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PREFACE

SPACE CONQUEST: MAN'S MOST AUDACIOUS DREAM

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This is the second issue of *Annales Kinesiologiae* reporting research presented at the International Meeting on *Living the space – The space a Human Habitat*, which took place in Naples on December 1–2, 2011. During the event, Space emerged as the target of men curiosity, creativity, intelligence and hard work, a place where to realize man's most audacious dreams. The meeting organized by the Italian Institute for Philosophical Studies, the Second University of Naples, the University of Salerno, the University Federico II in Naples and the Italian Space Agency discussed the hot topics of this enterprise, which appears capable to solve man's problems here on Earth.

The image of man as a figure well rooted into the ground but with an eye to heaven, the earthly nature but leaning towards the outer space, is old and established, and still retains all its living actuality. Albeit in different forms, man has always considered cosmic space as a place to watch with interest, looking for both the causes and the relief of his own fears and anxieties. Even in the twentieth century, a secular and disenchanted writer, Albert Camus (1913–1960), in his *Wedding in Tipaza*, strongly emphasizes with grace the special spirit of complicity between earth and heaven, fostered by the Algerians, a race of men "born from sun and sea, lively and flavorful, which derives its greatness from simplicity and standing on the shores of the sea turns his knowing smile to the luminous smile of heaven (Camus, 1988). Man smiles at the heaven and the accomplice heaven responds with a beaming smile.

Two centuries earlier, Giambattista Vico (1668–1744) a Catholic thinker among the most important innovators of philosophy in the eighteenth century (Vico, a) in Europe, in search of the first glimmer of humanity and the first glimpse of civilization in the mind of those solitary beasts wandering in the woods retrieves the old theory attributed by Sextus Empiricus (160–210 AD)` to Democritus of Abdera (470–370 BC) that "men in the distant past, observing the celestial phenomena, thunder and lightning, thunderbolts and clusters of stars, eclipses of sun and moon, were frightened, thinking they were provoked by the gods" (Diehls-Kranz, a). An additional testimony, at the time of Clement of Alexandria (c150–c215 AD), attests to Democritus "a few wise men, raising their hands up where we, the Greeks, say that air is, ´Zeus decides and knows everything, he gives and takes away and is the Lord of all things` " (Diehls-Kranz, b). For Vico in *The New Science* and for Democritus – according to the testimony of Sextus and Clement – man looks at the sky, – the limitless space that surrounds him,– and populates it with his imagination with powerful and menacing divinities (Vico, b).

This is perhaps one of the first ways in which man tries to conquer the space, transferring in the unlimited space not himself physically, but his supposed psychical tensions. And it is perhaps one of the first times that he elaborates those circular reasonings, the hermeneutic "vicious" circles, consisting of a premise which justifies the conclusion, and this, in turn, justifies the premise. The fear (*phobos*), and the hope or the benefit (*chreia*) lead men to imagine the existence of gods in the heavens and to consider them as both cause and relief of their passions.

Before being considered as the psychological and ethic paradigm – as in Democritus – the outer space inhabited by gods was utilized by many peoples and many cultures, as a political paradigm, defined by Antonio Capizzi (1982) as *cosmic monarchy*.

To provide credible assurance of eternal life and absolute perfection to monarchical institutions in force in ancient societies – Capizzi says – a parallelism between state organization and cosmic organization was speculated. In the unlimited and uncircumscribed cosmic space men project the model that governs the order and the hierarchical relationships in the confined space of the State. It is told through the Bards of the absolute power of a god – Lord of all – on air, earth, water and fire, even when the power on some of these elements, constituting the Whole, is delegated to minor divinities. In the myth the model of absolute monarchy, wherein the individuality (the king) means royalty and the community (the people) means obedience, is transformed. The vicious circle for which human and historical models provide the basis for divine paradigms, believed to be eternal, and, in turn, are used to confirm and guarantee the human model which produced them – is put once again in place.

This parallelism between State and Cosmos is present in Egyptian religion, in Mesopotamian mythology, in Minoan Crete, in the culture of the antique Egypt where the king himself is deified, as also happens in the Persia of Cyrus and Xerxes. In Persia – as Herodotus recounts – Cyrus and Xerses, convinced to possess divine powers, exercise judicial functions even on nature. The former divides the river Ginde into 180 channels with little flow of water as punishment for having drowned his sacred horse. The latter sentenced the Aegean sea to a total of 300 lashes for having destroyed during a storm the bridges he had built (Herodotus, a and b).

In Greece, the first political celestial model was created by Hesiod (750–650 BC). In the *Theogony,* the formation of this model is followed in its progressive form and development. At the beginning, in the space occur veritable civil wars between Abyss, Night, Ether, Light, Sea and Ocean, and there are Cyclops, Furies, Giants, Nymphs, and Titans. In the cosmos unsociability and terror are the rules. Political order begins with Hecates (Hesiod, a) and the name of king appears with Chronos. The monarchic model takes place after Gigantomachy, after the victory of Zeus over the Titans (Hesiod, b). Homer, in turns, describes the *cosmic monarchy* established with Zeus at the head of all gods. Once again cosmic space and political space are organized and ruled by the same monarchist and absolutist, paradigms.

Whereas governors urge scholars and poets to develop models of organization of the cosmos to be used as examples to enhance and provide assurance of eternity to their power in the State, city planners, architects, sailors, soothsayers, augurs, astrologers and interpreters of divine desires, look at the sky and stars to draw lessons and recommendations for their work.

Among the astrologers, should be remembered Tommaso Campanella (1568–1639). In *The City of the Sun*, the Calabrian philosopher says that 24 priests remain all day in the temple to sing psalms and to watch the stars. Their task is to "mark by means of astrolabes their movement and its effects, so they know the countries in which mutations will occur. They are able to decide the hours of generation and the days of seeding and harvesting, they serve as intermediaries between God and men, among them is selected the Sun (chief of the city), they write important things and experiment in science. They never descend from their place, except for eating, they are not interested in the female sex, unless women are needed as healings for the body. Every day the Sun (the priest, head of the city) goes to the temple and talks to them about what they have investigated on the benefits of the city and of all the nations of the world" (Campanella, 2001).

Since ever and for any activity men project themselves into Space with the acuteness of vision and the creativity of imagination consider the unlimited space around them and the celestial bodies within as the whole of their own world, and draw theirttention toward it, for the benefit of their existence.

Cosmic space and terrestrial space are thought by Democritus as made of the same elements, very small particles, infinite in number and in perpetual motion. The heavens, the stars, planets, Earth, animals, humans and all things in nature are composed of atoms, indivisible bodies spinning in the empty space. Between Heaven and Earth there is no ontological difference. In fact terrestrial physics and celestial physics are governed by the same laws of aggregation and disaggregation of atoms. All existing things, all things that we see, including humans, are the product of the combination of identical substances (Diehls-Kranz, c). Nothing is perceived as alien to man. Man is a full participant of the unity of the Whole. And with Leucippus, Democritus' mentor, he feels he has found a way, by using sensible experience and rational procedures, to understand generation and destruction, the movement and the multiplicity of things (Diehls-Kranz, d).

This model of the infinite universe, of infinite worlds spinning in it and made by the same "substance", by others "called the stars", will be taken up by Giordano Bruno (1548–1600), the great thinker from Nola, who by magnifying the cosmic space to the infinite, shatters the sky of fixed stars, identified by Aristotle as the limit of the cosmos, thus lousing up any absolute reference. In the universe each point is related to another "thus we being are on Earth assert that the Earth is in the middle [ ]. Those living on the moon think the Earth, the sun and the other stars rotate around them, who are in the middle and at the end of their half diameters of their horizons" (Bruno, 1985). As a consequence, we are heaven for the hypothetical inhabitants of other planets, just like they are heaven for us. For Bruno, the outer space and all the celestial bodies can be inhabited. Of course the inhabitants of such celestial bodies can grow and express their point of view on the rest of the universe around them.

In a destabilizing epoch due to a phenomenon of globalization produced by the enlargement of the Greek civilization to Middle East and to East, after Alexander the Great, a refined and cautious intellectual, Epicurus of Samos, between the fourth and the third century B.C., tries to pacify the spirits of his contemporaries. His philosophical model is simple and ambitious at the same time. To maintain a serene mind we must neutralize the fear that comes from ignorance and superstition, enabling the true knowledge. He takes over and corrects the theory of Democritus about atoms, discarding any form of determinism due to necessity. In the physical as well as in the moral world nothing is needed in a fatalistic manner. Men to be happy must free themselves from traditional concerns, starting with the fear of the gods and death. We should never take care of death because when we are here she is absent, and when she comes we are not here any longer. Gods, however, do exist, says Epicurus, but being blessed, immortal, immune to business and anxiety, are not concerned at all with human affairs, which would disturb their state of bliss and imperturbability (Epicurus, 1970). These gods, perpetually happy, live far away from men in the Cosmos, in the spaces between the infinite worlds that populate the universe, the *Intermundia* (the spaces between the worlds" (Cicero, *De Natura deorum*). Epicurus represents them as "the paradigm of the excellent and of a perfectly self-sufficient, blissful life that a wise man has to achieve." He, therefore, uses "the existence between world and world of empty spaces, the inter worlds […].to locate the ideal home of the gods" (Masi 1981).

Once again, the cosmic space is the place where people project their desire and dream of peace and heavenly bliss by attributing both conditions to their surrogates, the gods. Albeit through a third party, through the *dramatis personae* (the actors of the tragedy), men move into space to achieve happiness, quiet pleasures that are hard to achieve in their historical world, let alone during periods of alienation and impoverishment due to processes of globalization. And there, in space, through the images of the gods, is also confined the cause of many of their fears and their anxieties. It becomes the place where to relegate and keep away the reasons generating such anxieties and fears.

