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Effects of 30-Day Head-Down Bed Rest on Ocular Structures and Visual Function in a Healthy Subject

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Abstract

Introduction—We report ocular changes occurring in a healthy human subject enrolled in a bed rest (BR) study designed to replicate the effects of a low-gravity environment.

Case report—A 25-year-old Caucasian male spent 30 consecutive days in a 6° head-down-tilt position at the NASA Flight Analogs Research Unit. Comprehensive ophthalmologic exams, optic disc stereo-photography, Standard Automated Perimetry (SAP) and optic disc Spectralis OCT scans were performed at baseline, immediately post-BR (BR+0) and 6 months post-BR. Main outcome measures: changes in best-corrected visual acuity, intraocular pressure (IOP), cycloplegic refraction, SAP and Spectralis OCT measures. At BR+0 IOP was 11 and 10 mmHg in the right (OD) and left eye (OS), respectively (a bilateral 4 mmHg decrease compared to baseline); SAP documented a possible bilateral symmetrical inferior scotoma; Spectralis OCT showed an average 19.4 μm (+5.2%) increase in peripapillary retinal thickness, and an average 0.03 mm^3 (+5.0%) increase in peripapillary retinal volume bilaterally. However, there were no clinically detectable signs of optic disc edema. 6 months post-BR, IOP was 13 and 14 mmHg in OD and OS, respectively, and the scotoma had resolved. Spectralis OCT measurements matched the ones recorded at baseline.

Discussion—In this subject, a reduction in IOP associated with subtle structural and functional changes compared to baseline were documented after prolonged head-down BR. These changes may be related to cephalad fluid shifts in response to tilt. Further studies should clarify whether decreased translaminar pressure (i.e., the difference between IOP and intracranial pressure) may be responsible for these findings.

Keywords

intraocular pressure; microgravity; optic disc swelling; Spectral-Domain OCT; translaminar pressure

INTRODUCTION

NASA's plan for long duration human missions to asteroids and Mars requires implementation of adequate countermeasures to manage physiological changes induced by spaceflight to ensure a successful human space exploration program. The integrity of astronauts' visual function is crucial for safe and successful conduct of space missions.

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Exposure to space radiation and ultraviolet rays, for example, may increase the risk of cataract formation (4). Recently, ocular abnormalities such as optic disc edema and/or signs of globe flattening with hyperopic shifts resulting in significant visual impairment were described in several astronauts involved in long-duration spaceflights (>30 days) (8). The reasons for such findings are largely unknown. It is hypothesized that, in predisposed individuals, spaceflight-induced cephalad shift of body fluids, possibly leading to elevated intracranial pressure (ICP), may be responsible for these changes.

Head-down tilt bed rest has long been utilized to simulate the effects of microgravity on the human body and to study possible countermeasures (13). Similarly to spaceflight, long-duration, 6° head-down tilt bed rest produces cephalad fluid shifts, muscle atrophy and bone loss, reduced metabolic needs and decreased sensory stimulation (13).

We report the ocular changes occurring in a healthy individual enrolled in a 30-day bed rest study designed to simulate the effects of a micro-gravity environment.

CASE REPORT

The study protocol was approved in advance by both the NASA Committee for the Protection of Human Subjects and UTMB Institutional Review Board. All methods adhered to the Declaration of Helsinki for research involving human participants and the Health Insurance Portability and Accountability Act (HIPAA). The subject provided written informed consent before participating.

Subject

A 25-year-old Caucasian male participated in a long-term integrated, multidisciplinary bed rest study conducted at the NASA Flight Analogs Research Unit (FARU), located at The University of Texas Medical Branch (UTMB), Galveston, TX.

Procedure

This subject participated in a 30-day bed rest study. Details of subject qualification criteria and conditions of bed rest are detailed elsewhere (10). A brief description will be provided here. To qualify for this study, subjects passed extensive physical and psychological exams. A standardized diet was fed to subjects throughout the study (7). To ensure nutritional intake, subjects were required to consume all food served to them. Subjects adhered to a strict sleep/wake schedule and did not nap during the day. Lights were turned on at 6:00 am and turned out at 10:00 pm. Subject health was monitored by the attending physician and nursing staff 24 hours each day for the duration of the study.

