

Heavy ions light flashes and brain functions: recent observations at accelerators and in spaceflight

This content has been downloaded from IOPscience. Please scroll down to see the full text.

2008 New J. Phys. 10 075010

(<http://iopscience.iop.org/1367-2630/10/7/075010>)

View [the table of contents for this issue](#), or go to the [journal homepage](#) for more

Download details:

IP Address: 128.6.218.72

This content was downloaded on 08/09/2015 at 22:28

Please note that [terms and conditions apply](#).

Heavy ions light flashes and brain functions: recent observations at accelerators and in spaceflight

L Narici

Department of Physics, University of Rome Tor Vergata,
and INFN Roma Tor Vergata, Via della Ricerca Scientifica 1, 00133 Rome, Italy
E-mail: livio.narici@roma2.infn.it

New Journal of Physics **10** (2008) 075010 (23pp)

Received 5 April 2008

Published 28 July 2008

Online at <http://www.njp.org/>

doi:10.1088/1367-2630/10/7/075010

Abstract. Interactions between ionizing radiation in space and brain functions, and the related risk assessments, are among the major concerns when programming long permanence in space, especially when outside the protective shield of the Earth's magnetosphere. The light flashes (LF) observed by astronauts in space, mostly when dark adapted, are an example of these interactions; investigations in space and on the ground showed that these effects can originate with the action of ionizing radiation in the eye. Recent findings from ALTEA, an interdisciplinary and multiapproach program devoted to the study of different aspects of the radiation–brain functions interaction, are presented in this paper. These include: (i) study of radiation passing through the astronauts' eyes in the International Space Station (≈ 20 ions min^{-1} , excluding H and fast and very slow He), measured in conjunction with reporting of the perception of LF; (ii) preliminary electrophysiological evidence of these events in astronauts and in patients during heavy ion therapy; and (iii) *in vitro* results showing the radiation driven activation of rhodopsin at the start of the phototransduction cascade in the process of vision. These results are in agreement with our previous work on mice. A brief but complete summary of the earlier works is also reported to permit a discussion of the results.

Contents

1. Introduction	2
2. Historical background	3
2.1. Measurement in space in the 1970s	4
2.2. Measurements in accelerators	5
2.3. Measurements on board MIR (SilEye)	8
3. The ALTEA program	9
3.1. The questionnaire	9
3.2. Alteino	10
3.3. ALTEA space hardware	10
3.4. The DOSI and CNSM modalities	10
3.5. ALTEA space preliminary results	12
4. The ground-based experiments in the ALTEA program	15
4.1. ALTEA—MICE	16
4.2. ALTEA—HIT	18
4.3. ALTEA—biophys	20
5. Discussion and conclusions	20
Acknowledgments	22
References	22

1. Introduction

The next two–three decades will see man again on the Moon and for the first time on Mars. These voyages will bring humans outside the protection of the Earth’s magnetic shield and atmosphere for a long time. Ionizing radiation which is mostly absent on the ground and moderate in space stations (MIR and the International Space Station (ISS)), may be above unacceptable risk levels, and is one of the major concerns for the realization of such long-term space travels (Cucinotta *et al* 2005).

Risks due to ionizing radiation traveling through biological tissue have been studied (Durante 2002) and increase with the increasing *dose* (dose: energy deposited per unit of mass). The definition of these risk assessments is under continuous evolution due to the specificity of the different possible damages and to the relations between effects and the ionization energy deposits in tissue (linear energy transfer (LET)) of the heavy ions.

Radiation may also have transient effects on brain functions. This is shown, for example, by the flashes of light perceived by astronauts in space, mostly while dark adapted, in the absence of real light—technically *phosphenes*, hereinafter *light flashes* or LF (Fuglesang 2007, Sannita *et al* 2006). Many experiments, as will be described later, linked these phenomena to the energy delivered to portions of the visual system by cosmic ionizing radiation. More generally, the delivery of an instantaneous amount of energy in a specific location of the brain or eyes may have a non-physiological influence on the working of the structures that are hit. This influence may cause unintended functioning of our senses or, worst, of our reactions or cognitive assessments. Several experiments suggest this kind of influence. For example, electrical pulses directly on the brain cortex are perceived by the blind as spots of light (Dobelle *et al* 1974); magnetic pulses on the visual cortex may lead to the transient inability to detect an otherwise

detectable stimulus (Amassian *et al* 1989). The interaction mechanism in these cases is likely to be different from the one between radiation and the visual system, however, this evidence shows that sensory pathways may be influenced by non-physiological energy deliveries.

Furthermore the LF phenomenon can be seen as an alarm system, signaling an activation of some otherwise hidden process which may constitute a *risk*. To deal with this issue it is necessary to study all the processes that may lead to a particle-triggered LF. Finally, ionizing radiation may influence sensory pathways, other than visual, as is also supported, for example, by olfactory sensations in coincidence with particle hits (Gauger *et al* 1986).

This paper will focus on the understanding of the LF perceptions in space. The aim is to characterize this effect both in space and in the supporting experiments on the ground. The questions related to the different possible mechanisms of interactions behind this effect will be discussed.

Following a short historical background, the results of the several experiments in space and on the ground performed in the 1970s and 1990s, will be summarized. Our latest measurements on the ISS will then be described together with the measurements on the ground performed within the framework of the ALTEA program. Discrepancies and concurrencies will be underlined with the aim of proposing strategies for bringing new information about this issue.

2. Historical background

A long time before any report from astronauts of anomalous phosphene perceptions in orbit, Tobias (1952) wrote 'It is conceivable that very densely ionizing tracks would produce small flash-like light sensations'. One year after Gagarin's flight D'Arcy and Porter (1962) reported the first measurement on the ground of visual sensations caused by cosmic muons¹.

It was Edwin Aldrin, on his return from the Moon, who first reported the perception of unexpected flashes of light (LF), while there was no real light (Pinsky *et al* 1974). Since then most astronauts and cosmonauts have confirmed and detailed these perceptions.

The recognition of the scientific problem was immediate; the light flashes experienced by the astronauts provided an increased impetus for radiobiological experimentation by direct exposure to heavy ions in space.

This evidence triggered a number of dedicated observations in space in the following missions, ranging from the mere report of the timing and number of LF perceived to the concurrent measurement of the radiation flux through the astronauts/cosmonauts' heads.

The awareness of the problem also started a long series of ground-controlled experiments in accelerators, where subjects aligned their eyes or brain on the beam line, and described their perceptions evoked by the passage of the ions.

The results of all these measurements immediately pointed to an interaction of ionizing cosmic radiation and some part of the visual system, primarily the retina, as a cause of the phenomenon. No other targets (brain and optic nerve) seemed to produce evidence, but these were less studied. The end of the space-race in the 1970s corresponded also to a halt in this research.

This topic only returned to the Space Agencies' agendas with our SilEye experiments on the MIR station in the 1990s. These works confirmed and refined what had already been described in the previous investigations.

¹ These findings were confirmed 2 years after Apollo 11 (Charman and Rowlands 1971); however, Tobias *et al* (1971) could not find similar effects.

Recently, at the end of the 1990s, we proposed the ALTEA program, aimed at providing a broader coverage of this issue. The rationale being that these interaction effects may go well beyond the clearly perceived LF and could constitute a new kind of risk for longer space voyages in less protected environments. The strategy being to perform objective measures in space (trying to avoid relying only on subjective reports), while designing new controlled experiments (*in vitro*, on animals and on humans) on the ground, to study the possible processes linked to these interactions.

2.1. Measurement in space in the 1970s

After the first LF reports, scientists programmed measurements in space, asking astronauts in the following Apollo missions to devote time for systematic observations of the phenomenon. To link LF perceptions to some specific ion traveling through the eyes, a new detector was designed and deployed (The Apollo Light Flash Moving Emulsion Detector or ALFMED, Pinsky *et al* (1974), Osborne *et al* (1975)).

Following the lunar missions, measurements were performed on the Skylab (1974), and during the Apollo-Soyuz Test Project (ASTP) in 1975.

The Apollo results are mostly summarized into three points: (i) almost everybody perceived LF (with a single exception: the Command Module pilot of Apollo 16); (ii) the rate was quite high (an average of about 14 in 1 h); and (iii) there was an impressive difference between the rate of LF perception during translunar coast (TLC) and during transearth coast (TEC), the former being about more than 60% higher than the latter. Astronauts also reported that the LF during TEC were much less brilliant.

The ALFMED detector provided the first identification of ion-candidates as the cause of LF perception. Analysis of the data showed two candidates heavier than oxygen (Osborne *et al* 1975). A later analysis (Fazio *et al* 1970) proposed Cherenkov radiation in the vitreous as the cause of the LF phenomena, showing a consistency between observed LF rate with the estimated flux rate. A direct excitation of the retina was considered possible with relativistic $Z \geq 2$ radiation.

