

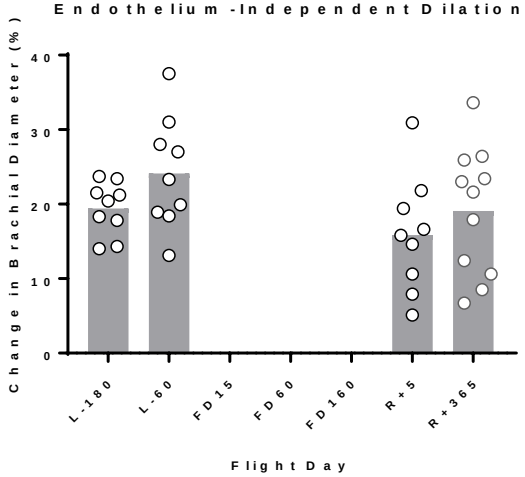












Relation of Biomarkers to Vascular Function

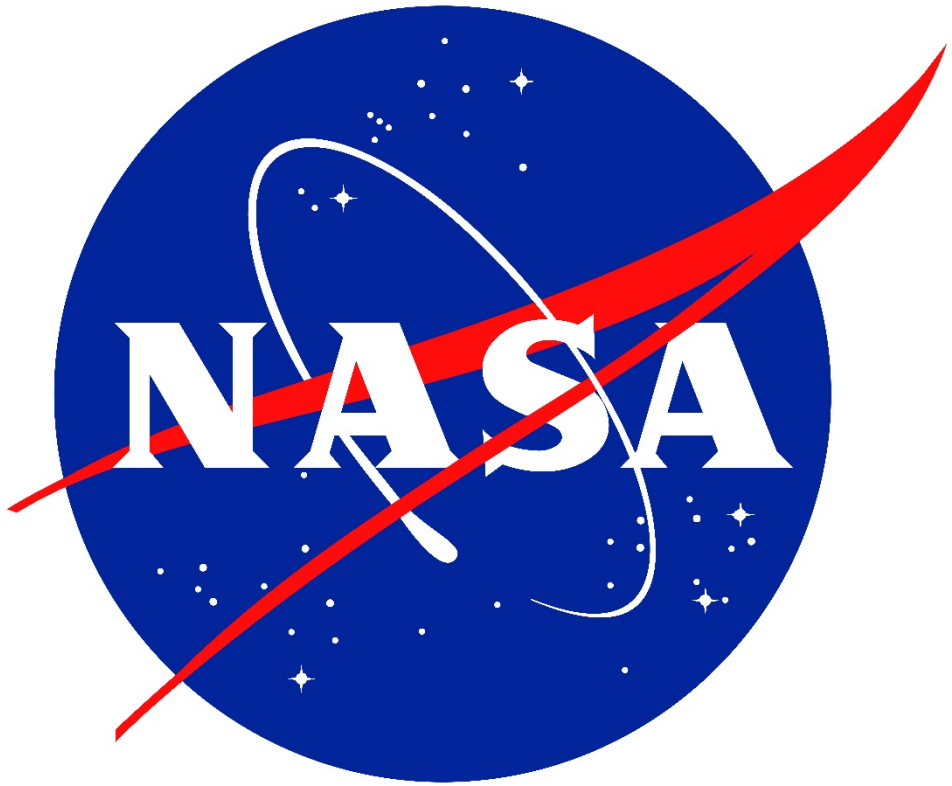
		D	95% CI	P_{inc}
Endothelium-Dependent Vasodilation	hs-CRP	0.23	-0.20 , 0.59	0.62
	IL-6	**0.39**	0.01 , 0.67	0.70
	8-OHdG	-0.13	-0.57 , 0.37	0.44
	PGF2α	-0.33	-0.62 , 0.03	0.33
	Oxidized LDL	0.28	-0.25 , 0.69	0.64
	Malondialdehyde	-0.15	-0.61 , 0.38	0.42
	Protein Carbonyls	-0.18	-0.61 , 0.33	0.41
Endothelium-Independent Vasodilation	hs-CRP	0.28	-0.29 , 0.71	0.64
	IL-6	0.57	-0.12 , 0.89	0.78
	8-OHdG	0.04	0.33 , 0.27	0.38
	PGF2α	**-0.38**	-0.61 , -0.10	0.31
	Oxidized LDL	0.23	-0.29 , 0.65	0.62
	Malondialdehyde	-0.10	-0.44 , 0.26	0.45
	Protein Carbonyls	-0.33	-0.62 , 0.04	0.33

Conclusions

- Biomarkers of inflammation and oxidative stress are elevated during spaceflight, and most returned to preflight values soon after landing.
- Total cholesterol and LDL are elevated during spaceflight but return to preflight levels during recovery. Insulin sensitivity tended to decrease during flight and at landing, but was not different at R+30.
- cIMT decreased during spaceflight secondary to a dilation of the carotid artery but cIMT was not different after landing.
- Carotid distensibility decreased and stiffness increased on R+5, but were similar to preflight values at R+365.
- There appear to be no changes in brachial artery function as a result of spaceflight.

Acknowledgments

- Astronaut volunteers
- NASA JSC Cardiovascular and Vision Laboratory
- NASA JSC Nutritional Biochemistry Laboratory
- ISS Medical Project
- Lifetime Surveillance of Astronaut Health Staff
- NASA Human Research Program


NASA

Carotid and Femoral Arterial Wall Distensibility During Long-Duration Spaceflight

Philippe Arbeille; Romain Provost; Kathryn Zuj

AEROSPACE MEDICINE AND HUMAN PERFORMANCE Vol. 88, No. 10 October 2017