The subject spent 13 days in the pre-bed rest phase. In this phase, the subject became acclimated to the hospital unit and underwent baseline assessments of their nutritional, cardiovascular, neurological and fitness status.

The bed rest phase included 30-days of confinement to bed in the 6° head-down tilt position. All daily activities were performed in this position including showering and toileting (10). During this phase monitoring of nutritional status, cardiovascular status and neurological status continued.

During the post bed rest phase, the subject remained on the unit for 14 more days. Once again, assessment of nutritional, cardiovascular, neurological and fitness status was completed. The subject was also provided with rehabilitation to compensate for the deconditioning that occurs with bed rest.

Ocular examinations were performed 13 days prior to starting bed rest (BR-13), immediately post bed rest on the morning of the first day out of bed (BR+0), and 6 months post bed rest by the same examiner. At each visit, the subject underwent a comprehensive ophthalmologic examination, including best corrected visual acuity (BCVA), cycloplegic refraction, slit-lamp biomicroscopy, Goldmann applanation tonometry, gonioscopy, dilated fundoscopic examination with a 78 D lens, optic disc stereo-photography with a digital fundus camera (Topcon TRC-NW6S, Tokyo, Japan), Standard Automated Perimetry (SAP) and Spectral-Domain (SD) Optical Coherence Tomography (OCT).

Equipment

SAP tests were obtained using the 24-2 SITA Standard strategy of the Humphrey Field Analyzer II (Carl Zeiss Meditec, Dublin, CA). Changes in the Visual Field Index (VFI) were evaluated. The VFI is a novel parameter of the Humphrey Field Analyzer (HFA) designed to stage perimetric damage and to calculate the rate of visual field deterioration. The VFI can range from 100% (normal visual field) to 0% (perimetrically blind visual field) (1).

SD-OCT scans were obtained with Spectralis OCT (software version 5.1.3.0, Heidelberg Engineering, GmbH, Heidelberg, Germany). The device uses a superluminescent diode with a wavelength of 870 nm to acquire 40,000 A-scans per second with an axial resolution of 3.9 μm and a transverse resolution of 14 μm. Spectralis OCT minimum detectable change is 1 μm (19). At each visit, the Volume Scan acquisition protocol (512 A-scans × 19 B-scans) was used to analyze a 20° × 15° area centered on the optic disc. Retinal thickness and volume measurements were compared at different time points using the AutoRescan™ feature. The feature utilizes a retinal map created by a real-time eye tracking system that combines confocal scanning laser ophthalmoscopy and SD-OCT scans to compensate for eye movements, allowing for automatic placement of follow-up scans in the same location as baseline.

The software automatically overlays a calculation grid in the center of the fundus image to evaluate the retinal thickness and volume of nine different sectors. The calculation grid is composed of three concentric circles (diameter of 1, 3 and 6 mm, respectively) defining the central, inner and outer regions, and four perpendicular radial lines that divide both the inner and outer regions into four quadrants (temporal, superior, nasal and inferior, respectively). Since the diameter of the external circle exceeds the 20° × 15° scanning area, only the retinal thickness and volume of the central and inner sectors were considered for further evaluation.

All SD-OCT funduscopic images were evenly illuminated with signal-to-noise ratio >15 dB, which represents the minimum quality score as per manufacturer's recommendation. In addition, the automated segmentation algorithm correctly identified the internal limiting membrane and Bruch's membrane in all SD-OCT scans.

The subject remained asymptomatic throughout the course of the study. At all visits, BCVA was 20/20 or better in both eyes with no significant changes in cycloplegic refraction (Table I) compared to baseline. In addition, slit-lamp examination was unremarkable and the anterior chamber angles on gonioscopy were open bilaterally (Shaffer grade 4 in all quadrants).

At BR+0, there was an average 28% decrease in IOP in both eyes (Table I). At 6 months post bed-rest, IOP returned to baseline levels.