Skylab and ASTP experiments were the first to report LF perceptions in low Earth orbit (LEO).

Skylab experiments were performed in two sessions, separated by a week, by the same astronaut during the last manned Skylab mission (Skylab 4) in early 1974 (Pinsky *et al* 1975). The sessions lasted 70 and 55 min. During both sessions the Skylab passed through the South Atlantic Anomaly (SSA), the portion of the low altitude Earth's inner trapped radiation belt. The results of these observations showed a dependency of LF perception rate on the radiation flux, as expected, and a significant increase (10–20 times) in the LF rate when passing over the SSA.

Experiments during the ASTP were performed jointly by the Apollo Commander and by the Apollo Command Module Pilot. Both were dark-adapted using a light-tight mask for about 10 min. The astronauts perceived a total of 82 LF in 90 min for an average rate of 0.46 LF min^{-1} . During the SSA passage the astronauts perceived a total of 4 LF. The results confirmed the correlation of the LF rate with the modulation of the radiation flux during the orbit and proposed a LET lower threshold for LF generation of about $5 \text{ keV } \mu\text{m}^{-1}$ (Budinger *et al* 1975). The absence of rate increase in the SSA, in contrast with the Skylab findings,

Table 1. LF experiments in space.

Mission (experiment)	Altitude (inclination)	Sessions, astronauts	Approximate shielding	Session time (min)	Number of LF (in SAA)	Mean time between LF (min)	Approximate min–max time between LF (min)
Apollo	–	20,12	3–5.5 g cm ⁻² Al	1161	268	4.3	1.3–8.6
Skylab	443 (50)	2,1	1.5–2 g cm ⁻² Al	105	168 (124)	0.6	1.1–4.4 (3.8 s in SAA)
ASTP	225 ^a	2,2	3–5.5 g cm ⁻² Al	180	82 (4)	2.2	0.8–6.0
MIR (SilEye)	350–400 (51.6)	29,6		1579	233 ^b	6.8	3–13
ISS Pirs (Alteino)	350 (51.6)	6,1		461	44	10.5	6.4–22
ISS USLab (ALTEA)	350 (51.6)	7,3	≈ 10–15 g cm ⁻² Al	414	20 (0) ^c	20.7	5–>60

^aAt 225 km altitude the low energy proton flux is 14 times less than that at the 443 km altitude of Skylab (Budinger *et al* 1975).

^bThe rate in the SAA is about twice the rate measured outside the SAA (Avdeev *et al* 2002).

^cOnly one session passed through the SAA.

was explained with considerations about the lower orbit and higher shielding of the ASTP (see table 1).

2.2. Measurements in accelerators

Several experiments in particle accelerators were performed concurrently with the space investigations. The experimenters received a minimal quantity of ionizing radiation in their eyes and psychophysiological responses were recorded. These works were published from 1970 to 1978. The many parameters used could be grouped into two families: beam parameters and target parameters.

Beam parameters were mostly Z (including neutrons), fluence, length of the burst, energy. Target parameters define the specific physiological target and the direction and versus of the beam bursts, with reference to the target. Of this multidimensional space only limited regions have been explored, so that describing a complete picture from these results is quite a difficult task. Giving a complete account of all these works is not within the scope of this paper. A schematic summary is given in table 2.

With reference to the table, the particles explored have been μ , π , He, C, N and neutrons. The beams were directed almost always towards the eye. Almost all were able to cause LF sensations in some configuration of the parameters. Only non-energetic neutrons (3 MeV) and very energetic π (1.5 GeV c⁻¹) failed to produce LF at the chosen set of the parameters. In two cases the beams passed through the visual cortex (N at 266 MeV n⁻¹ and cosmic μ) and in both cases there was no LF perception. Detection thresholds were searched for in a few measurements: with μ and π at least 150–300 particles in each burst were needed for LF perception. This appears to be in contrast with cosmic μ where detection (in darkness) was

Table 2. Results of the ground experiments in the 1970s.

Ref	Particle	Energy/ momentum	Number/ fluence	Direction	LF	Description	Comments/suggested mechanism
a	μ cosm	n.a.	Single	\approx F	Y	'Bright points of light' Efficiency \approx 24%	No Cherenkov Direct excitation of retina Probably no Cherenkov
b	μ Cosm	n.a.	Single	F B L L(cort)	Y N		
c	N	3 MeV	10^5	F B	Y	Faint points F: few/s; B: 5 times more	Knock on ^+H on retina (or early part of visual system)
d	N N	3 MeV 14 MeV	2×10^4	F L F L B	N Y Y	Rates 0.3 s^{-1} 10 s^{-1} white–bluish, no color Rate 0.3 s^{-1} (only one observer)	No Cherenkov Speculations on HZE
e	n π^+ X-rays	20–640 MeV 1.5 GeV c^{-1}	1.4×10^4 200	F L	Y N	Point mov/stars blue–white approaching	He from n on CNO Not able to see flashes at ground level from cosmic particles (see above) Scintillation 7000 photons needed for one LF High Z and low E needed (but shielded by cutoff in LEO)
f	He	5.3 MeV		in eye (freshly killed bullocks)	n.a.	n.a.	
g	μ	6 GeV c^{-1}	$3 \times 10^3 \text{ pulse}^{-1}$	L B	Y N	Bright diffuse flashes	most plausible mechanism is Cherenkov
h	n	$<25 \text{ MeV}$ (pkd at 8)	10^3 – 10^4	F B	Y Y	Bright stars, colorless As above fewer and weaker	Recoil H, He from n on C O
i	He N	240 MeV 266 MeV n^{-1}	10 – 20 pulse^{-1}	L Cort (900 ions)	Y N	Efficiency 40% Different shapes	Flashes only when beam in posterior part of the eye
j	N	531 MeV n^{-1}	$\approx 1 \text{ pulse}^{-1}$	25°	Y	Efficiency 10% Different shapes	Cherenkov
k	μ π^-	7.2 GeV c^{-1} 725 MeV c^{-1}	1 – 400 burst^{-1}	F	Y	Threshold at 150 – 250π per burst; large flashes with dark center	Cherenkov
l	μ	7.2 GeV c^{-1}		F L B	Y	All colorless; threshold ≈ 300	Cherenkov
m	Π	725 MeV c^{-1}	1 – 1000 burst^{-1}	F	Y	Threshold 250 – 300	Cherenkov
n	C	470 MeV n^{-1} 595 MeV n^{-1}	1 – 2 burst^{-1}	60°	Y	As π and μ ; efficiency $1/10$ – $2/3$; (single and multiple particles \approx the same)	Cherenkov

F, front; L, lateral; B, back.

a, D'Arcy and Porter 1962; b, Charman and Rowlands 1971; c, Fremlin 1970; d, Charman *et al* 1971; e, Tobias *et al* 1971; f, McAulay 1971; g, McNulty 1971; h, Budinger *et al* 1971; i, Budinger *et al* 1972; j, McNulty *et al* 1972; k, McNulty *et al* 1975; l, McNulty *et al* 1976a; m, McNulty *et al* 1976b; n, McNulty *et al* 1978.

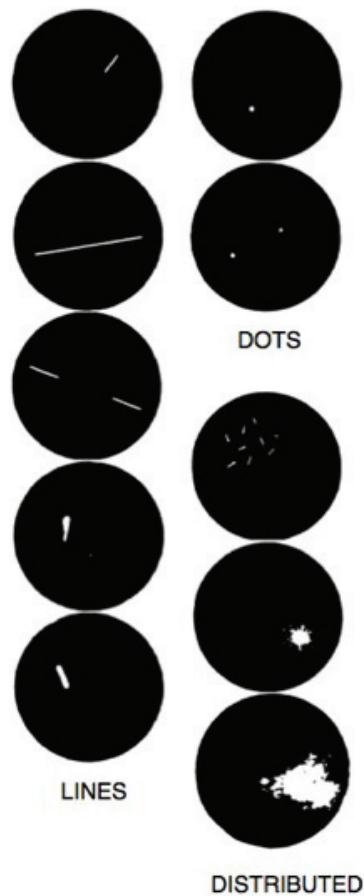


Figure 1. Sketch of different kinds of LF perceived by astronauts.

reported even for a single particle, with a 25% efficiency (D’Arcy and Porter 1962, Charman and Rowlands 1971). As mentioned (see footnote 1), these rather surprising findings (if this were true we should often experience LF on the ground) could not be confirmed later by Tobias *et al* (1971). The two heavier ions (N and C) were used in single–few particle mode: N (240 MeV n^{-1} , lateral incidence) 15 per burst, 40% efficiency; N (531 MeV n^{-1} , 25° incidence), single, 10% efficiency; C (470 and 595 MeV n^{-1} , 60° incidence), 1–2 per burst, 10–67% efficiency.