With the advent of Christianity nothing changes. The sky is still populated by many divine figures, and is the place from which men receive laws and ethical-political paradigms. In addition to the three persons of the mystical unity of God, there are angels, archangels, seraphim, and cherubim, saints and the souls of believers who died in Lord's divine grace and there is Mary, the mother of Jesus, taken up into heaven in the unit of body and soul. Angels move in the infinite spaces of the Cosmos. Sometimes, they reach the Earth and communicate to men Lord's will and protect them from evil. God descends to meet Moses, who led the Jews out of slavery, to which they were subject in Egypt, and on Mount Sinai God gives the table of laws, the Decalogue (*Exodus*, a), the Covenant Code (*Exodus*, b) to Moses who finds it difficult to turn a crowd of slaves into a people, led by a recognized authority and held together by a law indisputable because of its divine origin. Once again the infinite space, "the highest", is the place of perfection, of the eternal happiness, the prize that "every wish advances", and is the place where men seek the solution, or at least the alleviation to their problems on Earth.

The interest of the Catholic Church for space, however, is not only of a strictly ethical and metaphysical nature. It is also fuelled by scientific reasons. The desire to explore the created universe led the church to establish many astronomical observatories. At the beginning of the 18th century, the Church contributed to the creation of the Institute of Science in Bologna, where astronomical observation was prominent. In 1952, Pious XII (1876–1958), addressing the general assembly of the International Astronomical Society, praised the study of astronomy thanks to which "human spirit has exceeded the limits of physical senses". Also John Paul II (1920–2005) had a strong interest in science and astronomy, in the belief that faith and science, separately and independently, may "purify" each other.

Besides religious means, there are endless means by which men have sought salvation in space and escape from the fears of life, especially from the greatest of all, the fear of death for ever. Poets and literates have dreamed of inter-spatial flights, landings on the moon or other planets. In *Orlando enraged* of Ludovico Ariosto (1474–1635), Astolfo is forced to go to the Moon where all things lost on Earth are, to retrieve the lost wits of Orlando.

The interpretative framework of this desire to conquer the Space, however, seems to be always the same: to use the sky to solve the problems here on Earth. Even today, the race for the conquest of space is not only aimed to make visible and feared the power of individual States, but also to satisfy the insatiable human thirst for knowledge and mastery of the forces and of the unexplored regions of nature to use them at our own advantage, for instance by colonizing space, just like the great European powers colonized the new lands overseas since the discovery of America. The idea, born from the dream of a Russian scientist to colonize the "Milky Way" (Tsiolkovsky, 1928), is to broaden the "cradle too small" in which humanity feels increasingly closed and almost confined. (Genta, 1980).

Space still appears as the way of adventure to realize Faustian dreams, today as never before supported and encouraged by the power of technology. The dreams that help men to expand their knowledge, which has an impact on many branches of human knowledge, from physics to medicine, from astronomy to philosophy, because any innovation in any one branch of knowledge implies a redefinition, a redirection and an acceleration of all disciplines. This is easily understood by analyzing the changes occurred in the world of science, philosophy, technology, literature and the arts since the "Copernican revolution" or Einstein's theory of relativity. All this demonstrates the enormous creative power of human mind, "this greatest gift, this divine light", as in the words of Baruch Spinoza (1632–1677).

As outlined in the preface to the previous issue of *Annales Kinesiologiae* in the short term space conquest will be facilitated and driven by hyper-specialization, although the latter sometimes may fail in catching the complexity. It is evident that space conquest is one of the few human enterprises capable to catch complexity by utilizing sectorial knowledge and this should be regarded as a great merit deserving credit. Space science, which has been successful although at high economic costs, seems to hold the capacity to achieve Edgar Morin's dream for a "planetary education" through a process of "humanization". We are happy to stress that the French interdisciplinary thinker, in the last page of *La voie/ The way*, his latest masterpiece (Morin, 2012) ponders about the many possibilities offered to humans looking into Cosmos among which: i. travelling into space for thousands years to come, ii. the possibility of human migration into liveable planets, iii. the possibility to investigate on the existence of additional forms of intelligence distinct from man, iv. the existence of parallel cosmoses, v. the possibility to investigate whether the reality space-time is embedded in a reality lacking space and time, and vi. the continuity of the symbiosis between man and his technical production.

So to move to Mars we need to create new sciences, new technologies, new materials (De Santo, 2011), but this will be not detrimental to the enterprise for the time ongoing.

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Finally, warmest thanks to Matej Plevnik, editorial board member of this Journal, for the time he devoted to bringing this project to its fulfilment. It has been a privilege and a pleasure to work with him.

ABBREVIATIONS

Diehls-Kranz. *Die Fragmente der Vorsokratiker*, 3 vols. Kranz W, Ed., 6th Edition, Zurich, Weidman 1951–52. This book includes all extant writings of all Presocratic authors. Each author is assigned a number. Entries are numbered as (a) testimonia, that is ancient accounts of the author's life and doctrine, (b) *ipsissima verba* reporting the exact words of the author, and (c) imitations that false the author as a model.

PREDGOVOR

OSVAJANJE VESOLJA: ČLOVEKOVE NAJDRZNEJŠE SANJE

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Pred vami je druga izdaja raziskovalnega poročila *Annales Kinesiologiae*, ki je bilo predstavljeno na mednarodni konferenci Živeti vesolje – vesolje kot človeški življenjski prostor (Living the Space – The Space a Human Habitat), ki je bila organizirana v Neaplju od 1. do 2. decembra 2011. Na tej konferenci je bilo vesolje središče človeške radovednosti, ustvarjalnosti, inteligence in težkega dela, prostor, kjer se lahko uresničijo človekove najdrznejše sanje. Konferenco so organizirali Italijanski inštitut za filozofske študije Druge univerze v Neaplju, Univerza v Salernu ter Univerza Federico II v Neaplju. Udeleženci so razpravljali o vročih temah te iniciative, ki se zdi zmožna reševati človekove težave tu na Zemlji.

Podoba človeka kot bitja, ki je dobro zakoreninjeno na Zemlji, vendar z enim očesom vedno obrnjeno proti nebesom, z zemeljsko naravo, ki pa se nagiba k vesolju, je stara in uveljavljena, vendar še vedno ohranja vso aktualnost v današnjem svetu. Človek se je vedno zanimal za kozmično vesolje, četudi v različnih oblikah, kjer je iskal tako razloge kot tudi rešitve za svoje strahove in bojazni. Tudi v 20. stoletju je sekularni in razočarani francoski pisatelj Albert Camus (1913–1960) v svojem delu *Poroka v Tipazi* močno in sofisticirano poudaril poseben duh povezanosti Zemlje in nebes, ki ga hranijo Alžirci, tekmovanje človeka, „*rojenega iz sonca in morja, živahnega in polnega okusov, katerega izjemnost izhaja iz enostavnosti in postavanje na obalah morja spremeni njegov poznavalski nasmeh v žareč nasmeh nebes*" (Camus, 1988). Človek se smehlja nebesom, ta pa mu odgovorijo z žarečim nasmehom.

Dve stoletji poprej katoliški mislec Giambattista Vico (1668–1744), eden izmed najpomembnejših evropskih inovatorjev v filozofiji 18. stoletja (Vico, a), med iskanjem prvega prebliska človečnosti in prvega bežnega pogleda civilizacije v mislih osamljenih zveri, ki so pohajale po gozdovih, ponovno obudi staro teorijo, ki jo je Sekstus Empirik (160–210 pr. n. št.) prisodil Demokritu iz Abdere (470–370 pr. n. št.), in sicer, da so "bili možje v daljni preteklosti med opazovanjem zemeljskih pojavov, neviht in udarov strel, bliskov z gromom ter nakopičenih zvezd, sončnih in luninih mrkov prestrašeni, saj so mislili, da so jih povzročali bogovi" (Diehls-Kranz, a). Še eno pričevanje, tokrat s strani Klementa Aleksandrijskega (pribl. 150–215 pr. n. št.), izpričuje Demokritovo teorijo, namreč "nekaj modrih mož, ki svoje roke iztegujejo visoko, kjer mi, Grki, pravimo, da je zrak, pravi: Zevs se odloča in ve vse, daje in vzame, on je gospodar vsega" (Diehls-Kranz, b). Vico v svoji *Novi znanosti*, tako kot Demokrit – glede na pričevanja Sekstusa in Klementa – pravi, da človek gleda proti nebu, neomejenemu prostoru, ki ga obkroža, ter ga napolni s svojo domišljijo in močnimi ter grozečimi božanstvi (Vico, b).

To je najbrž eden prvih načinov, s katerimi človek želi osvojiti vesolje in kjer se, ne telesno, vendar s svojimi domnevnimi telesnimi napetostmi, preseli v "kozmos". In to je najbrž prvič, ko človek oblikuje krožna sklepanja, hermenevtične "začarane" kroge, ki vsebujejo premiso, ki opravičuje sklep, in obratno, ko sklep opravičuje premiso. Strah (*phobos*) in upanje ali korist (*chreia*) vodita človeka, da si domišlja obstoj bogov v nebesih in da jih upošteva kot razlog in olajšanje za svoje strasti.

Preden se je vesolje obravnavalo kot psihološko in etično paradigmo – kot pri Demokritu –, so vesolje, ki so ga naseljevali bogovi, ljudje in mnoge kulture, uporabljali kot politično paradigmo, ki jo Antonio Capizzi (1982) opisuje kot *kozmična monarhija*.

Capizzi pravi, da je za zagotavljanje kredibilnosti večnega življenja in absolutne popolnosti monarhističnim institucijam, ki so vladale starodavnim družbam, potrebno vzpostaviti vzporednice med organizacijo stanja in organizacijo kozmosa. V neomejenem in neopisanem kozmičnem vesolju si ljudje zamišljajo model, ki vlada redu in hierarhičnim razmerjem v omejenem prostoru Države. Bardi govorijo o absolutni moči boga – gospodarja vsega – zraka, zemlje, vode in ognja, tudi ko je moč nad nekaterimi izmed teh elementov, ki tvorijo Celoto, razporejena med nižja božanstva. V mitu je model absolutne monarhije, kjer individualnost (kralj) pomeni kraljestvo in skupnost (ljudje) pomeni pokorščino, preoblikovan. Začarani krog, v katerem človeški in zgodovinski modeli predstavljajo osnovo za božanske paradigme, ki naj bi bile večne in ki se uporabljajo za potrditev in garancijo človeškega modela, ki jih je ustvaril, je zopet vzpostavljen.