Dilated fundoscopic examination at baseline revealed only mild venous tortuosity in the left eye as compared to the right with no signs of vascular engorgement (Fig. 1D). However, no

fundoscopic changes were observed during the course of the study. In particular, there were no clinically detectable signs of optic disc edema, defined as swelling of the optic disc associated with hyperemia, blurring of disc margin or papillary/peripapillary retinal hemorrhages (Fig. 1A–F).

HFA threshold sensitivity and pattern deviation probability maps are shown in Fig. 2. At each visit, the subject performed a reliable visual field test, defined as fixation losses and false negatives ≤33%, and false positives ≤15%. There were no visual field artifacts, such as lid or rim artifacts.

At BR+0, SAP documented the presence of a possible bilateral symmetrical inferior scotoma associated with a 2% decrease in the VFI bilaterally (Table I). At 6 months post bed rest the scotoma resolved and the VFI was 100% in both eyes.

Results of Spectralis OCT scans are shown in Fig. 3. Peripapillary retinal thickness and volume changes at BR+0 and at 6 months post bed rest are reported in Fig. 4. At BR+0, SD-OCT detected an average 17.4 μm (+4.4%) increase in peripapillary retinal thickness in the right eye and 21.4 μm (+5.9%) in the left eye compared to baseline. These changes were accompanied by an average 0.03 mm^3 (+4.6%) volume increase in the right eye and 0.02 mm^3 (+5.3%) in the left eye. The increase in retinal thickness from baseline is visibly noticeable on the thickness maps as an enlargement of the warm-colored areas (e.g., white, red and yellow areas) (Fig. 3D–F and J–L). Fig. 5 shows the retinal thickness profile of both eyes evaluated on a cross-sectional B-scan passing through the optic disc. The area displayed in red represents the retinal thickening noticeable 30 days after bed rest. At 6 months post bed rest, SD-OCT measurements matched the ones recorded at baseline. There was −0.4% and −0.3% change from baseline in average peripapillary retinal thickness and volume, respectively, in the right eye, while no changes were detected in the left eye.

DISCUSSION

This report describes the ocular changes that occurred in a healthy human subject after 30 consecutive days in a 6° head-down tilt position. An ophthalmological examination conducted one day post bed rest showed an apparent decrease in IOP in both eyes compared to baseline. Also, Spectralis OCT documented an increase in retinal thickness and volume at the level of the optic disc above the test-retest variability of the instrument (19). Furthermore, these changes were associated with the presence of a bilateral scotoma, as detected by SAP. All measurements tended to return to baseline values six months after bed rest.

Posture-related IOP changes are widely described in the literature for different durations and angles of tilt. It is well known, for example, that changes from a vertical position to a horizontal or reclined body position produce an acute rise in IOP (14). The amount of change depends on the degree of tilt and the time spent in the dependent position. This acute rise in IOP seems to be more pronounced in glaucomatous eyes (14). Although the mechanism is not completely understood, it is likely that the change in body position causes inhibition of choroidal venous drainage and vascular engorgement. The subsequent choroidal expansion against the rigid scleral tissue would lead to a sudden IOP elevation (9, 17). In addition, increased episcleral venous pressure results in increased outflow resistance (5). However, compensatory mechanisms that are currently disputed and require further investigation, such as decreased aqueous humor volume possibly resulting from reduced production (9), may remain active after 30 days of head-down bed rest as subjects slowly readapt to upright conditions. This appears to be the case in spaceflight, as anecdotal reports suggest that post-flight IOP may significantly decrease below pre-flight values (6). Chiquet

et al. reported a progressive IOP decrease during 7 days of 6° head-down bed rest associated with a parallel decrease in plasma volume over this time frame ($r = 0.61$, $p = 0.02$) (3). This parallel decrease in IOP and plasma volume suggests a compensatory response in IOP linked to cephalad fluid shifts produced by head-down tilt bed rest. Compensatory mechanisms may also explain the decrease in IOP found in our subject at the end of bed rest.

To our knowledge, this is the first report documenting ocular changes in a healthy human subject after prolonged head-down bed rest using SD-OCT. Studies have shown that this technology provides automated, objective and reproducible evaluations of ocular microstructures (16). In addition, Spectralis OCT AutoRescan™ feature enables the identification of true change over time by correctly identifying and rescanning the same area at follow-up examinations (19).