A possible classification of the output of these experiments, beside perceptions and rate of LF, concerns the LF shape. As illustrated in figure 1, LF appeared to astronauts (and to subjects during ground experiments) in many shapes. They were either dot-like (single or many) and strikes, or diffuse. Also color is sometime reported, and often motion. During the many controlled experiments there had been an effort to link LF characteristics with the possible processes that might have generated them. As an example, the diffuse LF, sometimes with dark center, appeared to be related to Cherenkov radiation (McNulty *et al* 1975). However, again, the very partial coverage of the parameter space did not allow for final associations. The absence of LF moving vertically (see also Fuglesang *et al* 2006) appears to be one of the very few common characteristics of all the reports about LF.

Table 3. Ion candidates as LF triggers.

Mission	Number	Z
Apollo (ALFMED)	2	> 8
MIR (SilEye2)	8:	
	3	2
	2	2–3
	2	8
	1	≈ 24
ISS (ALTEA)	3 ^a	3–4 ^a

^aPreliminary, low LET ions (3–6 keV μm^{-1}).

2.3. Measurements on board MIR (SilEye)

Starting from the mid-1990s we designed SilEye, a new space experiment to clarify some of the LF issues. From 1995 to 1999, we carried out the longest LF observation campaign on board the MIR station (Avdeev *et al* 2002). A total of 29 sessions, involving six cosmonauts and spanning almost 26 h (with 233 LF perceptions), were performed. The overall rate was about 9 LF h⁻¹ (average time between LF: 6.6 min). Two different SilEye apparatuses were used. They included an active particle telescope which was able to measure particles, identifying Z, trajectory and energy released (Bidoli *et al* 2001). The telescope was positioned either in front of the eye (SilEye1) or laterally to the right eye (SilEye2), permitting the detection of particles passing through the eye. SilEye1 was a prototype and pioneer experiment (Bidoli *et al* 2000). SilEye2 detected a total of about 116×10^3 H, 858 nuclei ($Z \geq 2$) and 4434 showers passing through eyes in the 814 min of observation. In the same time window 116 LF were perceived (Avdeev *et al* 2002). Using as reference the signal recorded from a pushbutton, pressed when a LF was perceived, 8 ions have been reported as candidates for the generation of the LF (see table 3). The ratio of the number of candidates to the number of perceived LF was shown to be in good agreement with the estimate for the relative geometrical acceptance of the eyes and the detector (6–7%). An analysis of the LET distribution showed that the probability of generating a LF increased with increasing LET, suggesting a LET higher than 10 keV μm^{-1} was needed to generate a LF (Avdeev *et al* 2002), in agreement with previous measurements (Tobias 1973). The probability for an ion ($Z \geq 2$) traveling through the eye to generate a LF was found to be $\approx 1\%$, while the same probability for a proton with $E < 200$ MeV was found to be about 750 times smaller. About 90% of the flashes were described as lines or lines with gaps. The rate of LF in the SAA was about twice as large as the rate outside the SAA. There was no apparent long-term dynamics with the permanence in space, as confirmed by a later survey among astronauts (Fuglesang *et al* 2006). It should be mentioned that two astronauts out of the ten involved in the experiment did not report any LF. A further analysis of the data collected in the SAA (Casolino *et al* 2003) proposed that high proton fluxes have a role in LF generation suggesting knock on processes on C N O, whereas outside the SAA high charge and energy (HZE) particles have the leading role. As discussed in the last section, the contribution of high LET stopping protons should also be taken into account.

3. The ALTEA program

ALTEA is a full-scale interdisciplinary program aimed at investigating the LF phenomena, and more generally the interaction between cosmic radiation and brain functions (Narici *et al* 2003, 2004).

The ALTEA program is searching for answers to several questions:

- 1) What kind of *functional* effects on the brain can be elicited by radiation? Which of these effects may have associated risks?
- 2) What kind of radiation (Z , energy) is more likely to produce such effects?
- 3) What is the radiation environment the astronauts are experiencing in the ISS?
- 4) What portion of this radiation is produced by interactions in the spacecraft hull?
- 5) What are the specific interactions causing these *functional* effects?
- 6) Can we quantify the *functional* risk due to these effects in LEO?
- 7) What are the best countermeasures that should be taken to minimize these risks?
- 8) Can we extrapolate these findings to outer space (Moon, Mars), and with what level of confidence?

In order to provide answers to these questions new space hardware has been developed and a series of supporting ground experiments have been designed.

The ALTEA space particle detector is a natural development of our previous SilEye detectors, with a much larger solid angle coverage for the particles passing through the head. To obtain objective information about the LF perception we included in the system the possibility of recording electrophysiological signals via a high definition electroencephalographer (EEG). To monitor the status of the visual system in microgravity a visual stimulator was also added. Due to the end of the operational life of MIR, the natural site of the ALTEA space project has been the ISS.

Finally a series of experiments based on measurements in particle accelerators was designed with the aim of supporting the space measurements and providing detailed information on the possible mechanisms of the radiation–brain functions interaction.

The program in the current form will not give exhaustive answers to all the questions mentioned above; however, it is providing valuable information concerning all the raised problems and for some of the topics it is also providing final answers.

3.1. The questionnaire

The ALTEA program started with the collection of the subjective experiences of the many astronauts who have flown since the Apollo missions. These represent important information for the understanding of the phenomena related to these perceptions.

A 29 item questionnaire was prepared and distributed to 98 astronauts who have flown in different missions (Fuglesang *et al* 2006). Of them 58 responded and of these 47 reported experiencing LF (in agreement with the percentage found during the SilEye experiment on MIR). The answers to this survey show clearly the broadness of the characteristics of these effects: from the astronauts who never observed LF, to the ones whose sleep was disturbed by them ($\approx 20\%$), or to those who reported LF visible even in bright light (for 1–2 cases). LF have been described with many shapes, several different colors, steady or moving. Interestingly, no

astronaut has ever reported an apparent vertical motion (motion has been reported only in the horizontal plane, in the two directions or a combination of them). If we associate the ‘diffuse’ LF shapes with the Cherenkov effect, we could infer that about 5–10% of the LF might be due to this process.

3.2. *Alteino*

Alteino/SilEye3 was the first experimental achievement of the program providing the first measurement with full Z discrimination of the radiation environment in the ISS (Pirs module, in the Russian Segment, Casolino *et al* (2002), Narici *et al* (2004)).

Alteino featured a 16-channel EEG and an active particle detector, an upgrade of the SilEye ones, placed nearby the astronaut so as to measure the radiation flux, however, without the possibility of retrieving timed particle data through the eyes. Six LF sessions were performed in April–May 2002, in the Pirs module of the ISS (see table 1). The total observation time was 7 h 41 min and the LF rate ranged from 3 to 9 LF h⁻¹. Alteino permitted us to master EEG measurements in space.

3.3. *ALTEA space hardware*

The ALTEA hardware has been operating in the ISS–USLab since August 2006. It features six identical silicon particle telescopes assembled on a helmet-shaped holder (silicon detector system, SDS). Each telescope is made with six silicon planes—each composed of two $8 \times 8 \text{ cm}^2$ and $380 \mu\text{m}$ thick wafers—striped alternately in the x - and y -directions, in order to be able to reconstruct the trajectory of the particle. A 32 electrode EEG cap, including three floating electrodes for retinogram measurements, and high resolution electronics allow for electrophysiological readings. A visual stimulator is used to deliver standard stimuli. Electrophysiological responses to these stimuli (evoked potentials) are measured to test the status of the visual system. A three-button pushbutton is used to signal the LF perception. At the highest sensitivity, the SDS is able to detect particles from He to relativistic Mo, and protons between 25 and 200 MeV (Zaconte *et al* 2008).

3.4. *The DOSI and CNSM modalities*

ALTEA space is mounted on an express rack in the USLab and can be utilized in two modalities: dosimetry (DOSI) and central nervous system monitoring (CNSM).

In the DOSI unmanned modality, the six detectors on the helmet (silicon detector system, SDS), tilted flat on the rack as shown in figure 2, continuously measure the environmental radiation. Data are downlinked in real time to the ground, to the User Home Base in the Department of Physics of the University of Rome ‘Tor Vergata’. Real time and off line software provides tools to discriminate the kinds of particles, calculate trajectories and energy of the particles, constructing spectra of the measured radiation. ALTEA operated in DOSI mode almost continuously from August 2006 to July 2007.²

The manned experimental modality (CNSM) is specifically aimed at the study of the interaction between particle passages and brain electrophysiological dynamics. The detector is extended normal to the rack. The astronaut wears the EEG cap, inserts the disposable pregelled

² A recent agreement between NASA and the Italian Space Agency will permit the use of ALTEA for monitoring radiation during operations from the beginning of 2009.