Ta vzporednica med Državo in Kozmosom je predstavljena v egipčanski veri, mezopotamski mitologiji, v minojski Kreti, v kulturi starodavnega Egipta, kjer je kralj oboževan, prav tako je prisotna v Perziji v času Cirusa in Kserksesa. V Perziji – kot pripoveduje Herodot – sta Cirus in Kserkses prepričevala ljudi, da imata božanske moči in da lahko svoje pravne funkcije izvajata tudi v naravi. Cirus je razdelil reko Ginde v 180 potokov z malo pretočnosti kot kazen za svojega potopljenega svetega konja (Herodotus, a and b). Kserkses je obsodil Egejsko morje na 300 udarcev z bičem, ker naj bi med nevihto uničilo mostove, ki jih je bil zgradil.

V Grčiji je prvi politični božanski model ustvaril Hesiod (750–650 pr. n. št.). V svoji *Teogoniji* sledi oblikovanju tega modela v zelo progresivni obliki in razvoju. Na začetku se v vesolju pojavijo prave civilne vojne med Breznom, Nočjo, Eteričnostjo, Morjem in Oceanom, kjer pa se pojavijo Kiklopi, Furije, Giganti, Nimfe in Titani. V kozmosu sta nedružabnost in teror pravili. Politični red se začne s Hekatom (Hesiod, a) in ime kralja se pojavi pri Kronosu. Monarhični model se pojavi v Gigantomahiji, po zmagi Zevsa nad Titani (Hesiod, b). Homer pa opisuje *kozmično monarhijo*, ki jo je Zevs ustvaril kot vladar vseh bogov. Še enkrat se kozmično vesolje in politično vesolje ravnata po enakih paradigmah – monarhističnih in absolutističnih.

Medtem ko vladarji silijo učenjake in pesnike, da razvijajo modele kozmosa, ki se uporabljajo kot primeri za zagotavljanje večnosti njihovega vladanja Državi, pa mestni načrtovalci, arhitekti, mornarji, preroki, vedeževalci, astrologi in interpreti božanskih želja gledajo proti nebu in zvezdam, kjer iščejo navdih za svoja mnenja in priporočila za svoje delo.

Med astrologi se moramo spomniti Tommasa Campanelle (1568–1639). V svojem *Mestu Sonca* ta kalabrijski filozof pravi, da je 24 duhovnikov ves dan v templju, kjer pojejo psalme in opazujejo zvezde. Njihova naloga je, da „s pomočjo kotomerjev označijo njihove premike in učinke, da bodo vedeli, v katerih državah se bodo dogajale spremembe. Tako se lahko odločijo o ustreznem času in dnevih, ko se seje in žanje, služijo kot posredniki med bogom in človekom, med njimi je izbranec Sonce (gospodar mesta), pišejo o pomembnih stvareh in poskusih v znanosti. Svojih mest nikoli ne zapustijo, razen ko se odpravijo k jedi, ne zanimajo se za ženske, razen če so le te potrebne kot zdravilke. Sonce (duhovnik, vodja mesta) vsak dan obišče tempelj in se z njimi pogovarja o njihovih izsledkih, ki so dobri za mesto in vse narode sveta" (Campanella, 2001).

Že od nekdaj in za katerokoli dejavnost se je človek s pomočjo ostrine vida in ustvarjalnosti domišljije postavljal v vesolje, tako da je neomejen prostor okoli sebe in božanska telesa v njem razumel kot celoto svojega sveta, ter tako pozornost usmerjal proti tem božanstvom v korist njihovemu obstoju.

Kozmično vesolje in zemeljsko vesolje Demokrit definira kot celoto enakih elementov, zelo majhnih delcev, ki so neomejeni v številu in v stalnem gibanju. Nebesa, zvezde, planeti, Zemlja, živali, človeška bitja in vse stvari v naravi so sestavljene iz atomov, nedeljivih teles, ki se vrtijo v praznem prostoru. Med Nebesi in Zemljo ni ontološke razlike. V zemeljski fiziki in božanski fiziki veljajo enaki zakoni združitve in razdružitve atomov.

Vse stvari, ki obstajajo, vse, kar vidimo, vključno s človeškimi bitji, je proizvod kombinacije identičnih snovi (Diehls-Kranz, c). Človeku ni nič tuje. Človek je del enotnosti Celote. Leucip, ki je bil Demokritov mentor, meni, da je s pomočjo čutnih izkušenj in racionalnih postopkov našel način, kako razumeti ustvarjanje in uničenje, gibanje in množtvo stvari (Diehls-Kranz, d).

Ta model neskončnega univerzuma, neskončnih svetov, ki se v univerzumu vrtijo in jih tvori ista "snov", ki jih drugi imenujejo "zvezde", prevzame Giordano Bruno (1548–1600), veliki mislec iz Nole. Ta je povečeval kozmični prostor v neskončnost in tako izničil nebo, ki ga tvorijo fiksne zvezde, po Aristotelu skrajna meja kozmosa, ter tako iztrebil tudi vsakršno absolutno referenčno točko. V univerzumu je vsaka točka povezana z drugo, "pri čemer mi, ki smo na Zemlji, izjavljamo, da je Zemlja v sredini […]. Tisti, ki živijo na Luni, mislijo, da se Zemlja, Sonce in druge zvezde vrtijo okoli njih, in da so v sredini ter na koncu polmerov svojih horizontov" (Bruno, 1985). Posledično smo mi nebesa hipotetičnim naseljencem na drugih planetih, tako kot so oni nebesa nam. Bruno pravi, da je možno naseliti vesolje in vsa nebeška telesa. Seveda lahko naseljenci takšnih nebeških teles rastejo in izražajo svoje mnenje o univerzumu, ki jih obkroža.

V dobi, ki je postala nestabilna zaradi pojava globalizacije, ki jo je povzročilo širjenje grške civilizacije na Srednji Vzhod in Vzhod po Aleksandru Velikem, imenitni in previdni intelektualec Epikur iz Samosa med četrtim in tretjim stoletjem pred našim štetjem skuša pomiriti duhove svojih sodobnikov. Njegov filozofski model je enostaven in hkrati ambiciozen. Če želimo ohraniti vedrost, moramo nevtralizirati strah, ki izhaja iz ignorance in praznoverja, tako da dovolimo pot pravemu znanju. Tako prevzame in popravi Demokritovo teorijo atomov, kjer zavrača vsakršno obliko determinizma, ki nastane zaradi nuje. V fizičnem in moralnem svetu nič ni potrebno na fatalističen način. Če človek želi biti srečen, se mora osvoboditi tradicionalnih skrbi, začenši s strahom pred bogovi in smrtjo. Nikoli ne bi smeli skrbeti o smrti, saj ko smo tu, smrt ni prisotna, ko pa pride, nas ni več tu. Bogovi pa kljub temu obstajajo, vendar so blagoslovljeni, nesmrtni, imuni za posel in bojazni, ne obremenjujejo se s človekovimi zadevami, saj bi to zmotilo njihovo stanje blaženosti in ravnodušnosti (Epicurus, 1970). Ti bogovi večno in srečno živijo stran od človeka v Kozmosu, v prostorih med neskončnimi svetovi, ki naseljujejo univerzum, t. i. *Intermundiji* (prostori med svetovi) (Cicero, *De Natura deorum*). Epikur jih predstavlja kot „paradigma izjemnega in popolnoma samozadostnega, blaženega življenja, ki ga mora doseči moder človek". Tako uporablja „obstoj med svetom in svetom praznih prostorov, medsvetovi […], s katerimi določi popoln dom za bogove" (Masi 1981).

Še enkrat, kozmični prostor je prostor, kjer ljudje izražajo svoje želje in sanje o miru in nebeški blaženosti tako, da ta stanja pripisujejo svojim namestnikom, bogovom. Četudi prek tretje osebe, t. i. *dramatis personae* (igralci v tragediji), ljudje potujejo v vesolje, da dosežejo srečo, tihe užitke, ki jih je težko doseči v njihovem historičnem svetu, še posebej med obdobji odtujenosti in osiromašenja zaradi globalizacije. In prav tam, v vesolju, se v podobah bogov skriva vzrok mnogih strahov in bojazni ljudi. To je prostor, kamor odženejo razloge, ki povzročajo te bojazni in strahove.

S prihodom krščanstva se nič ne spremeni. Nebo še vedno naseljujejo božanska bitja, prav tako je to kraj, od koder človek sprejema zakone ter etično-politične paradigme. Poleg treh oseb, ki tvorijo mistično enotnost Boga, so tu še angeli, nadangeli, serafini in kerubini, svetniki in duše vernikov, ki so umrli v božji milosti, prav tako je tu Marija, Jezusova mati, ki se je z dušo in telesom povzdignila v nebesa. Angeli se gibajo v neskončnih prostorih Kozmosa. Včasih dosežejo Zemljo in posredujejo božjo voljo človeku in ga tako ščitijo pred zlom. Bog pride na Zemljo, kjer sreča Mojzesa, ki je vodil Jude iz suženjstva v Egiptu. Na gori Sinaj mu Bog izroči seznam zakonov, t. i. dekalog (*Exodus,*a 8) oziroma deset zapovedi (*Exodus*, b), saj Mojzes le stežka skuša spremeniti množico sužnjev v ljudi, ki jih je vodila priznana avtoriteta in so se ravnali po nespornem zakonu, ki je veljal prav zaradi božanskega izvora. Še enkrat je neskončni prostor, torej „najvišji", prostor popolnosti, večne sreče, nagrade, ki jo „vsak želi doseči", prav tako je to kraj, kjer človek išče rešitev oziroma vsaj lajšanje težav na Zemlji.