In our head-down bed rest subject, structural and functional changes appeared to be correlated. At BR+0, SD-OCT showed signs of bilateral optic disc swelling while SAP evidenced a possible bilateral inferior scotoma associated with 2% bilateral reduction in the VFI. It has been shown that the VFI is a more robust index than the Mean Deviation (MD) and a reduction of the VFI generally occurs in the presence of substantial changes in the HFA pattern deviation map (1). The reliability of SAP tests and the absence of any noticeable artifacts are two additional elements in support of a “true” functional change that occurred at BR+0. Finally, a complete resolution of both structural and functional abnormalities was noted at 6-month post bed rest.

Although the subject remained asymptomatic during the course of the study and no other significant changes were seen on exam, it is possible that longer bed rest phases may show abnormalities of a greater magnitude. It is conceivable that the duration of bed rest may be associated with the severity of retinal changes. In fact, time appears to be a crucial factor in determining the severity of ocular findings after exposure to microgravity. Recently, ophthalmological changes experienced by astronauts who participated in the Space Shuttle and the International Space Station missions have been reported (8). Some astronauts who participated in the Space Shuttle Program (generally 10 to 14-day missions) complained of reduction of near visual acuity that resolved upon landing. However, several astronauts returning from long duration International Space Station missions (average 6–month duration) showed signs of various degrees of optic disc edema. Severe cases presented additional signs, such as globe flattening with hyperopic shifts, choroidal folds and cotton wool spots, resulting in some cases in permanent visual impairment. Interestingly, these changes seemed to be associated with elevated ICP (8).

Similarly, ocular changes found in our subject may be the result of cephalad shift of body fluids in response to tilt, possibly favored by the absence of valves in the upper venous system. Another postulated contributing mechanism is decreased cerebrospinal fluid and aqueous humor outflow resulting from compression of the internal jugular veins, which likely does not occur in the 1G head-down tilt bed rest analog, and may help explain why the subject remained asymptomatic (18). Postural and venous pressure changes exert an effect not only on IOP, but also on ICP. It has been suggested that translaminar pressure, i.e., the difference between IOP and ICP, may play a crucial role in the pathophysiology of optic nerve damage (2, 15). Eyes in which the lamina cribrosa and/or the peripapillary sclera may be abnormally thin (e.g., myopic eyes) are likely to be more susceptible to damage caused by changes in translaminar pressure (11). ICP may counteract the effects of IOP on the optic nerve head and vice-versa. As a consequence, disruption of the translaminar pressure balance may ultimately lead to the development of optic disc changes. For example, reduced translaminar pressure may occur in case of decreased IOP associated with increased ICP, thus producing optic disc swelling. This could potentially explain our findings.

However, ICP measurements or other useful measurements, such as brain Magnetic Resonance Imaging for evaluation of ventricular size or optic nerve sheath diameter, or ultrasonographic assessment of the optic nerve sheath diameter, could not be obtained for this subject.

We are aware of the intrinsic limitations of a single case report with regard to the generalization of the results. However, structural and functional changes were detected in this subject after 30-day head-down bed rest. In order for the subject to comply with the rigid study protocol one day post bed rest, it was not possible to repeat SAP for confirmation of visual field abnormalities. However, repeated SAP after 6 months showed resolution of findings, suggesting that changes seen on the previous exam were likely the result of prolonged head-down bed rest. In addition, structural and functional changes seemed to correlate at each visit.

In-bed measurements, such as IOP, central corneal thickness and other useful measures, were not obtained for this study due to research protocol constraints. Further studies are necessary to better characterize the patterns of IOP change during prolonged head-down bed rest.

Despite the above mentioned limitations, we were able to demonstrate the presence of ocular modifications likely induced by head-down bed rest. The relevance of this study is not confined to aerospace medicine alone. The bed rest analog may help advance our knowledge in the pathophysiology of certain optic neuropathies, including but not limited to glaucoma, with direct clinical implications. For example, ischemic optic neuropathy is a cause of permanent perioperative vision loss associated with spine surgery, which is commonly performed in a tilted position (12). Similarly to bed rest experiments, numerous other procedures, such as abdominal or gynecological surgeries, are conducted in a head-down tilted position for a prolonged time.

