Comparison of Structural and Functional Ocular Outcomes Between 14- and 70-day Bed Rest

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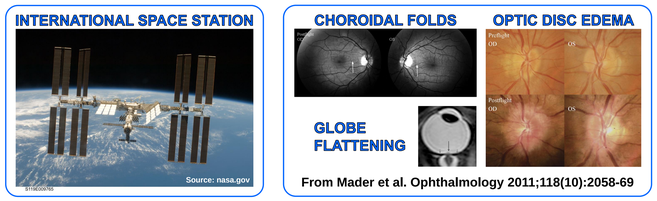
BACKGROUND

- Ophthalmological changes have been recently reported in some astronauts involved in long-duration space missions:



- Elevated intracranial pressure resulting from µG-induced cephalad fluid shifts may be responsible for most of these findings
- Head-down tilt bed rest (HDTBR) produces cephalad fluid shifts; used to simulate the effects of µG on the human body

PURPOSE

- To compare structural and functional ocular outcomes between 14- and 70-day HDTBR in healthy human subjects
- Hypothesis: the amount of ocular changes induced by HDTBR is affected by the time spent in the HDTBR position

METHODS

- Two integrated, multidisciplinary studies conducted at NASA Flight Analogs Research Unit (FARU): 14- and 70-day 6º HDTBR
- NASA standard HDTBR screening procedures (healthy adults)

NASA bed rest studies **STANDARDIZED CONDITIONS**

- ✓ Subject to rest in bed **at all times**
- ✓ Monitoring by a subject monitor and an in room camera **24-hour a day**
- ✓ Daily measurement of vital signs, body weight, fluid intake and fluid output
- ✓ No napping permitted between 6:00 am and 10:00 pm
- ✓ Standardized diet

NASA Flight Analogs Research Unit (FARU)

70 days	HDTBR Duration	14 days
	OCULAR EXAMS:	
YES 2 office visits	Pre-BR	**YES** 2 office visits
YES Weekly (FARU)	During BR	**YES** Weekly (FARU)
YES 2 office visits	Post-BR	**YES** 1 office visit

METHODS

- Mixed-effects linear models compared pre- and post-HDTBR observations between 14- and 70-day HDTBR in:
  - Near best-corrected visual acuity
  - Spherical equivalent
  - Goldmann and iCare (Icare Finland Oy, Espoo, Finland) intraocular pressure (IOP)
  - Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany) average retinal nerve fiber layer thickness (RNFLT), peripapillary retinal thickness and macular thicknesses
- Statistical analyses were conducted using Stata (StataCorp LP, College Station, TX; software version 14.0)

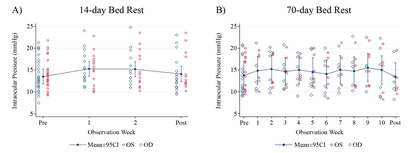
RESULTS

Baseline demographic characteristics of the participants

	14-day HDTBR (n = 16)	*70-day HDTBR (n = 6)*
Age	37.8 (8.8)	39.5 (7.8)
Gender (Male/Female)	12/4	5/1
Height, cm	174.9 (8.3)	171.3 (5.9)
Weight, Kg	76.4 (10.4)	76.2 (8.4)

Data presented as mean (sd).
One subject participated in both bed rest campaigns

Intraocular Pressure (iCare)