Zanimanje Katoliške cerkve za vesolje pa nima zgolj etične in metafizične narave. Prav tako to zanimanje žene znanstvena motivacija. Želja po raziskovanju ustvarjenega univerzuma je vodila Cerkev k ustanovitvi mnogih astronomskih observatorijev. V začetku 18. stoletja je Cerkev prispevala k ustanovitvi Znanstvenega inštituta v Bologni, kjer je bilo astronomsko opazovanje zelo razširjeno. Leta 1952 je papež Pij (1876–1958) nagovoril generalno skupščino Mednarodnega združenja za astronomijo, kjer je pohvalil preučevanje astronomije, zaradi česar je «človekov duh presegel meje fizičnih čutov». Janez Pavel II. (1920–2005) se je prav tako zanimal za znanost in astronomijo, saj je verjel, da vera in znanost, ločeno in samostojno, lahko «očistita» druga drugo.

Poleg religioznih načinov obstaja tudi nešteto drugih načinov, s pomočjo katerih je človek iskal odrešitev v vesolju in tako ubežal življenjskim strahovom, še posebej največjemu strahu – strahu pred smrtjo. Pesniki in književniki so sanjali o poletih v medsvetove, pristankih na Luni in drugih planetih. V delu Ludovica Ariosta (1474–1533), Besneči Roland, je Astolfo prisiljen, da odide na Luno, kjer lahko najde vse stvari, ki so izgubljene na Zemlji, in tako ponovno najde svojo izgubljeno razsodnost.

Interpretativno ozadje želje po osvojitvi vesolja pa kljub vsemu ostaja enako: uporabiti nebo, da bi rešili probleme na Zemlji. Še danes tekmovanje za osvojitev vesolja ni le dokazovanje in ustrahovanje drugih pred močjo posameznih držav, vendar pa predstavlja tudi nenasitno žejo po znanju in obvladovanju sil ter neraziskanih področij narave, ki bi jih lahko uporabili v lastno prid, na primer s pomočjo kolonizacije vesolja, podobno kot so velike evropske sile kolonizirale nove prekomorske dežele že od odkritja Amerike naprej. Ideja, ki se je porodila iz sanj ruskega znanstvenika, da kolonizira „Mlečno pot" (Tsiolkovsky, 1928), pomeni, da je potrebno širiti "*premajhno zibelko*", v kateri se človeštvo počuti vedno bolj zaprto in že skoraj omejeno (Genta, 1980).

Vesolje je še vedno nek pustolovski način uresničevanja faustovskih sanj, ki pa ga danes kot še nikoli prej podpira in spodbuja moč tehnologije. Sanje, ki pomagajo človeku, da širi svoje znanje, imajo močan vpliv na mnoge veje človeškega znanja; od fizike do medicine, od astronomije do filozofije, saj vsaka inovacija v kateri koli veji znanja predstavlja ponovno opredelitev, drugačno usmerjenost in pospešitev vseh disciplin. To zlahka razumemo s pomočjo analize sprememb, ki so se zgodile v svetu znanosti, filozofije, tehnologije, literature in umetnosti že od Kopernikove revolucije ali Einsteinove relativnostne teorije. Vse to kaže ogromno ustvarjalno moč človeškega razuma, "to izjemno darilo, to božansko svetlobo", kot ga opisuje Baruch Spinoza (1632–1677).

Kot je bilo opisano v predgovoru prejšnje izdaje revije *Annales Kinesiologiae*, se bo na kratek rok osvajanje vesolja izvajalo in vodilo s pomočjo izjemne specializacije, čeprav se ta lahko včasih izjalovi prav zaradi svoje kompleksnosti. Jasno je, da je osvajanje vesolja eno izmed številnih človeških dejanj, ki lahko zajame kompleksnost s pomočjo uporabe specializiranega znanja, to pa bi lahko upoštevali kot izjemno odliko, ki si zasluži vsako spoštovanje. Zdi se, da vesoljska znanost, ki je bila uspešna, čeprav ob zelo visokih stroških, lahko doseže sanje Edgarja Morina po „planetarni izobrazbi" skozi proces „humanizacije". Veseli nas, da lahko poudarimo, da francoski interdisciplinarni mislec na zadnji strani svojega zadnjega dela *Pot* (*La Voie*) (Morin, 2012) razmišlja o številnih možnostih, ki so na voljo ljudem, ki stremijo proti Kozmosu, med drugim: i.) potovanje v vesolje v prihodnjih tisočih letih, ii.) možnost migracije človeka na naseljive planete, iii.) možnost raziskovanja obstoja drugih oblik inteligence, ki se razlikujejo od človeka, iv.) obstoj vzporednih kozmosov, v.) raziskovanje dejstva, ali je stvarnost prostor-čas vtisnjena v stvarnost, kjer prostor in čas manjkata, in vi.) kontinuiteta simbioze med človekom in tehnično proizvodnjo.

Če se želimo preseliti na Mars, moramo ustvariti nove znanosti, nove tehnologije, nove materiale (De Santo, 2011), kar pa sedaj še ne bo škodljivo za to področje človekove dejavnosti.

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RAZLAGA KRATIC

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VIBRATION AND BONE – AN OPTION FOR LONG-TERM SPACE MISSIONS?

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ABSTRACT

Bone is lost during sojourns in microgravity. In order to prevent fractures in future manned inter-planetary missions, efforts are currently being made to develop effective countermeasures. Bones adapt to mechanical stimuli, and biomechanical analysis suggests that muscle forces play an important role. Thus, resistance training is advocated as a first option for a countermeasure modality. In addition, vibration has certain characteristics (well controllable, rapid stretch-shortening and large number of contractions) that could be of interest. Studies in the past decade have shown that conventional resistive exercise may be sufficient to maintain bone when performed on a daily basis, but not when performed only every other day. Whole body vibration without additional load seems to be ineffective, but it shows good potential, and probably will have a genuine effect upon bone when combined with additional loads in the order of twice the body weight. There is now accumulating evidence to suggest that effective exercises exist to counteract microgravity-related bone loss. At least for bed rest, forceful muscle contractions seem to be a prerequisite. They may be fortified, but probably not replaced, by vibration exposure.

Keywords: *immobilization, human physiology, physical medicine, bed rest*

VIBRACIJA IN KOST – MOŽNOST ZA DOLGOTRAJNE MISIJE V VESOLJE?

IZVLEČEK

Kostna gostota se zmanjšuje med bivanjem v mikrogravitacijskem prostoru. Z namenom, da bi preprečili zlome med prihodnjimi medplanetarnimi misijami, se trenutno vlaga precej truda v razvoj učinkovitih protiukrepov. Kosti se prilagodijo mehaničnim stimulansom, biomehanična analiza tako predvideva, da mišične sile tu igrajo pomembno vlogo. Zato se trening odpornosti priporoča kot prvo možnost med načini protiukrepov. Poleg tega bi nas lahko zanimale tudi določene značilnosti vibracij (dobro nadzorljivo, hitro in neprekinjeno kratko in daljše trajanje kontrakcij). Študije v preteklem desetletju so pokazale, da konvencionalna telovadba za odpornost zadostuje za ohranjanje kostne gostote, če se telovadba izvaja redno, vendar le, če se izvaja vsak drugi dan. Vibracije celotnega telesa brez dodatne obremenitve so očitno neučinkovite, vendar pa kažejo dober potencial oziroma bodo lahko imele dejanski vpliv na kosti, ko jih bomo združili z dodatnimi obremenitvami po načelu dvojne telesne teže. Tako obstaja več dokazov, ki navajajo, da obstajajo učinkovite vaje, ki delujejo proti izgubi kostne gostote, ki je pogojena z mikrogravitacijo. Vsaj v primeru ležanja v postelji je prvi pogoj za to silovito krčenje mišic. Takšne vaje lahko okrepimo, vendar jih najverjetneje ne moremo zamenjati z izpostavljenostjo vibracijam.

Ključne besede: *imobilizacija, človeška fiziologija, fizikalna medicina, ležanje v postelji*

STATEMENT OF THE PROBLEM

It was a surprising result of the Gemini program that astronauts seemed to lose bone tissue from their legs at an astounding rate. The awareness of Space as a particularly 'hostile' environment for bone was borne. This connotation has been substantiated during the Skylab era, even though the rate of bone loss found was not as severe as initially feared (Vogel, 1975). Systematic research in the Spacelab, on the Mir station and on board the International Space Station (ISS) has provided us with valuable descriptive information (Lang, Leblanc, Evans, & Lu, 2006; Vico et al., 2000), even though the exact mechanisms of bone loss are still under debate. The existing evidence can be briefly summarised as follows: In humans, bone is lost at a rate of approximately 1% per month from the legs, but not from the arms. Animals, including monkeys, however, lose bone from all extremities. As to the consequences, it is evident that removing tissue from the bone reduces its strength and increases the likelihood of fracture. Given the deleterious consequences of a fracture during manned planetary exploration, development of effective countermeasures is mandatory before embarking on such missions.

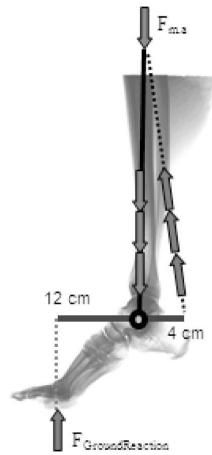
Why, then, would one lose bone in microgravity? The initial suspects were hormonal and nutritional alterations, in particular in relation to Vitamin D and calcium metabolism (Globus, Bikle, Halloran, & Morey-Holton, 1986; Halloran et al., 1985). However, this idea did not prevail, and 'immobilisation' of the astronauts' legs is now widely held as the cause. In parallel to research on bone losses in astronauts, and probably stipulated by it, it has been established that bone is also lost in clinical cases of leg immobilization, such as spinal cord injury (Eser et al., 2004; Griffiths, Bushueff, & Zimmermann, 1976), stroke (Jorgensen, Crabtree, Reeve, & Jacobsen, 2000), anterior cruciate ligament injury (Leppala et al., 1999) – and bed rest (LeBlanc, Schneider, Evans, Engelbretson, & Krebs, 1990; Rittweger et al., 2005; Vico et al., 1987). The latter is of particular interest, as experimental bed rest in combination with -6° head-down tilt (HDT) has been proposed as a ground based model for the cardiovascular alterations induced by space flight (Kakurin, Kuzmin, Matsnev, & Mikhailov, 1976; Kakurin, Lobachik, Mikhailov, & Senkevich, 1976), and it is currently also recognized as a model for the musculo-skeletal effects of microgravity (Pavy-Le Traon, Heer, Narici, Rittweger, & Vernikos, 2007).