In conclusion, in this subject, a reduction in IOP associated with subtle structural and functional changes compared to baseline occurred after 30 days of head-down bed rest. SD-OCT can be used to detect changes at the level of the optic disc possibly due to cephalad shifts of body fluids in response to body tilt. Further studies are required to better characterize the underlying process.

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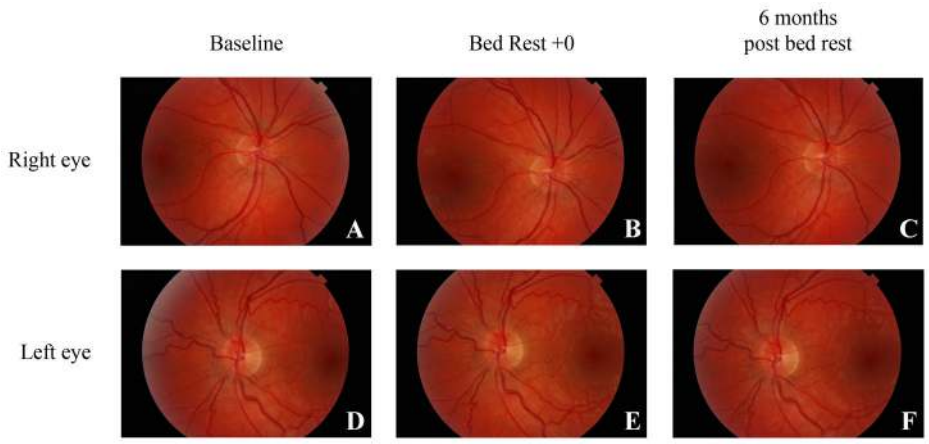

Fig. 1.
Optic disc photographs at baseline, 1 day post bed rest (Bed Rest +0) and 6 months post bed rest for the right (A–C) and left eye (D–F).

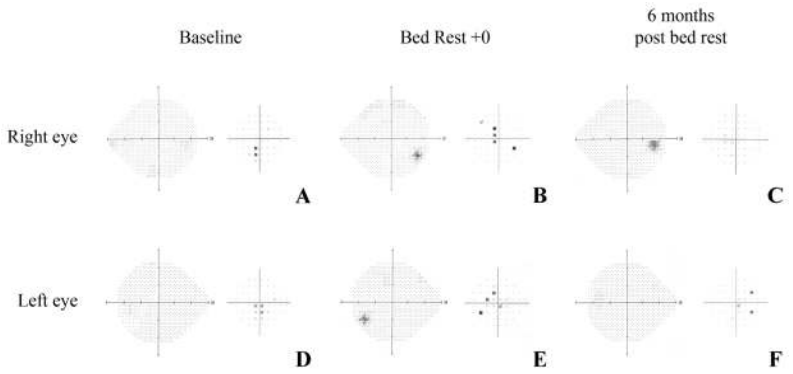

Fig. 2.
Humphrey Field Analyzer grey-scale and pattern deviation probability maps at baseline, 1 day post bed rest (Bed Rest +0) and 6 months post bed rest for the right (A–C) and left eye (D–F).