Figure 2. ALTEA in DOSI mode in the ISS–USLab.



Figure 3. ALTEA in CNSM mode in the ISS–USLab, during a measurement.

electrodes, slides into the SDS helmet and wears the visual stimulator which also permits dark adaptation (figure 3). In this configuration, the SDS measures the particles passing through the astronaut's head. For about 25 min he/she is presented with a standard set of visual stimuli, then the astronaut relaxes; after about 5–10 min of dark adaptation the observing session starts: each perception of a LF is signaled with the pushbutton. The observing session lasts about one hour.

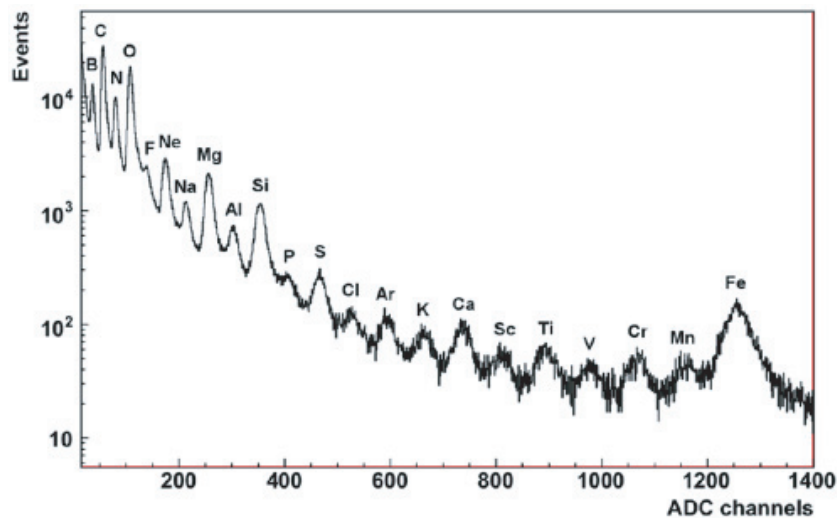


Figure 4. A spectrum of the radiation environment of the ISS showing the nuclear discrimination capability of the ALTEA detector. Only particles releasing an almost constant energy (<10% difference between the two outer planes) are counted. The spectrum refers to about six months acquisition with 10 MIP threshold.

Total measurement time is about 1.5 h: one orbit. Seven sessions with three astronauts have been performed. The last one was lengthened to allow a measurement with a full passage in the SAA (the other six did not pass over the SAA during the observing time).

3.5. ALTEA space preliminary results

Data analysis for the ALTEA-space measurements is still in progress and will be the topic of focused papers in preparation.

Here preliminary results are reported. These may have already provided insights on the LF phenomena and, in general, on the interaction of ionizing radiation with brain functions. These findings will be discussed in the panorama of the previous results.

When operating in the DOSI mode ALTEA allowed for a quite detailed view of the radiation environment in the USLab. In figure 4, we show the spectrum from six months acquisition, with a threshold of 10 MIP (MIP: minimum ionizing particle = 109 keV/380 μm of silicon). In this configuration, ions from B to Fe are discriminated. Lower thresholds permit lighter ions to be discriminated.

The seven sessions of CNSM measurements produced 20 LF perceived in about 7 h of observing time (see tables 1 and 4), less than expected considering the previous LEO measurements (see table 1). More than half of these LF were perceived in a single session. Only the last session passed over the SAA. The astronaut paid particular attention during the transit; however, he reported to have seen no LF during that period.

Using the discriminating and tracking capability of ALTEA, during the CNSM sessions the ionizing radiation passing through the eyes and the brain of the astronauts has been measured and characterized for the first time. Analysis is still in progress, however, preliminary results from the first session show a measured rate of about 2.8 ions min^{-1} in the eyes.

Table 4. The ALTEA–CNSM sessions.

Astronaut	LF	Duration (min)	Mean interval between LF (min)
1	12	58	5
2	4	65	16
3	1	18	–
2	0	63	–
3	1	61	–
2	1	62	–
2	1	87	–
Total	20	414	21

Table 5. Ions through both eyes (total rate per minute) in one CNSM session (no SAA). Values in *italic* show our estimate for a preliminary discrimination in Z and energy. These total rate values are obtained by multiplying the measured rate by the ratio of eye acceptance to SDS acceptance (≈ 6.3).

	All	$E \leq 100 \text{ MeV n}^{-1}$	$E > 100 \text{ MeV n}^{-1}$
All	18	<i>2</i>	<i>16</i>
$Z < 6$	<i>16</i>	<i>2</i>	<i>14</i>
$Z \geq 6$	<i>1.5</i>	<i>0.07</i>	<i>1.4</i>

We evaluated in different ways the total rate of radiation hitting the astronauts' eyes in the energy range detected by ALTEA, taking into account the geometrical factors of the SDS ($1190 \text{ cm}^2 \text{ sr}$, [Zaconte et al 2008](#)) and of the eyes, and found consistently $\approx 2 \times 10^1 \text{ ions min}^{-1}$ through the eyes (the ratio of eye acceptance to SDS acceptance is ≈ 6.3) and $4\text{--}5 \times 10^2 \text{ ions min}^{-1}$ in the brain. These figures are lower limits: instrument dead times and multiple traces have not yet been considered. Furthermore the detectors are not triggered by most protons and high energy He, however, these low LET ions (less than $1.5 \text{ keV } \mu\text{m}^{-1}$) should not have an important role in LF generation ([Avdeev et al 2002](#), [Budinger et al 1975](#), [Tobias et al 1973](#)).

When the analysis is completed we will also be able to estimate the charge of each of the measured ions. Work is in progress to determine the energy discrimination ability of the device both at low and high input energies. Our goal is to calculate the dose per diem in the eye/brain of the astronauts. Preliminary results permit the radiation in the eyes to be detailed as shown in table 5.

These values are in principle applicable to any ISS orbits (excluding SAA), and to any astronaut.

To compare these findings with estimations in the literature some evaluation of the amount of shielding of the USLab, where CNSM and DOSI are performed, is needed. From comparison of our measured relative ion abundances inside the ISS to ion spectra outside the ISS ([Simpson 1983](#)) propagated through the Station hull, this shielding can be estimated to be about $10\text{--}15 \text{ g cm}^{-2}$.

We compared our measured eyes rate (with $Z \geq 6$) with previously published estimations. For example, Fazio *et al* (1970) reported an estimate of $0.5\text{--}1.0 \text{ ion cm}^{-2} \text{ min}^{-1}$ for heavy ions ($Z \geq 6$) reaching the eyes, in the Apollo command module, which was a factor of 3–5 less shielded than the USLab (see table 1). Our figure of $1.5 \text{ ions min}^{-1}$ should be compared with $2.3\text{--}4.5 \text{ ion min}^{-1}$ (considering both eyes) estimated in the reported paper. Considering the higher shielding of the USLab and that our measurement have been performed in LEO, while the mentioned estimates were for a lunar flight outside the magnetosphere, our figure appears compatible with the previous evaluations.

This measured rate of ions in the eye in ALTEA–CNSM produced an averaged rate of $\approx 5 \times 10^{-2} \text{ LF min}^{-1}$ (20 in about 7 h of observation). Assuming that each of the ions in the eyes could cause a LF, we can calculate an efficiency of $\approx 2 \times 10^{-3}$. This figure is an upper limit, due to the non-considered dead-times, multiple tracks and other possible brain targets (that may produce visual sensations, such as in the optic nerve, or the visual cortex). One way to interpret this data is to assume a simple geometrical efficiency, leading to a sensitive surface of about 7 mm^2 , which might be consistent with some portion of the retina. This assumption would be compatible with an interaction model requiring specific areas within the retina as targets.

The observed LF rate is lower than expected. SilEye findings, for example, would suggest about three times more LF. There is also a lower efficiency in ALTEA in the production of LF by particles impinging the astronauts' eyes in comparison to SilEye (a factor of 5 less). This may suggest that the observed lower LF rate may not be due to the possibly higher USLab shielding (and consequently lower fluence), indicating interindividual variability and physiological parameters as conceivable reasons for this discrepancy.