Rationale for exercise countermeasures

There is compelling evidence to suggest that mechanical stimuli per se can elicit a so-called 'osteogenic' response, i.e. a reaction by which bone accrual leads to an enhancement of bone rigidity and strength. It is straightforward to regard the immobilization-induced bone losses as the reverse of this, and to integrate bone strengthening and losing reactions into the concept of a self-adaptive system – commonly known as Wolf's Law (Wolff, 1870). But which is the decisive signal within the mechanical environment that drives bone adaptation? Most researchers would currently agree that it is 'strain' (a dimensionless number that quantifies the deformation of bone), or a signal that is related to the generation of strain. The evidence for this view came initially from the striking observation that peak bone strains center around 2000[1] µstrain across a wide range of species the mass of which spans several orders of magnitude. More compellingly, even, Rubin et al. (1987) have demonstrated in the 'isolated-ulna' model in Turkey that daily loading leads to modelling[2] -based bone accrual when the strains are in excess of 1000 µstrain, but that bone will be lost to disuse-mode remodelling when that threshold is not achieved. Viewing strain as the invariant of a feed-back control system makes sense also from an engineering point of view, as it is the strain that is ultimately destructive. The mechanostat theory (Frost, 1987) was the first to conceptualize this relationship between strains, modelling and remodelling as a semi-quantitative model of bone adaptation. It predicts that bone rigidity varies in direct relationship to the peak loads experienced by bones.

1 One µstrain means deformation by 10^{-6}, hence 2000 µstrain signify 0.2% of the original length.

2 Modelling is shapes and strengthens bone structures – here, formation normally outweighs resorption.



	Standing	Hopping
Body Mass [kg]	70	70
Ground reaction force [kN]	0.7	2.5
Torque [Nm]	84	300
Acceleration [g]	1	3
$Force_{AchillesT}$ [kN]	2.1	7.5
$Force_{Tibia}$ [kN]	2.1	10

Figure 1: Free body diagram of the human ankle. This simplified diagram suggests that loading of the tibia by the mere body weight is only around 700N, whilst a load of 10,000N is achieved when calf muscles accelerate the body, e.g. in hopping. One important aspect herein is the short lever (1:3) against which the calf muscles work. Figure adapted from Maganaris et al. (2011).

So, where do the peak loads arise from? The commonly-used term ‘weight bearing’ bone suggests that, at least in the leg bones, they may arise from the accelerated body mass. Let us remember, though, that weight is defined in physics as mass · gravitational acceleration. Thus, the body weight of a 70 kg person is approximately 700 N on Earth. However, as can be seen from Figure 1, forces more than 10 times greater than body weight can arise from muscle contractions when these muscles accelerate our body mass, as e.g. during hopping. Accordingly, weight-bearing in itself engenders comparatively small forces on the tibia. Countermeasure interventions to prevent bone loss should thus require forceful muscle contractions in order to replicate the bone’s mechanical environment on Earth. Accordingly, resistance training is usually advocated as the first option (Frost, 1997).

Vibration as an exercise modality

Although the mechanostat theory has been the first formal model of bone adaptation, and it continues to be the most popular one, other authors have focused on various aspects not covered by this theory (Schriefer, Warden, Saxon, Robling, & Turner, 2005). One important aspect not covered by that theory is the question of how many strain cycles are required to elicit a response and how many to saturate it, and also whether only supra-threshold cycles contribute to the adaptive process. Moreover, it seems certain nowadays that not only strain magnitude, but also other strain-related entities such as strain energy density, and strain rate have a role to play (Mosley & Lanyon, 1998). This notion has been further elaborated to propose that many small-magnitude strain cycles could be as efficient as few cycles of large strain magnitude – provided the former have greater strain rate than the latter (Qin, Rubin, & McLeod, 1998). It was further proposed that strain rate could be increased with constant amplitude in sinusoidal vibration by increasing the frequency of vibration – which was the birth of vibration as a therapeutic modality for bone (C. Rubin, Turner, Bain, Mallinckrodt, & McLeod, 2001).

The current concepts of vibration exercise have been recently reviewed (Rittweger, 2010). Most vibration devices are meant to be used for 'whole-body vibration', meaning that people usually stand with their feet on a platform. This can be by imposing mechanical oscillations in a synchronous or in a side-alternating fashion (Rauch et al., 2010), as illustrated in Figure 2. Vibration transmission to the trunk and head is more pronounced with synchronous mode vibration (Abercromby et al., 2007). Strictly speaking, ISO norms 2631–1 (for occupational exposure) and 5349 (for hand-held devices) need to be considered, although it is evident that therapeutic (Rittweger, Just, Kautzsch, Reeg, & Felsenberg, 2002) and exercise applications do not strictly fall into their remit (Rittweger, 2010).

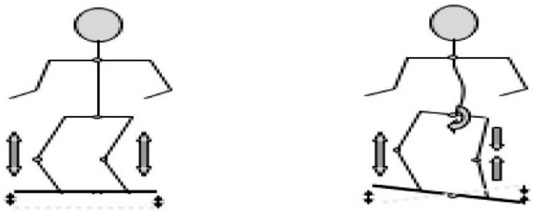


Figure 2: The two principle ways of applying vibration for whole body vibration exercise. The synchronous applies a purely linear acceleration, thus compressing both legs at the same time. In the side-alternating mode, the legs operate anti-phase, which introduces a rotary component to the lumbar spine, and therefore reduces vibration transmission to the trunk. Figure adopted from Rittweger (2010).

Vibration exposure leads to rhythmic elongation and shortening of the musculature (Cochrane, Loram, Stannard, & Rittweger, 2009). Oxygen uptake is moderately enhanced during vibration exposure (Cochrane et al., 2008; Rittweger, Schiessl, & Felsenberg, 2001), and the latter effect can be parametrically controlled by adjustment of frequency and amplitude of vibration (Rittweger et al., 2002). These observations are compatible with the idea of vibration eliciting monosynaptic stretch reflexes, although it has to be considered that the H-reflex, as well as probably the stretch reflex amplitude are mitigated during vibration exposure itself (Ritzmann, Kramer, Gollhofer, & Taube, 2011).

Thus, even though our understanding is not complete, we can outline the following salient features of vibration as an exercise modality in the context of a space-flight countermeasure:

1. Well controllable force and displacement profile
2. Rapid stretch-shortening cycles
3. Large number of muscle contractions per unit time

Evidence from bed rest studies

The scene for a resistive-type of exercise as a countermeasure against bed rest-induced muscle atrophy and bone loss was set by the 90-days HDT Long Term Bed Rest (LTBR) study carried out in Toulouse in 2001 and 2002 (Rittweger et al., 2005). In this study, a gravity-independent ‘flywheel’ ergometer was used as an exercise device 2–3 times per week, resulting in good preservation of the knee extensor, but not of the plantar flexor muscles (Alkner & Tesch, 2004). Bone loss from the tibia was halved in the group that performed the exercise as compared to those who were on bed rest only, which however was not significant because of the huge inter-individual variability (Rittweger et al., 2005). The 17-week study by Shackelford et al. (2004) has been more successful: conventional exercise performed on 6 days per week with a custom-made 'horizontal exercise machine' led to enhanced muscle strength (at least as tested on the horizontal exercise machine), prevented muscle atrophy and bone loss from the heel, and mitigated bone loss from the hip.

Vibration as a countermeasure was first tested at the German Aerospace Centre in Cologne in the 14-day VBR-study, which failed to demonstrate any effect of whole body vibration (twice daily, no additional load) upon muscle atrophy (Zange, Mester, Heer, Kluge, & Liphardt, 2008). Similarly, no effect was observed on bone (Baecker, Frings-Meuthen, Heer, Mester, & Liphardt, 2011). Good results were achieved, however, when whole body vibration was combined with resistive exercise in the 56-day Berlin Bed Rest study, performing exhaustive exercises 11 times per week, with an additional static load equivalent to twice the body weight (Rittweger et al., 2006): atrophy of the calf muscle was prevented and plantar flexor strength maintained (Blottner et al., 2006), and bone loss from the tibia, and probably also from the hip were likewise prevented (Rittweger et al., 2010). A recent study by Wang et al. (2011) in which vibration, albeit with much smaller peak acceleration than in the BBR study, was applied once daily in combination with a static load equivalent to 1.5 times body weight corroborates these findings and shows good efficacy for bone.

The pertinent question, of course, is whether the benefits of these latter two studies were an effect of the vibration (probably not, in the light of results from the VBR study), of the resistive exercise component (possibly, as indicated by Shackelford's study), or a result of both. A case for the latter view can be made on basis of the results from the BBR-2 study. In this 60-day HDT study, the group that performed resistive exercise 3 days per week in combination with whole body vibration depicted a significantly smaller bone loss than the group that performed resistive exercise only (Belavy et al., 2011). Thus, there seems to be a benefit in vibration, although 3 exercise sessions per week may not be sufficient to completely counteract bed-rest induced bone loss.

CONCLUSION

Whilst the exact physiological mechanisms of bone losses induced by space flight and immobilization may still be under scientific debate, the past decade has seen the development of countermeasures that are becoming increasingly effective, at least in a bed rest scenario. Although the recognition of such effective countermeasures cannot invalidate the quest for the establishment of the exact physiological mechanisms behind the bone loss, it will certainly inform and guide future research. In this sense, skeletal forces as induced by muscle contractions should be regarded as an important determinant of bone health. At least for bed rest, the effects of muscle contractions may be fortified, but probably not replaced, by vibration exposure.