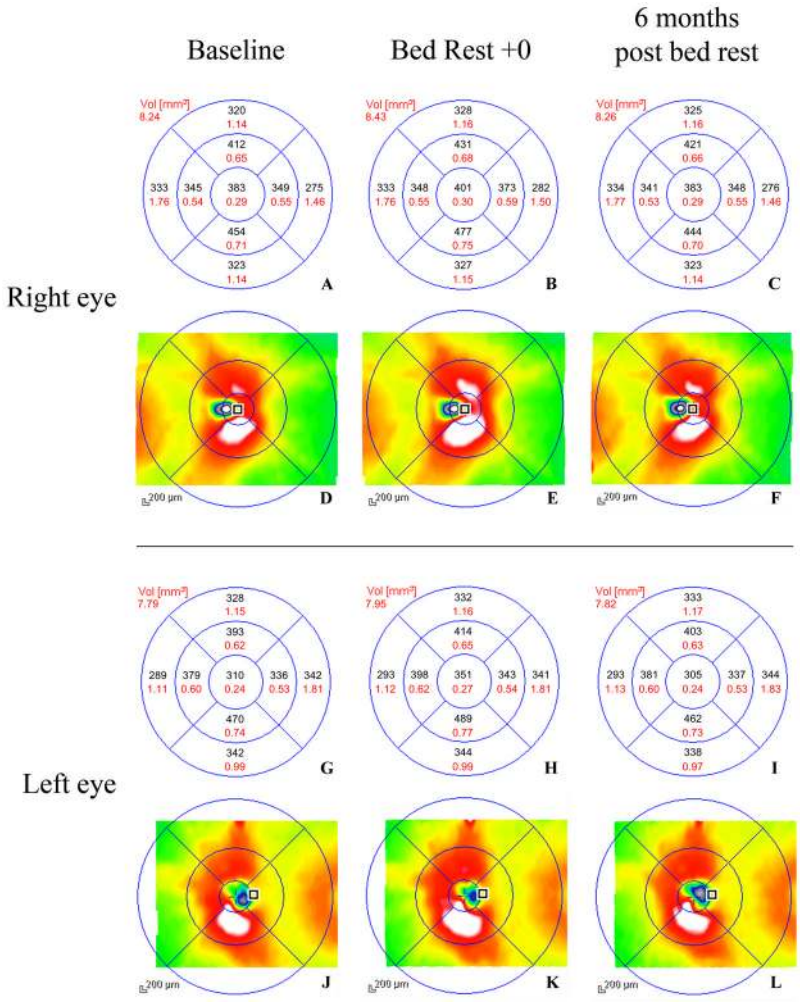

Fig. 3.

Results of Spectralis OCT scans centered on the optic disc at baseline, 1 day post bed rest (Bed Rest +0) and 6 months post bed rest. Retinal thickness and volume (Right eye: panels A–C; Left eye: panels G–I) and retinal thickness maps (Right eye: panels D–F; Left eye: panels J–L) are shown. Thicker areas are represented with warm colors (e.g., red or yellow), while thinner areas are represented with cool colors (e.g., green or blue). At BR+0, the increase in retinal thickness form baseline is noticeable on the thickness maps as an enlargement of the warm-colored areas (Panels E and K).