Pre- and post-HDTBR ophthalmological data

	14-day HDTBR		*70-day HDTBR*	
	Pre	*Post*	*Pre*	*Post*
Near BCVA, logMAR	-0.12 (-0.15, -0.09)	-0.17 (-0.20, -0.14)	-0.16 (-0.21, -0.11)	-0.19 (-0.24, -0.14)
Spherical Equivalent, D	-0.25 (-0.87, 0.37)	-0.45 (-1.07, 1.51)	0.77 (-0.25, 1.79)	0.49 (-0.53, 1.51)
Goldmann IOP, mmHg	15.17 (13.64, 16.70)	14.67 (13.14, 16.20)	15.42 (12.92, 17.91)	14.96 (12.41, 17.51)
iCare IOP, mmHg	13.78 (11.91, 15.66)	14.09 (12.21, 15.96)	13.21 (10.15, 16.27)	13.62 (10.52, 16.73)
Peripapillary retinal thickness				
Temporal, µm	304.31 (293.06, 315.56)	307.41 (296.15, 318.66)	307.17 (288.79, 325.54)	311.83 (293.49, 330.17)
Superior, µm	386.91 (372.60, 401.21)	391.59 (377.29, 405.90)	407.25 (383.89, 430.61)	418.75 (395.46, 442.04)
Nasal, µm	356.38 (345.19, 367.56)	361.00 (349.82, 372.18)	351.67 (333.40, 369.93)	363.13 (345.00, 381.25)
Inferior, µm	397.03 (382.45, 411.61)	401.38 (386.79, 415.96)	400.92 (377.11, 424.73)	411.00 (387.25, 434.75)
Central, µm	306.67 (261.27, 352.07)	310.69 (265.30, 356.08)	299.60 (218.41, 380.79)	312.10 (231.02, 393.18)
Average RNFL thickness, µm	96.94 (92.56, 101.32)	98.09 (93.71, 102.48)	103.42 (96.26, 110.57)	105.13 (98.00, 112.26)
Macular thickness, µm	279.45 (270.22, 288.67)	276.97 (267.75, 286.19)	268.25 (253.19, 283.31)	266.63 (251.59, 281.66)

Data presented as mean (95% Confidence Interval).
BCVA, best corrected visual acuity; IOP, intraocular pressure; RNFL, retinal nerve fiber layer.

- In both studies:
  - Subjects remained asymptomatic throughout HDTBR
  - Modified Amsler grid, red dot test, color vision, confrontational visual field were within normal limits throughout
  - No changes from baseline were detected on stereoscopic color fundus photography
- LogMAR and spherical equivalent decreased during and after HDTBR (p's < 0.001)
- Overall, iCare IOP increased during HDTBR (+1.42 mmHg, p < 0.01), but no differences from baseline were observed post-HDTBR (p = 0.46)

RESULTS

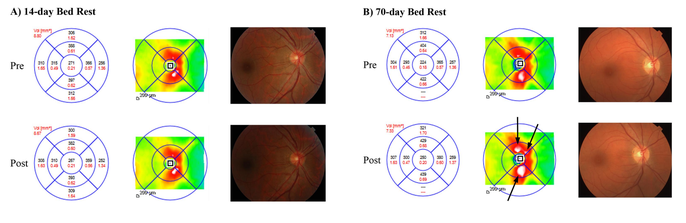
- In the superior, nasal and inferior peripapillary sectors, the magnitude of retinal thickening post-HDTBR was greater after 70-day HDTBR (p's < 0.01):

Pre/post Δ Retinal Thickness, µm

Peripapillary Sector	*14-day HDTBR*	*70-day HDTBR*
Temporal	NS	NS
Superior	+4.69 (+2.12, +7.26)	+11.50 (+7.87, +15.13)
Nasal	+4.63 (+1.49, +7.76)	+11.46 (+7.02, +15.90)
Inferior	+4.34 (+1.97, +6.72)	+10.08 (+6.72, +13.45)
Central	NS	NS

Data presented as mean (95% Confidence Interval). NS, non-significant.

Case Example



Pre/post-bed rest Spectralis OCT peripapillary retinal thickness and volume, retinal thickness map and color fundus photography of two sample eyes from the 14- and the 70-day bed rest campaigns

- Overall, average RNFLT increased (p = 0.002), while macular thickness decreased from baseline (p < 0.01)

CONCLUSIONS

- 70-day HDTBR induced greater peripapillary retinal thickening than 14-day HDTBR, suggesting that the time spent in the 6º HDTBR position may affect the amount of optic disc swelling
- There was a slight RNFL thickening post-HDTBR, without signs of optic disc edema. Such changes may have resulted from HDTBR-induced cephalad fluids shift.
- HDTBR induced a small non-progressive increase in IOP, which subsided post-HDTBR
- HDTBR duration may be critical for replicating ophthalmological changes observed in astronauts on ≥6-month spaceflights.
- Further research is necessary to elucidate the interaction of HDTBR duration and the angle of tilt to study microgravity-related ophthalmological changes

SUPPORT

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DISCLOSURE

All Authors, None

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