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FROM SPACE FLIGHTS TO OSTEOPOROSIS

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ABSTRACT

Space missions (microgravity) alter the balance between bone formation/resorption and induce bone loss. This effect represents a major limiting step in the realization of long-term space missions. A similar picture is induced by prolonged immobilization in bed (bed rest). The Osteoporosis and Muscular Atrophy project (OSMA) was a research program sponsored by the Italian Space Agency which included 35-day bed rest experiments in healthy young men. Anthropometric data of these experiments indicated the expected bone mass reduction in some segments of the leg and body mass redistribution from non-fat mass to fat mass. According to the current view, the bone mass reduction due to microgravity/bed rest is associated with the release of calcium from the bone into the bloodstream (hypercalcemia) which, in turn, lowers the secretion of parathyroid hormone and increases urinary calcium excretion. One of the main unsolved issues in this view is that hypercalcemia is mild and transient during microgravity/bed rest whereas parathyroid hormone reduction is sustained. Bone mass reduction could also be dependent on parathyroid hormone reduction as this hormone affects both formation and resorption of bone tissue. The research on the mechanisms underlying bone mass loss during microgravity/bed rest could be of help, not only to space medicine, but hopefully also for prevention and control of bone ageing and osteoporosis.

Keywords*: bed rest, space mission, microgravity, bone metabolism*

OD POLETOV V VESOLJE DO OSTEOPOROZE

IZVLEČEK

Misije v vesolje (mikrogravitacija) spremenijo ravnotežje med kostno formacijo/resorpcijo in povzročajo izgubo kostne gostote. Ta učinek predstavlja zelo omejujoč korak v realizaciji dolgotrajnih misij v vesolje. Podoben rezultat povzroči daljša imobilizacija v postelji (t. i. „bed rest“). Projekt OSMA ali Osteoporoza in mišična atrofija je bil raziskovalni program, ki ga je sponzorirala Italijanska vesoljska agencija in je vključeval poskuse 35-dnevnega ležanja v postelji na mladih zdravih moških. Antropometrični podatki teh poskusov so pokazali pričakovano zmanjšanje kostne gostote na nekaterih predelih noge ter tudi prerazporeditev telesne mase s področja, kjer ni bilo maščob, na področje z maščobami. Glede na trenutne vidike se zmanjšanje telesne mase, ki ga povzroča mikrogravitacija/ležanje v postelji, povezuje z izločanjem kalcija iz kosti v krvni obtok (hiperkalcemija), kar pa zmanjšuje izločanje obščitničnih hormonov in povišuje izločanje kalcija z uriniranjem. Eno izmed glavnih nerešenih vprašanj ostaja, zakaj se hiperkalcemija med mikrogravitacijo/ležanjem v postelji pojavlja v blagi in začasni obliki, medtem ko je zmanjšanje obščitničnega hormona trajno. Zmanjšanje kostne gostote bi lahko bilo odvisno od zmanjšanja obščitničnega hormona, saj le ta vpliva na formacijo in resorpcijo kostnega tkiva. Raziskave o mehanizmih, ki delujejo v času izgube kostne gostote oziroma mikrogravitacije/ležanja v postelji, bi lahko bile v pomoč tako vesoljski medicini ter mogoče tudi preprečevanju in nadzoru staranja kosti in osteoporoze.

Ključne besede: *»bed rest«, misije v vesolje, mikrogravitacija, kostna presnova*

INTRODUCTION

The normal metabolism of the bone is maintained thanks to the equilibrium between formation/mineralization of new tissue and resorption of pre-existing tissue. In healthy children, teenagers, and young adults, this equilibrium is shifted toward a positive balance during growth and maturation (formation/mineralization > resorption). This equilibrium progressively shifts with ageing toward a negative balance in middle and older ages leading to a progressive loss of bone mass (formation/mineralization < resorption) (Firestein et al., 2008). Space missions alter this equilibrium and induce a substantial reduction in bone mass which is progressively more severe with the increasing duration of a mission (Smith & Heer, 2002). At present, this effect represents a major limiting step in the realization of long-term space missions. It is generally accepted that the determinant of the changes in bone metabolism during space missions are due to the lack of gravity (microgravity) and in particular due to the reduction of the gravitational load on the bone (Le Blanc, Spector, Evans & Sibonga, 2007). The bone mass reduction induced by microgravity is characterized by the loss not only of the organic component of the bone but also of its mineral content. The mineral component of the bone is hydroxyapatite, a salt which contains calcium (Ca) and phosphorus (P). Thus, a reduction in bone mass and in bone mineralization implies the inevitable release of an excess of Ca and P from the bone. As far as Ca, this excess is detectable in the urine as space missions are usually associated also with a substantial increase in urinary Ca excretion. The prolonged immobilization in bed (bed rest) is used as a model to simulate the effects of microgravity on the bone because it induces the loss of bone mass in some segments of the skeleton together with some changes in the bone metabolism with the inclusion of an increase in urinary Ca. The existence of high urinary Ca during immobilization has actually been well known in nephrology for at least 30 years (Stewart, Adler, Byers, Segre & Broadus, 1982).

THE BED REST OF THE OSMA PROJECT

The OSMA project is a multicentre program of investigation on Osteoporosis and Muscular Atrophy sponsored by the Italian Space Agency. The project included the realization of two different bed rest experiments which consisted of the continuous immobilization in bed of 10 healthy young men for a period of 35 days. The bed rest period was preceded by a week for adaptation and pre-bed rest measurements and was followed by a week for post-bed rest measurements and recovery. In these three different periods, the protocol included the collection of blood and urine samples together with measurements of anthropometry, medical parameters, and bone densitometry (Biolo et al., 2008). The design aimed to analyze the time-course of the changes induced by bed rest and, in particular, to assess if the prevailing mechanisms responsible for or associated with the reduction in bone mass vary (or not) from the early phases to the later phases of immobilization.

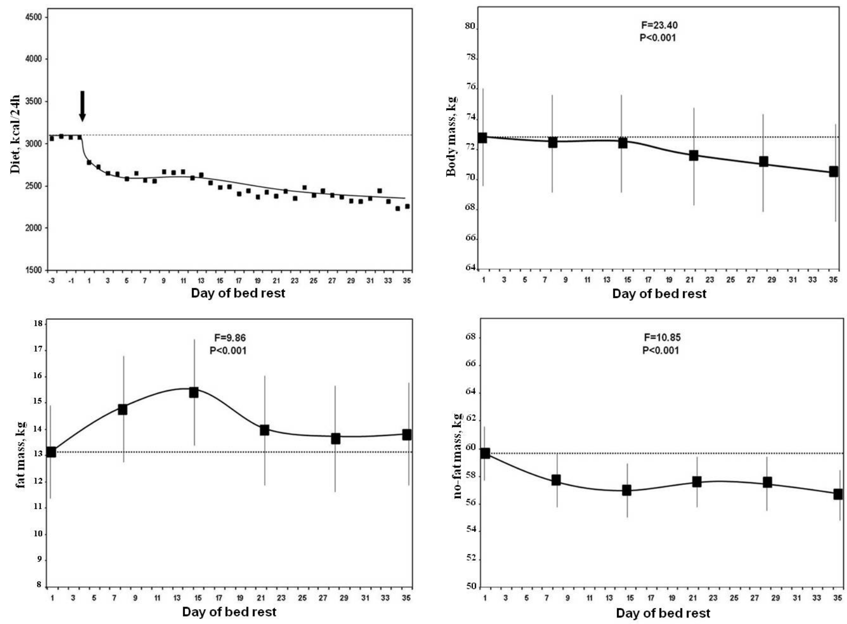

Figure 1: Descriptive data of changes in calorie intake, body mass, fat mass, and non-fat mass during first bed-rest experiment of the OSMA Project (sponsor Italian Space Agency).

Figure 1 shows calorie intake and anthropometric indices during the first experiment. Starting from the bed rest initiation, the study protocol included a reduction in calorie intake to prevent an increase in body mass and fat mass secondary to immobilization, hence, a reduction in the calorie expenditure. Body mass did not increase throughout bed rest and actually decreased in the last weeks. Despite of the lack of a body mass increase, fat mass increased indicating a re-distribution of the weight from the muscular mass to the fat mass compartment. This change was obviously due to immobilization and could not be prevented by a simple restriction of caloric intake. Figure 1 also shows that caloric intake progressively declined after day 15 of bed rest, a decline which was not designed by the protocol and reflected an uncontrolled reduction in appetite due to bed rest.

A previous paper reported the effects of this first experiment on bone densitometry (Rittweger et al., 2009). Briefly, bone mass reduction was not uniform across all segments of the leg skeleton and tended to be greater in the patella and in the tibia epiphyses (Rittweger et al., 2009). Altogether, the data confirmed that a bed rest intervention induces a negative balance mainly in the lean components of the body with inclusion of some leg segments of the skeleton. At present, there is no definite mechanism to explain these differential effects of bed rest.

BONE MASS LOSS DUE TO MICROGRAVITY / BEDREST: THE PRESENT VIEW

As stated above, one of the aims of the OSMA project was to assess if the prevailing mechanisms responsible for or associated with bone mass reduction vary (or not) from early phases to later phases of bed rest taken as a model of microgravity on Earth. In this area of research, the current view is that the loss of bone mass due to bone unloading is mainly explained by an acceleration of bone resorption (Lueken, Arnaud, Taylor & Baylink, 1993). The dissociation of this event from a compensatory increase in bone formation would lead to a progressive reduction in the organic component of the bone and in its mineralization. In other words, the exposure to microgravity or to a bed rest experiment would accelerate the physiologic process of bone ageing due to the progressive prevailing of bone resorption over bone formation. According to the view of an excess of bone resorption, the load of Ca ions available in the bone would be released from the bone into the bloodstream leading to hypercalcemia and eventually to hypercalciuria thanks to the compensatory increase in Ca excretion via the kidneys (Drummer et al., 2002). Another important piece in this mosaic is the regulation of parathyroid gland activity. Parathyroid hormone (PTH) plays a pivotal role in the control of Ca homeostasis and bone metabolism. It is well established that PTH secretion is reduced or suppressed by hypercalcemia (Potts, 2005). Therefore, the observation of PTH down-regulation during space missions or bed rest is in full agreement with the view of a primary increase in bone resorption leading to hypercalcemia and, in turn, to PTH suppression and hypercalciuria (Figure 2).