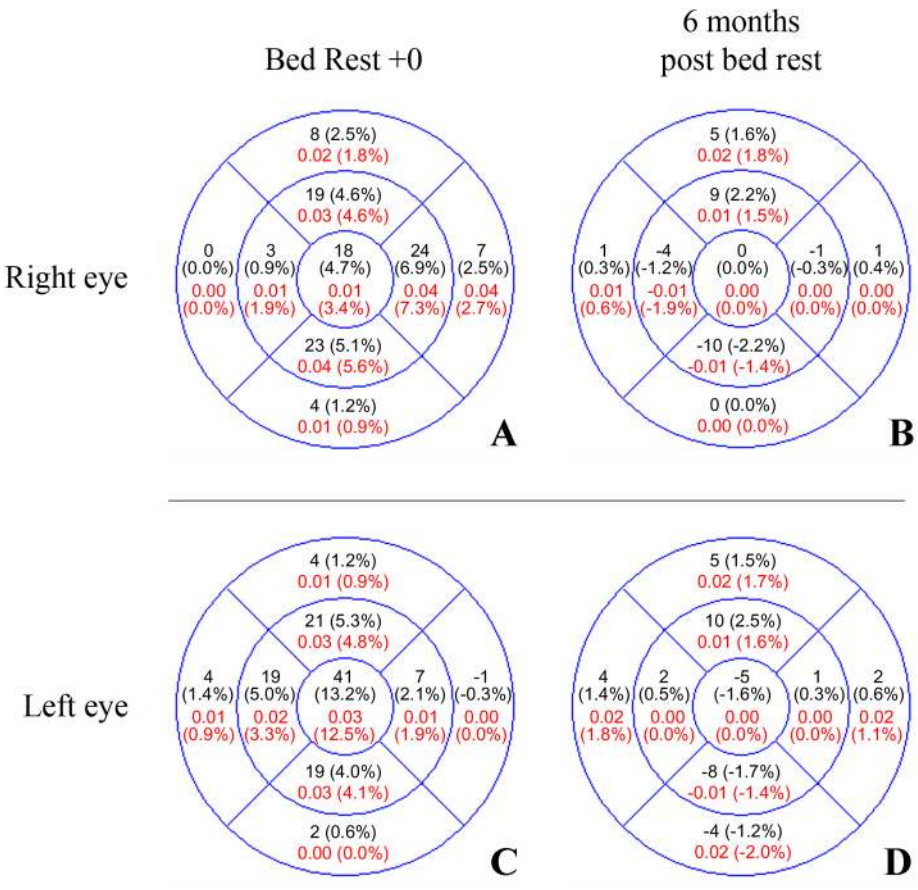

Fig. 4.

Spectralis OCT retinal thickness (μm, in black) and volume (mm^3, in red) changes at 1 day post bed rest (Bed Rest +0, Right eye: panel A; Left eye: panel C) and at 6-month post bed rest (Right eye: panel B; Left eye: panel D). Percentage changes are reported in parenthesis.

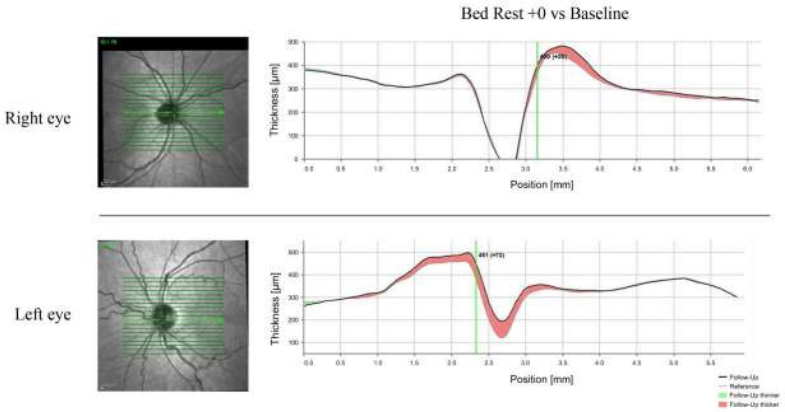

Fig. 5.
Retinal thickness profile evaluated on a cross-sectional B-scan passing through the optic disc. For the right and left eye, the area displayed in red represents the retinal thickening that occurred 1day post bed rest (Bed Rest +0).

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Table I

OPHTHALMOLOGICAL DATA AND VISUAL FIELD RESULTS OF THE STUDY SUBJECT AT BASELINE, 1 DAY POST BED REST (BR+0) AND 6 MONTHS POST BED REST.

	Right Eye			Left Eye		
	Baseline	**BR+0**	**6 months post BR**	**Baseline**	**BR+0**	**6 months post BR**
BCVA	20/20	20/20	20/20	20/20	20/15	20/20
Cycloplegic Refraction						
Sphere (D)	−3.25	−3.25	−3.50	−3.00	−3.00	−2.75
Cylinder (D)	+0.25	+0.25	+0.50	+0.75	+0.75	+0.75
Axis (degrees)	80	80	80	90	90	90
IOP (mmHg)	15	11	13	14	10	14
MD (dB)	+0.87	+1.05	+1.81	+1.43	+0.38	+1.31
PSD (dB)	1.59	1.63	1.39	1.73	1.71	1.66
VFI (%)	100	98	100	99	97	100
GHT	WNL	WNL	WNL	BL	WNL	WNL

BCVA, Best Corrected Visual Acuity; BL, Borderline; BR, Bed Rest; D, Dioptres; GHT, Glaucoma Hemifield Test; IOP, Intraocular Pressure; MD, Mean Deviation; PSD, Pattern Standard Deviation; VFI, Visual Field Index; WNL, Within Normal Limits.