The electrophysiological measurements in space (ALTEA–CNSM) are providing the first links between radiation and its effects on electrophysiology. Geometrical considerations show that only about 1 particle will be measured for every $\sim 6\text{--}7$ passing through the eye, so we expect to be able to identify ≈ 3 ion candidates for the 20 LF perceived. We have been first analyzing the electroretinograms (ERG), looking for features in the ERG traces linked to the particle passages in the eye. Results from the first session indicate one, possibly two candidates. Both ions are light ($Z \approx 3\text{--}4$) and appear to produce an ERG signal which in morphology is similar to the one measured after light stimulation. Analysis is still in progress and results will be published soon.

The electrophysiological response from one of these candidates is shown in figure 5 (ERG from right eye, following one particle (estimated $Z \approx 3$) which is hitting the same eye; see top right inset for the trajectory). In figure 5 we can follow the time behavior of the retinal response from the arrival of the ion ($t = 0 \text{ ms}$) to the signal from the pushbutton ($t = 880 \text{ ms}$), and the possible underlying activities. The processes we are most interested in are probably in the first 10^2 ms . We know that the ion will release some energy in the eye, and that sometime in the following 500 ms the astronaut perceives the LF, prepares to move his finger, and finally presses the PB. The electrophysiological retinal response at $\approx 10^2 \text{ ms}$, similar in morphology to known responses to light, suggests that the energy released is routed into a quasi-physiological path producing a response compatible with the known light-induced responses.

Note that our preliminary findings (backed by the previous results) seem to indicate that the most probable ions for generating LF are light ions (see table 3).

We are also analyzing signals from the visual cortex (visual evoked potentials, VEP) searching for correlations with ions in the retina, in the optic nerves and in the cortex, regardless of the perception of LF. The final analysis goal will be to investigate the brain

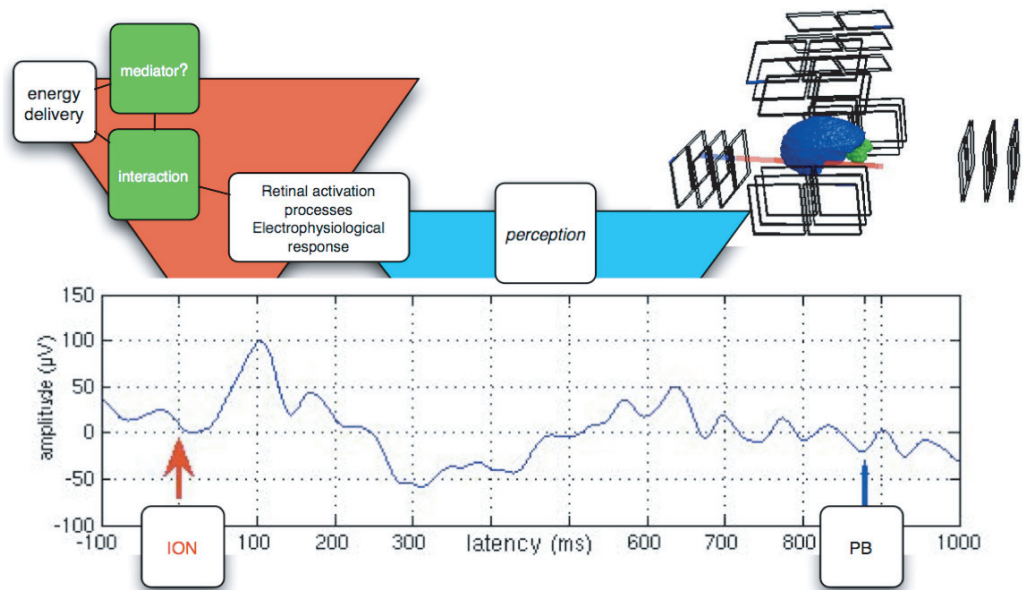


Figure 5. A retinal signal (right eye) following the hit on the right eye of an ion ($Z \approx 3$), (see top right for a sketch of the trajectory). PB indicates the instance at which the astronaut pressed the push button. Above is a diagram of the processes which are assumed to be concurrent to the response dynamics (see text).

electrophysiological dynamics following ionizing radiation impacts in all brain regions (not only in the visual areas), regardless of the generation of LF. The rationale is the assumption that: (i) there might be direct effects on the retinal/brain electrophysiology that do not trigger cognitive events such as perception; and (ii) regions of the brain other than visual areas may be affected as well by incident radiation. In both cases electrophysiological signals will provide useful information for understanding the biophysical interaction at the start of these processes. Analysis in this sense is in progress.

4. The ground-based experiments in the ALTEA program

Several ground experiments provide a controlled environment for these investigations.

The appropriate first step would be to repeat the 1970's experiment using objective EEG recordings. However this would likely encounter vetoes from ethical committees.

Therefore we designed and performed experiments on animal models, patients and *in vitro*.

We set up an animal model using mice, irradiated with very short bursts of heavy ions while concurrently acquiring electrophysiological data from the retina and from the cortex (ALTEA-MICE). We also measured EEG and ERG of those patients undergoing tumor heavy-ion therapy at GSI (Darmstadt, FRG) who reported perceiving LF during the therapy (ALTEA-HIT). Finally, we started *in vitro* investigations of the behavior of rhodopsin, at the start of the phototransduction cascade in the process of vision, when hit by heavy ions (ALTEA-biophys).

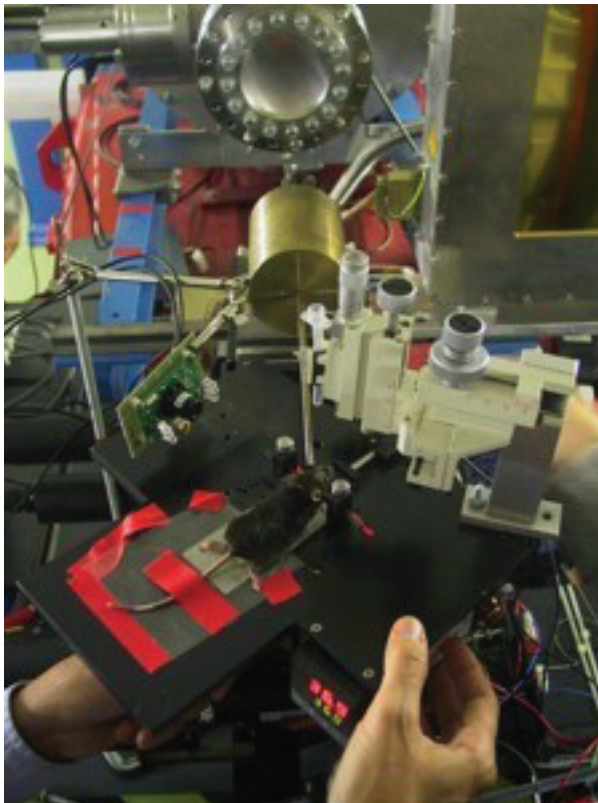


Figure 6. Setup of the MICE experiment at GSI.

4.1. ALTEA—MICE

This project proposes an animal *in vivo* model for the study of the origin of the radiation-induced phosphenes (Sannita *et al* 2004). It is aimed at studying the electrophysiological dynamics of mice, while the eye or the cortex is irradiated with very short bursts of heavy ions. To assume that the mouse visual system interprets each burst as a single-energy delivery, the burst length is kept below 2 ms.

A setup has been designed and built to hold the mouse and provide capability for remote controlled alignment to the beam (figure 6). The same setup permits the animal to be stimulated with light (with a white LED), to monitor the experiment with an infrared video camera, to precisely position the electrodes (cortical and retinal), to control the temperature of the animal, and to quickly change the animal maintaining the alignment set. The whole measurement is remotely controlled from the beam line control room.

Several preliminary measurements have been performed at GSI (Darmstadt, FRG) and at Brookhaven National Laboratories (AGS, NSRL).