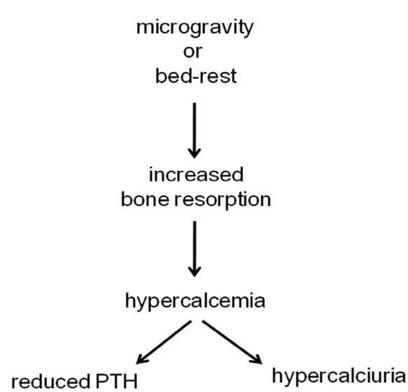

Figure 2: Present view of the chain of events linking bone unloading to alterations in indices of calcium homeostasis.

BONE MASS LOSS DUE TO MICROGRAVITY / BEDREST: THE UNSOLVED ISSUES

The main unsolved issue in the current view is that, at its best, hypercalcemia is very mild and only transient during space missions and bed rest (LeBlanc et al., 1995). In other words, a key component is lacking in the chain of events from the excess of bone resorption to PTH suppression and the excess of urinary Ca. This lack appears even more important considering that PTH suppression could have a primary role in bone mass reduction because of the favorable effects of PTH on bone metabolism. Another unsolved issue is the change in P homeostasis. As stated above, the mineral component of the bone is rich not only in Ca, but also in P. Therefore, if an excess of Ca ions is reabsorbed and released from the bone, the same should also be true for P. However, a reliable conclusion has not been achieved regarding this issue because P homeostasis has not been extensively investigated during space missions or bed rest. The largest series of data regarding P homeostasis during bed rest was reported by Zerwekh et al. who found a non-significant increase in serum and urinary P over a pre-bedrest baseline (Zerwekh, Ruml, Gottschalk & Pak, 1998). Finally, another important unsolved issue is the possibility that during space missions or bed rest experiments, early changes are different from subsequent changes (Lueken, Arnaud, Taylor & Baylink, 1993). In most physiologic and pathologic processes, a substantial change in the environmental conditions is followed first by a set of rapid effects and later by a sequence of compensatory adaptations which lead to a new equilibrium. Is this true also for bone metabolism and Ca/P homeostasis during space missions or bed rest? Does a primary excess in bone resorption exist also when space missions or bed rest experiments last for more than a few days?

BONE MASS LOSS DUE TO MICROGRAVITY / BEDREST: THE PRACTICAL IMPLICATIONS

The existence of bone mass loss during space missions or bed rest could be considered a problem of importance confined to the limits of space medicine and clinical practice for immobilized patients. This may not be the case. The available evidence suggests that bone mass reduction in those particular settings represents in many aspects an acceleration of the normal ageing of the bone. Thus, research in this field could be of help in the prevention and control of osteoporosis, a disorder which is highly prevalent in the populations of industrialized countries and results in high social and economic costs (Smith et al., 2003). In other words, as often with space research, the comprehension of the mechanisms underlying bone mass loss during space missions and bed rest could favor the development of diagnostic tools and therapeutic countermeasures of potential use also for millions of people "in the real world".

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HEART RATE REPRODUCIBILITY ASSESSED BY SURROGATE DATA ANALYSIS

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ABSTRACT

Purpose: Combinations of head up tilt (HUT) and lower body negative pressure (LBNP) have been used to study syncope. Since HUT invokes initial, partly transient cardiovascular responses, in this work we employed the HUT phase (5 min in all subjects) to arrive at a state of orthostatic loading to be used as a reference load for subsequent added LBNP phases. We investigated the pattern of cardiovascular responses during the LBNP phase across four runs for test subjects using surrogate data analysis. Methods: Ten healthy young males were subjected to HUT + LBNP to achieve a presyncopal end-point in four runs, each separated by ≥2 weeks. Beat to beat continuous hemodynamic variables were measured and analyzed. Results: Expected heart rate increases, in response to the decreases in stroke volume induced by graded LBNP, were observed. Heart rate was the only variable that showed reproducibility between subjects across four runs. Conclusion: During LBNP phase of the combined HUT+ LBNP protocol, heart rate was the only reproducible variable, thus confirming its central role during added LBNP in upright tilted men. Surrogate data analysis is useful tool to differentiate physiological responses from chance events in repeated runs.

Keywords: *lower body negative pressure, presyncope, hemodynamics, stroke volume, blood pressure*

OCENA REPRODUCIBILNOSTI SRČNEGA UTRIPA Z NADOMESTNO ANALIZO PODATKOV

IZVLEČEK

Za raziskovanje sinkope so bile uporabljene kombinacije testa z nagibanjem (HUT) in testa z negativnim tlakom spodnjega dela telesa (LBNP). Ker test HUT sproži najprej deloma začasne odzive krvožilnega sistema, smo v tem projektu uporabili fazo HUT (5 minut za vse preiskovance), da smo dosegli stanje ortostatične obremenitve, ki se uporablja kot referenčna obremenitev za nadalje dodane faze LBNP. Preiskali smo vzorec odzivov krvožilnega sistema med fazo LBNP tekom štirih ponovitev na preiskovancih, pri čemer smo uporabili nadomestno analizo podatkov. Na desetih zdravih mladih moških smo izvedli testa HUT in LBNP, da bi dosegli presinkopo v štirih poskusih, med vsakim poskusom sta minila najmanj dva tedna. Izmerili in analizirali smo kontinuirane hemodinamične spremenljivke utripa. Ugotovili smo, da pričakovani srčni utrip naraste kot odziv na zmanjšanje obsega udarcev, kar sproži postopni test LBNP. Srčni utrip je bil edina spremenljivka, ki je pokazala reproducibilnost med preiskovanci v času vseh štirih ponovitev. Med fazo LBNP v okviru kombiniranega protokola HUT in LBNP je bil srčni utrip edina reproducibilna spremenljivka, kar potrjuje njegovo osrednjo vlogo med dodajanjem LBNP pri moških, ki so med testom nagibanja obrnjeni vertikalno. Nadomestna analiza podatkov je uporabno orodje za diferenciranje psiholoških odzivov od priložnostnih dogodkov med ponovitvami postopkov.

Ključne besede: *negativni tlak spodnjega dela telesa, presinkopa, hemodinamika, obseg udarcev, krvni tlak*

INTRODUCTION

Like hypergravity (induced by centrifuge) (Evans et al, 2006), head up tilt (HUT) combined with lower body negative pressure (LBNP) challenges the maintenance of blood pressure stability and can force the control system to exploit the full spectrum of cardiovascular compensatory mechanisms, revealing characteristics of individual blood pressure control that might go unnoticed with conventional orthostatic stress. The combination of HUT followed by LBNP (HUT + LBNP) induces cardiovascular and neuroendocrine changes, which are dependent on stress intensity and duration (Al-Shamma & Hainsworth1987; el-Bedawi, & Hainsworth, 1994).

Orthostatic tolerance has been typically studied using either graded LBNP or HUT alone or combination of both. When HUT + LBNP is employed, extensive central hypovolemia leading to presyncope is seen in most test subjects underlining the fact that HUT+LBNP represents a significant challenge to the cardiovascular system (Hainsworth, & el-Bedawi, 1994). There exists a considerable body of evidence regarding hormonal and hemodynamic changes due to HUT and LBNP in presyncopal state (Howden et al., 2001; Lelorier et al., 2003; Lightfoot et al., 2001) but little is known about the individual stability of orthostatic tolerance in subjects. Wide variance in inter-individual reproducibility but high intra-individual reproducibility of responses to orthostatic tolerance has been previously observed in our test subjects, induced by HUT + LBNP across multiple runs for test subjects (Evans et al., 2006; Goswami et al., 2009b).

We have previously shown that heart rate and stroke volume responses are reproducible across HUT+ LBNP (Goswami et al., 2009c). Since HUT invokes initial, partly transient cardiovascular responses, in this work we used the HUT phase (5 min in all the subjects) to arrive at a state of orthostatic loading that acts as a reference load for the following consecutively added LBNP phases. While the data used here are from the study (Goswami et al., 2009c) [which used data of the entire HUT + LBNP phases], in this paper we focus solely on the cardiovascular responses during the graded LBNP phase (“hypergravity” or added orthostatic loading phase) in subjects who were tilted upright at 70 degrees. While we observed reproducibility in heart rate and stroke volume during the entire HUT + LBNP protocol (Goswami et al., 2009c), in this paper we examined only the LBNP phase to investigate whether this reproducibility was present across the four runs. It was not the aim to identify the underlying physiological mechanisms causing a given response but to analyze the measured data by statistical means. To our knowledge, we are not aware of any study that has examined only the LBNP phase of a combined HUT + LBNP paradigm to investigate the reproducibility of hemodynamic responses across several runs. We believe that this is important, as the added orthostatic loading caused by increasing LBNP would provide useful information on how the physiological systems behave during extreme (or what the body is not normally used to) stress and across repeated runs. Indeed, reproducibility of heart rate and stroke volume during the LBNP phase would indicate that the system behaves the in the same manner under added orthostatic loading as under normal head up tilt.

METHODS

Subjects

Because gender and age may affect orthostatic and stress responses (reviewed in Goswami et al., 2008), we focused on young healthy men whose physical characteristics were homogeneous. The study was done in healthy, non-obese, non-medicated, non-smoking males who were free from any somatic or mental symptoms or diseases. Ten men of age 25±3 years, weight 75±12 kg, height 179±6 cm, and with a supine heart rate of 69±10 bpm met these criteria. They were advised to keep their fluid and salt intake according to their usual dietary habits and to refrain from alcohol during any part of the study period. Subjects were familiarized with the test protocol and gave written informed consent to participate in the study. The study was approved by the Medical University of Graz Ethics Board, and was performed in accordance with the 1989 WMA Declaration of Helsinki.

Protocol

The measurements were conducted on fasting subjects. Experimental tests were carried out in a semi-dark, quiet room with a temperature maintained at 23–24 °C, and humidity between 50–55%, between the hours of 9–11 am. Each subject was tested four times with a minimum of a two-week interval between test runs.