In a pilot experiment (Sannita *et al* 2006), we irradiated the retina of anesthetized wild-type mice with short bursts of carbon ions, below the Cherenkov threshold. ^{12}C ions evoked electrophysiological responses in the mouse retina and visual cortex comparable to those following light stimuli. Responses to ^{12}C ions were obtained with burst lengths of ≤ 2 ms, containing $\approx 10^3$ ions, 250 MeV n^{-1} ($\text{LET} = 14 \text{ keV } \mu\text{m}^{-1}$), in about 50% of the mice tested. The beam was collimated (diameter = 5 mm) and directed to the mouse eye. Latency of

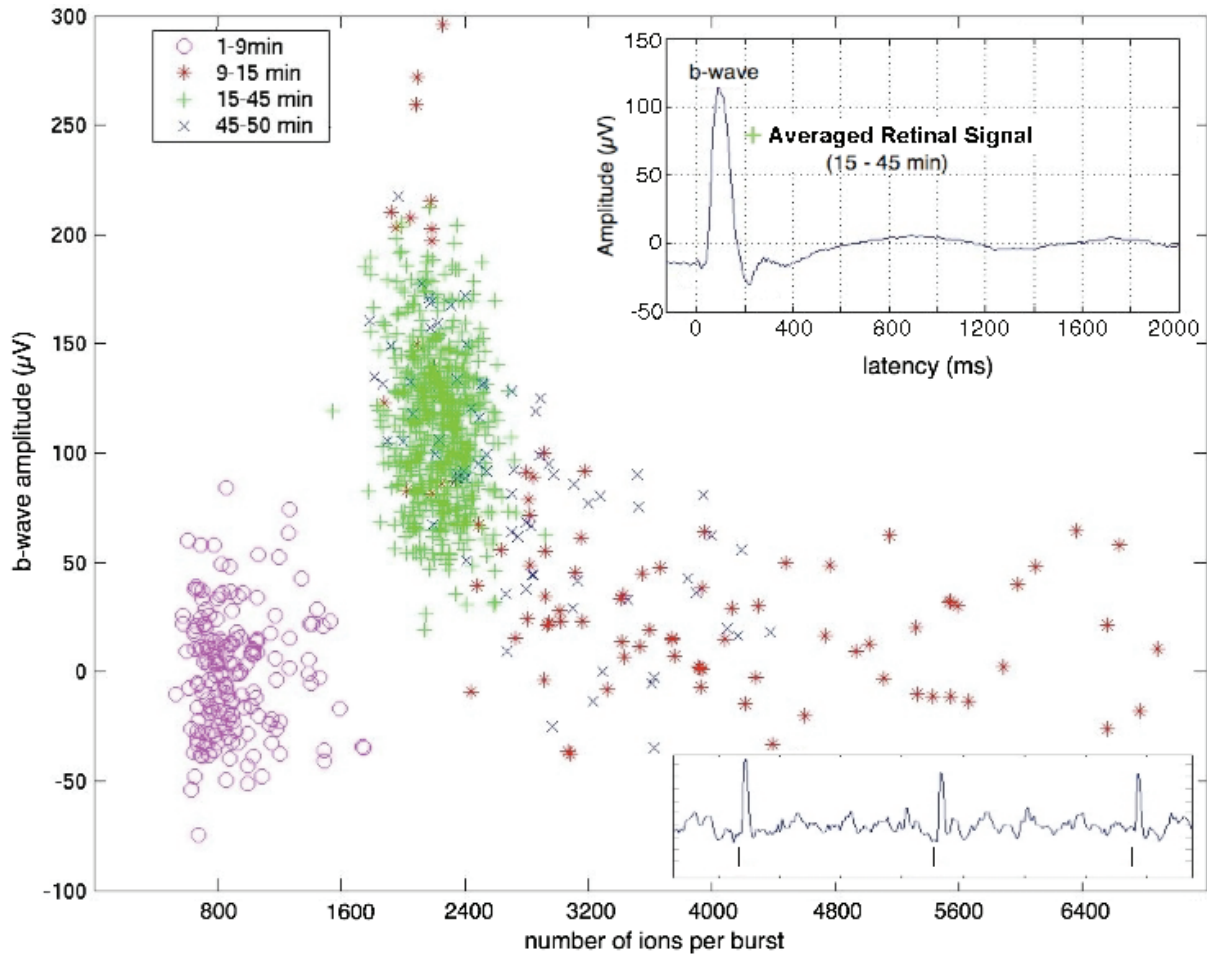


Figure 7. Amplitude of b-wave in one mouse as a function of the number of ions in each 2 ms burst. The different symbols indicate different times during the 50 min irradiation (see legend at the top left). The real time retinal signal is illustrated in the lower inset (the instant of the ion bursts is reported at the bottom, every ≈ 3 s). In the top inset, the average of the retinal responses is shown (indicated in the main plot with green crosses: from 15 to 45 min).

responses was ≈ 35 ms longer than the ones following light bursts. This difference might be accounted for by the weakness of the ion-induced stimulus. This has been the first evidence of electrophysiological responses comparable to that of light from a particle passing through the eye.

We did not detect damage in the retinal architecture, staining intensity and distribution of various antigens of retinal samples studied by immunocytochemistry.

In one mouse, we recorded clear online retinal responses (see figure 7, lower inset), and we studied the response dependence with the number N of ions in the burst. We observed a threshold, at $N \approx 1700$ ions, a maximum with $N = 2000$ – 2500 , and then a clear decrease almost to zero with $N > 3000$ (figure 7). When $1700 < N < 2700$ (between 15 and 45 min) 98.6% of the bursts produced a response.

The threshold might be compatible both with: (i) a large net energy deposit from many particles within the same burst needed to generate the response, as well as to (ii) the low

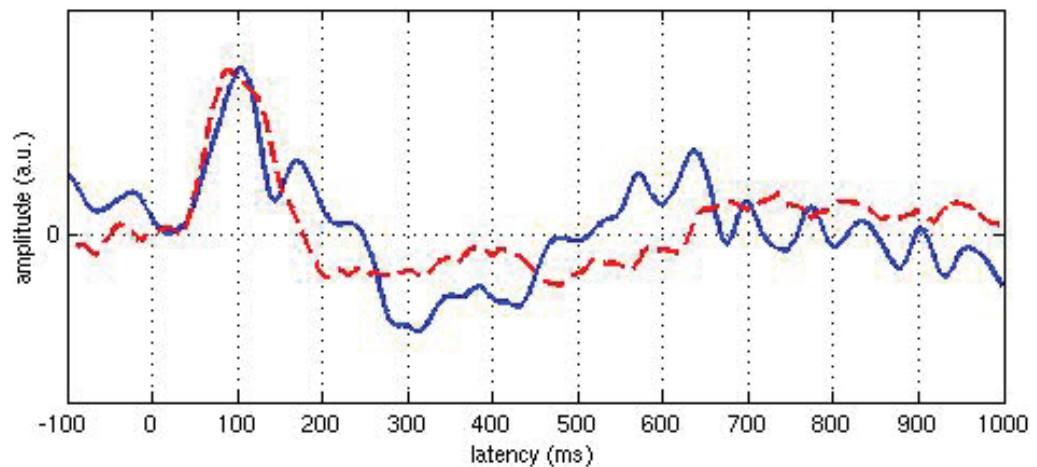


Figure 8. The same retinal signal as in figure 5 (blue continuous line) compared to one of the online responses from a mouse (red dashed line, see figure 7, lower inset). Amplitude of the two signals has been normalized (arbitrary units). Latency = 0 corresponds to the arrival of the ion(s).

probability that a single particle (or a small number of them) would produce a response, for cross-sectional reasons. However, when these data are seen in the panorama offered by the other ground and space results, only this second explanation survives. In this case, the threshold would be seen as the result of a $\approx 10^{-3}$ total efficiency value, in agreement with what was found for single-particle generation in the CNSM measurements (see above). The drop-off observed at higher rates might be due to a not yet identified saturation process.

One of the online responses is compared (figure 8) to the astronaut retinal response in figure 5. The morphology similarity is evident, and the slight latency delay (about 20 ms) is compatible with differences in latencies between human and mice responses.

The wide inter-animal response variation found in the mice experiment might suggest that we had scarce control on some unidentified parameter, or/and that we may be triggering more than one process leading to electrophysiological responses.

4.2. ALTEA—HIT

The intensity modulated heavy ion tumor therapy at GSI exploits the characteristic depth-dose profiles of heavy ions in matter to irradiate tumors with minimal effects on the surrounding tissues (Kraft 2000). The beam intensity is of the order of 10^{7-8} ions s^{-1} and a complex control system permits the dose of each irradiated voxel to be specified. Several patients undergoing heavy ion therapy reported the perception of LF during the irradiation (Schardt and Krämer 2002). Since then we started a collaboration with the GSI/Heidelberg medical and physics teams to measure EEG of the patients while they were being irradiated. Therapy is distributed over 20 sessions, in consecutive days. We usually tested a few patients each therapy run, for at least four sessions. The project started in August 2004, we have measured a total of 15 patients in four therapy runs between 2005 and 2007.

Patients' heads are anchored on a bed via a thermoplastic mask manufactured for each patient. The therapy masks of those patients who reported having perceived LF during therapy

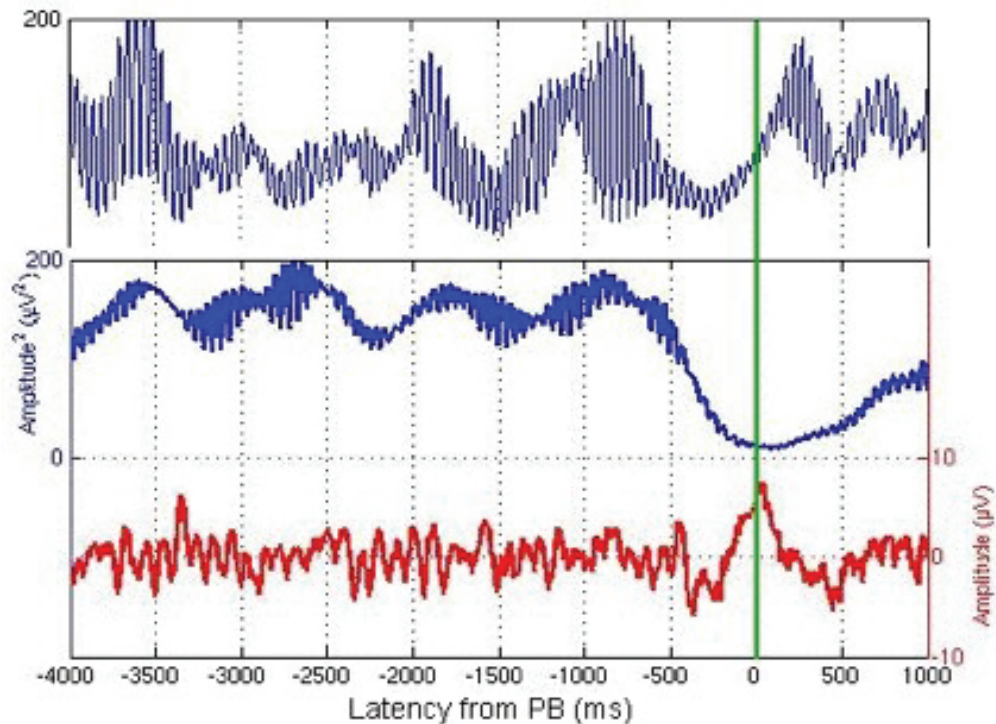


Figure 9. *Bottom two traces:* EEG from one electrode on the occipital cortex of one patient. Average over all the LF perceptions, aligned to the pushbutton signals (PB), in two different bandwidths: (i) filtered 1–45 Hz (bottom, red trace) and filtered in the 8–12 Hz band, squared and then averaged (middle, blue). Here, $t = 0$ ms (green bar) indicates the pushbutton signal. The bottom red trace shows a signal (about 300–400 ms before PB) which is a candidate to be produced by the ions generating the LF. The middle blue trace shows a possible depression of alpha-rhythm (8–12 Hz) starting about 500 ms before PB. For reference we show (*top trace*) a laboratory baseline (no beam) when a subject pressed the pushbutton following an acoustic stimuli, filtered and analyzed as the middle blue trace. The absence of the depression can be appreciated.

were equipped with electrodes to measure EEG and ERG during therapy. A pushbutton was used by the patients to signal the LF perception.

Data analysis is in progress. The main goal will be to assess the precise location(s) of the beam when the LF is generated. This will permit eye/brain areas where LF might be generated to be shown.

Preliminary findings show a large signal (same polarity of the ‘b’ retinal wave, about 10^2 ms long and about 300–1000 ms prior to the pushbutton signal) measured on the cortical/retinal electrodes (figure 9, red trace) when the beam is irradiating locations on the boundary of the tumor, possibly with a marginal interest of the posterior region of the eye (the exact location of the beam is still under analysis). Each single site is irradiated for a few milliseconds; however, it is quite conceivable that many adjacent sites could generate LF, and in this case we would have a multiple trigger, summing up to a long ‘particle stimulus’ which might modify the morphology of the response, probably increasing its length.

One of the most prominent rhythmical activities of the brain (the *alpha* rhythm), measurable over the occipital cortex, appears depressed before and after the pushbutton is pressed, while a control experiment, using no beam and with an acoustic stimulus to trigger the pressing of the pushbutton, does not show a similar depression (figure 9 blue traces).

4.3. ALTEA—biophys

Rhodopsin is at the start of the phototransduction cascade in the process of vision. It is one of the best molecular transducers for converting a visible photon into an electric signal. It is therefore the first candidate as the target for the radiation–visual system interaction. We have been working to study the possibility that rhodopsin can also be activated by irradiation with ^{12}C nuclei.

Intact rod outer segments (ROS) containing rhodopsin were isolated from bovine retina. Suspended ROS were irradiated with ^{12}C (200 MeV n^{-1} , well below the Cherenkov threshold) at GSI (Darmstadt, Germany). Spectrophotometric measurements investigated the activation (*bleaching*) of the rhodopsin. The functionality of the ROS after irradiation was checked by regenerating the rhodopsin *in vitro*. With these measurements we were able to show that radiation can induce *bleaching*, and that rhodopsin can be subsequently effectively regenerated.

Data analysis and work on the understanding of the interaction mechanism are in progress.

5. Discussion and conclusions

The LF phenomenon demonstrates that radiation may modify perceptions: light is seen where there is no light. This effect would be potentially critical in space under conditions requiring reliable visual processing. If LF disturb normal occurrence of sleep (Fuglesang *et al* 2006) this might also constitute a problem for long permanence in space. Similar interactions may also concern other sensory and possibly cognitive brain areas, producing different kinds of risks. Furthermore the underlying, and yet to be described, interactions producing LF may also be evidence of other processes constituting a hazard for prolonged missions. Discovering and describing such interactions is therefore of paramount importance when attempting to define the risk parameters.

The investigation of the radiation environment during the ALTEA–CNSM sessions is providing the first measurement of the amount of radiation traveling through the eye ($2 \times 10^1\text{ ions min}^{-1}$) and through the brain ($4\text{--}5 \times 10^2\text{ ions min}^{-1}$) of an astronaut in LEO. Further data analysis should permit the contributions of the different ions to be separated and the dose per diem in the eye/brain of the astronauts to be calculated.

An upper limit on the ‘LF generation efficiency’ ($\approx 2 \times 10^{-3}$) was calculated from the measured rate. This limit, if interpreted as a geometrical efficiency, would lead to a sensitive surface about the size of a portion of the retina ($\approx 7\text{ mm}^2$). This interpretation would require an interaction model where only specific locations in the retina can participate in LF generation. It will therefore be important to verify whether the model(s) that will be proposed from the ALTEA—biophys project will be compatible with interactions of this kind.

The threshold of about 10^3 particles in mice (figure 7, Sannita *et al* 2007) can be viewed also as a detection efficiency in agreement with what was found in the CNSM measurements.

The higher efficiency (up to $\approx 10\%$) claimed by a few experimenters in the 1970s ground-based experiments (see, for example, McNulty *et al* 1972) may be due to the beam alignments over the human retina which were more precise in those measurements in accelerators, as

compared with a collimated beam over the whole mouse eye, or with the tracking spatial resolution of the ALTEA system.

The large variability of the subjective LF reports of the astronauts seems unlikely to be entirely explained by differences in radiation kind and fluences (due to altitude, latitude and vessel shielding), providing strong hints toward the coexistence of many routes to LF generation, and for considering physiological (and psychological) parameters as important co-causes. This should be also taken into account when interpreting the low LF rate measured in ALTEA, which might be only partly explained by the better shielding of the ISS–USLab and by the possible non complete dark adaption as suggested by one of the astronauts.

The electrophysiological measurements in space and on the ground are providing insights into the mechanisms correlated to particle passages and LF perceptions. Astronauts, mice (figures 7 and 8) and patients undergoing heavy ion therapy (figure 9) seem to produce similar responses even in different environmental and experimental conditions.

A most important question, mainly addressed by the ALTEA—biophysics project, is whether an ion entering the eye tissue can couple directly with the sensorial pathway with a yet to be discovered mechanism, or produces a photon which acts as a transducer to turn the ion energy into a compatible form for the visual sensors in the retina, or, more likely, if both processes are possible. Our rhodopsin measurements demonstrate that rhodopsin can be *bleached* by radiation; work is in progress to describe compatible process(es) producing this *bleaching*.

There have been a large number of discussions about which particles are responsible for LF. The available particle candidates detected in space in coincidence with LF perceptions seem to indicate ions comprised between $Z = 3$ and $Z \approx 8$, with three exceptions (in the MIR experiments, one Cr candidate, and in the Apollo experiments two candidates with $Z > 8$). This of course also reflects the relative abundance of the ions (O is about 10^2 times more abundant than Fe). On the ground much lighter particles such as He nuclei and μ and π have also been shown to be able to elicit LF.

The discussion about the proton contribution is still open. Unfortunately, only one passage on the SAA (where the radiation environment is mostly low energy protons) has been measured in the ALTEA–CNSM sessions, however, in that passage no LF was reported. The striking difference between the findings in the Skylab and the ASTP measurements in the SAA (table 1) can be accounted for by a combination of different altitude and different shielding. Better shielding in the ISS–USLab might also be one explanation for the missing LF in the SAA.

The most accredited model for LF induced by protons refers to nuclear interaction in or near the retina (inelastic nuclear collision with C, H, O, Rothwell *et al* 1976, Casolino *et al* 2003), Cherenkov not being possible due to the low energy. Interestingly, in ground experiments no clear direct evidence of this effect was looked for. Helium nuclei have been shown to elicit LF (Budinger *et al* 1972), light ions (with $LET \approx 3\text{--}6 \text{ keV } \mu\text{m}^{-1}$) appear to be among the candidates for ALTEA–CNSM LF. Direct investigation on the ground of proton induced LF might add useful information about the underlying processes.

The large amount of ALTEA data under analysis, and the new measurements foreseen to start again at the beginning of next year, will provide further answers to the questions mentioned in section 3.

The working strategy will be to infer from the electrophysiological measurements possible generating processes and to investigate them in detail with *in vitro* measurements. This, and the

study of the radiation environment in the ISS, would allow a risk assessment to be provided and countermeasure strategies to be proposed.

Finally these data will be extrapolated for interplanetary voyages using simulations providing risk parameters for the next return to the Moon and for the flight to Mars.

Acknowledgments

The financial contribution of ASI (MoMa grant) is acknowledged. I also acknowledge the help of all the ALTEA team, in particular of L Di Fino, M Larosa, C La Tessa, A Rinaldi, V Zaconte, G Notaro and A Ciccotelli for help in providing several of the presented new results and P Picozza and W G Sannita for their revision of the manuscript. NASA is acknowledged as the source of figures 2 and 3.

References

- Amassian V E, Cracco R Q, Maccabee P J, Cracco J B, Rudell A and Eberle L 1989 Suppression of visual perception by magnetic coil stimulation of human occipital cortex *Electroenceph. Clin. Neurophysiol.* **74** 458–462
- Avdeev S *et al* 2002 Eye light flashes on the Mir space station *Acta Astronaut.* **50** 511–25
- Bidoli V *et al* 2000 Study of cosmic rays and light flashes on board space station MIR: the SilEye experiment *Adv. Space Res.* **25** 2075–9
- Bidoli V *et al* 2001 In-flight performances of SilEye-2 experiment and cosmic ray abundances inside space station MIR *J. Phys. G: Nucl. Part. Phys.* **27** 2051–64
- Budinger T F, Bichsel H and Tobias C A 1971 Visual phenomena noted by humans subjects on exposure to neutrons of energies less than 25 million electron volts *Science* **172** 868–70
- Budinger T F, Lyman J T and Tobias C A 1972 Visual perception of accelerated nitrogen nuclei interacting with the human retina *Nature* **239** 209–11
- Budinger T F, Tobias C A, Huesman R H, Upham F T, Wieskamp T F, Schott J U and Schopper E 1975 Light flash observation, experiment MA-106 *Apollo-Soyuz Test Project Summary Science Report* NASA SP-412 pp 193–209
- Casolino M *et al* 2003 Dual origins of light flashes in space *Nature* **422** 680
- Casolino M *et al* 2002 The Sileye-3/Alteino experiment on board the International Space Station *Nucl. Phys.* **113** 71–8
- Charman W N, Dennis J A, Fazio G G and Jelley J V 1971 Visual sensations produced by single fast particles *Nature* **230** 522–4
- Charman W N and Rowlands C M 1971 Visual sensations produced by cosmic ray muons *Nature* **232** 574–5
- Cucinotta F A, Kim M H Y and Ren L 2005 Managing lunar and Mars mission radiation risks Part I: cancer risks, uncertainties and shielding effectiveness *NASA/TP-2005-213164*
- D'Arcy F J and Porter N A 1962 Detection of cosmic ray μ -mesons by the human eye *Nature* **196** 1013–4
- Dobelle W H, Mladejovsky M G and Girvin J P 1974 Artificial vision for the blind: electrical stimulation of visual cortex offers hope for a functional prosthesis *Science* **183** 440–4
- Durante M 2002 Radiation protection in space *Nuovo Cimento* **25** 1–70
- Fazio G, Jelley J V and Charman W N 1970 Generation of Cherenkov light flashes by cosmic radiation within the eyes of the Apollo astronauts *Nature* **228** 260–64
- Fremlin J H 1970 Cosmic ray flashes *New Sci.* **47** 42
- Fuglesang C, Narici L, Picozza P and Sannita W G 2006 Phosphenes in low earth orbit: survey responses from 59 astronauts *Aviat. Space Environ. Med.* **77** 449–52

- Fuglesang C 2007 Using the human eye to image space radiation or the history and status of the light flash phenomena *Nucl. Instrum. Methods A* **580** 861–5
- Gauger E G, Tobias C A, Yang T and Whitney M 1986 The effect of space radiation on the nervous system *Adv. Space Res.* **11** 243–9
- Kraft G 2000 Tumorthrapy with ion beams *Nucl. Instrum. Methods A* **454** 1–10
- McAulay I R 1971 Cosmic ray flashes in the eye *Nature* **232** 421–2
- McNulty P J 1971 Light flashes produced in the human eye by extremely relativistic muons *Nature* **234** 110
- McNulty P J, Pease V P, Pinsky L S, Bond V P, Schimmerling W and Vosburgh K G 1972 Visual sensations induced by relativistic nitrogen nuclei *Science* **178** 160–2
- McNulty P J, Pease V P and Bond V P 1975 Visual sensations induced by Cerenkov radiation *Science* **189** 453–4
- McNulty P J, Pease V P and Bond V P 1976a Muon induced visual sensations *J. Opt. Soc. Am.* **66** 49–55
- McNulty P J, Pease V P and Bond V P 1976b Visual sensations induced by relativistic pions *Radiat. Res.* **66** 519–30
- McNulty P J, Pease V P and Bond V P 1978 Visual phenomena induced by relativistic carbon ions with and without Cerenkov radiation *Science* **201** 341–3
- Narici L *et al* 2003 ALTEA: anomalous long term effects in astronauts. A probe on the influence of cosmic radiation and microgravity on the central nervous system during long flights *Adv. Space Res.* **31** 141–6
- Narici L *et al* 2004 The ALTEA/Alteino projects: studying functional effects of microgravity and cosmic radiation *Adv. Space Res.* **33** 1352–7
- Osborne W Z, Pinsky L S and Bayley J V 1975 Apollo light flash investigations *Biomedical Results of Apollo NASA SP-368* ed R S Johnston, L F Dietlein and C A Berry (Washington, DC: NASA)
- Pinsky L S, Osborne W Z, Bailey J V, Benson R E and Thomson L F 1974 Light flashes observed by astronauts on Apollo 11 through Apollo 17 *Science* **183** 957–9
- Pinsky L S, Osborne W Z, Hoffman R A and Bailey J V 1975 Light flashes observed by astronauts on Skylab 4 *Science* **188** 928–30
- Rothwell P L, Filz R C and McNulty P J 1976 Light flashes observed on Skylab 4: the role of nuclear stars *Science* **193** 1002–3
- Sannita W G *et al* 2004 Effects of heavy ions on the visual function and electrophysiology of rodents: the ALTEA-MICE experiment *Adv. Space Res.* **33** 1347–51
- Sannita W G, Narici L and Picozza P 2006 Positive visual phenomena in space: a scientific case and a safety issue in space travel *Vision Res.* **46** 2159–65
- Sannita W G *et al* 2007 Implications for human space travel of mice retinal responses to ^{12}C ions *Neurosci. Lett.* **416** 231–5
- Schardt D and Krämer M 2002 Particle induced visual sensations in heavy-ion tumor therapy *GSI Scientific Report*
- Simpson J A 1983 Elemental and isotopic composition of the galactic cosmic rays *Annu. Rev. Nucl. Part. Sci.* **33** 323–81
- Tobias C A 1952 Radiation hazards in high altitude aviation *J. Aviat. Med.* **23** 345–72
- Tobias C A, Budinger T F and Lyman J T 1973 Biological effects due to single accelerated heavy particles and the problems of nervous system exposure in space *Life Sciences and Space Research XI* ed P H A Sneath (Berlin: Akademie-Verlag)
- Tobias C A, Budinger T F and Lyman J T 1971 Radiation-induced light flashes observed by human subjects in fast neutron, x-ray and positive pion beams *Nature* **230** 596–8
- Zaconte V *et al* 2008 ALTEA: the instrument calibration *Nucl. Instrum. Methods B* **266** 2070–8