Each experimental run started with a 30 min supine rest period to acquire cardiovascular steady state conditions. At minute zero of the stress protocol, the tilt table was brought to 70° head-up position. After five more minutes, -20 mmHg LBNP was added. LBNP was increased by 10 mmHg every 3 minutes, particularly as we wanted to drive the subjects to presyncope quickly. We chose this protocol, as LBNP stress duration influences stress responses and we also wanted to minimize the possible effects of rapid adaptation. As soon as presyncopal signs or symptoms occurred, the table was brought back to 0° and LBNP was stopped at once. The criteria of presyncope (Grasser et al., 2008a) were when all/either of the following occurred: a) Blood pressure drop below systolic 80 mmHg or by ≥25 mmHg/min, diastolic by ≥15 mmHg/min, and /or heart rate decrease by ≥15 bpm; b) Lightheadedness, dizziness, visual disturbances, nausea, stomach awareness, clammy skin, excessive sweating, or skin pallor.

During the test the subjects were instructed to avoid undue movements of the lower limbs and to breathe normally. Test subjects were secured and had access to an emergency shutdown (automatic return to supine and pressure neutralization) at all times.

Test Apparatus

The test was carried out at the Institute of Adaptive and Spaceflight Physiology (www.meduni-graz.at/iap/AHST.htm) using a combined tiltable-LBNP chamber device equipped with a footrest. Care was taken to maintain the sealing at the iliac crest, as sealing position has been shown to affect hemodynamic responses (Goswami et al., 2009a). A transition from supine to upright position as well as negative pressure buildup was complete within 5 seconds. Suction was provided using a commercially available vacuum cleaner located in an adjacent room. The execution of the pre-programmed test protocol and synchronous recording of all data from the cardiovascular monitoring system was done by LabView®.

Measurements

Electrodes were placed at the neck and thoracic regions, the latter specifically at the midclavicular line at the xiphoid process level. Continuous hemodynamic monitoring included systolic and diastolic blood pressure, heart rate (3-lead ECG), and thoracic impedance using the Task Force Monitor®, CNSystems, Graz, Austria. This monitor estimates arterial pressure using finger cuffs (the principle of vascular unloading technique was used to estimate the arterial blood pressure (Penaz principle)) and regular calibration to standard arm cuff measurements (by Task force monitor). Mean arterial blood pressure (MAP) was calculated from diastolic (DBP) and systolic pressures (SBP), respectively: MAP = DBP + 1/3 (SBP - DBP). Stroke volume was calculated from the impedance data.

Data Analysis and Interpretation

Sample Size

Using typical cardiovascular changes during orthostatic loading from previous studies (Evans et al., 2001; Gao et al., 2008; Grasser et al., 2008b), error probability (α) of 0.05, power (1-ß) of 0.80, we estimated the number of subjects required to be 10.

Data Preparation

Cross-correlation (CC) analysis was used to assess reproducibility of heart rate and stroke volume responses as a function of time, as well as heart rate to stroke volume relationships comparing consecutive runs per person using Matlabs XCORR algorithm. This algorithm produces an estimate of the correlation between two random sequences:

C(m) = E[A(n+m)*conj(B(n))] = E[A(n)*conj(B(n-m))]

XCORR, an unbiased estimator, normalizes the sequence so that the autocorrelations at zero lag are equal to unity (MatLab R2007a, The MathWorks Inc.).

To characterize the non-linear dynamic features of the protocol by appropriate statistical means, data sets were created from the original data by computing the Fourier transform and randomizing the imaginary part in the frequency domain. Following this randomization in the frequency domain, data were then transformed back to the time domain by inverse Fourier transformation. Such data have the same mean, standard deviation, and power spectrum as the original data (Theiler et al., 1992) and can be used as so-called surrogate data for statistical analysis. For every original data set 100 such data sets were calculated and correlated with the original signal. The 95^{th} percentile of the correlation coefficient of this comparison was then used to reject the null hypothesis, namely that there was no difference between a random signal produced by the original run and a signal from another run. Comparisons were done using a paired t-test. Thus, if the correlation coefficient of the 95^{th} percentile (taking in account alpha error $p<0.05$) of the randomized signal was lower than the correlation coefficient in another run, the differences between runs were more likely to be due to physiological mechanisms than to the randomization itself.

For each subject in a run, the period between the commencement of LBNP and the maximum heart rate was used to assess cardiovascular reproducibility. During this period, cross correlation of HR and SV was also done (Table 1). To compare the runs, we used the shorter time of the two respective pairings, to calculate the CC between the pairs and to calculate the surrogate data (see Table 2 & 3).

RESULTS

Figure 1 shows the relationship of MAP, HR and SV changes across the entire combined protocol (supine rest, HUT and graded LBNP). That is, the influence of HUT application on the subsequent LBNP induced hemodynamic changes.

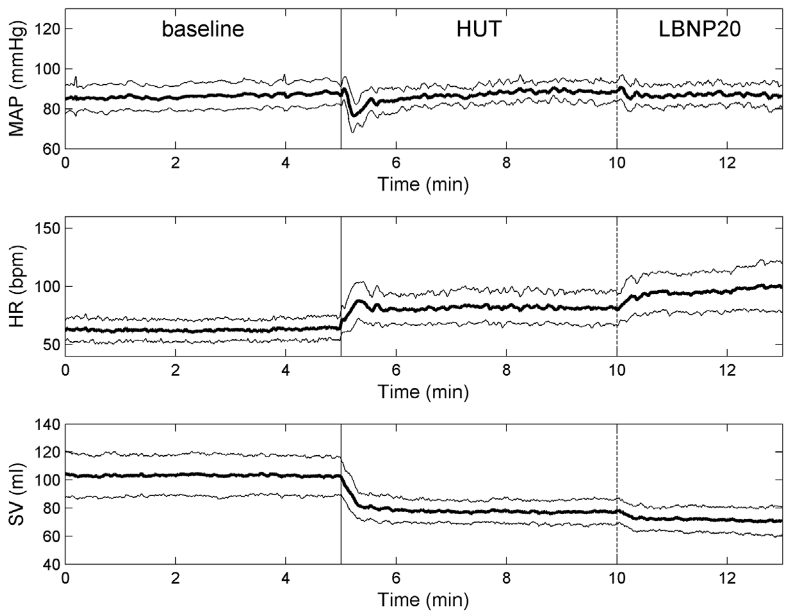

Figure 1: The influence of HUT application on the subsequent LBNP induced hemodynamic changes (MAP, HR and SV). The values indicated here are the means (SD) of all the 10 subjects across the four runs. LBNP20 represents only the initial phase of the graded LBNP. Legend: MAP: Mean arterial pressure; HR: Heart rate; SV: Stroke volume.

Overall cardiovascular effects of the HUT +LBNP are presented elsewhere (Goswami et al., 2009c).

The correlations of HR and SV during increasing LBNP phase for 10 subjects (A–J) are shown in the Table 1.

Table 1. Summary of cross correlation (CC) between heart rate and stroke volume in all subjects (A to J). # Refers to machine failure and shut down during run 1.

Subject	Heart rate : Stroke volume			
	$CC_{1,1}$	$CC_{2,2}$	$CC_{3,3}$	$CC_{4,4}$
A	-0.922	-0.915	0.903	-0.843
B	-0.934	-0.941	-0.925	-0.901
C	-0.649	-0.802	-0.684	-0.632
D	-0.901	-0.927	-0.932	-0.942
E	-0.617#	-0.633	-0.351	-0.533
F	-0.918	-0.913	-0.946	-0.946
G	-0.870	-0.870	-0.909	-0.924
H	-0.823	-0.845	-0.939	-0.942
I	-0.895	-0.906	-0.861	-0.793
J	-0.417	-0.668	-0.630	-0.719

Correlation between paired runs was significantly higher for HR data when compared to the corresponding surrogate data (Table 2).

*Table 2. Cross correlation of heart rate across runs (1–4). Paired T-test between Cross Correlation Coefficents of runs 1,2,3,4 (C1,2,C1,3, ... C3,4) to runs and surrogate (C1,surrogate, C2,surrogate, C3,surrogate) ; * ... p<0.05; ** ... p<0.01; *** ... p<0.001.*

	HR_2	HR_3	HR_4
HR_1	$C_{1,2}$ = 0.725 ± 0.153 **	$C_{1,3}$ = 0.728 ± 0.181***	$C_{1,4}$ = 0.740 ± 0.137 **
	$C_{1,surrogate}$ = 0.587 ± 0.108	$C_{1,surrogate}$ = 0.593 ± 0.134	$C_{1,surrogate}$ = 0.600 ± 0.123
HR_2		$C_{2,3}$ = 0.743 ± 0.206 **	$C_{2,4}$ = 0.707 ± 0.195 *
		$C_{2,surrogate}$ = 0.546 ± 0.131	$C_{2,surrogate}$ = 0.557 ± 0.119
HR_3			$C_{3,4}$ = 0.804 ± 0.109***
			$C_{3,surrogate}$ = 0.537 ± 0.094

Table 3. Cross correlation of stroke volume across runs (1–4). Designations as in Table 2.

	SV_2	SV_3	SV_4
SV_1	$C_{1,2}$ = 0.575 ± 0.264	$C_{1,3}$ = 0.578 ± 0.291	$C_{1,4}$ = 0.582 ± 0.229
	$C_{1,surrogate}$ = 0.533 ± 0.131	$C_{1,surrogate}$ = 0.549 ± 0.126	$C_{1,surrogate}$ = 0.552 ± 0.131
SV_2		$C_{2,3}$ = 0.624 ± 0.269	$C_{2,4}$ = 0.586 ± 0.241
		$C_{2,surrogate}$ = 0.499 ± 0.135	$C_{2,surrogate}$ = 0.495 ± 0.130
SV_3			$C_{3,4}$ = 0.584 ± 0.260
			$C_{3,surrogate}$ = 0.443 ± 0.162

However, no differences in the CC were seen for SV data when compared to the corresponding surrogate data (Table 3).

Blood pressures, particularly diastolic and systolic, showed poor correlation between runs. Therefore, no differences, or an even higher correlation, to the corresponding surrogate data was found. For example, we calculated the CC of run 1 vs 2 and run 1 vs surrogate data, etc. See Table 2 for details.

DISCUSSION

The application of LBNP, to subjects who are already in HUT position, is an additional significant orthostatic challenge. We observed that heart rate responses were reproducible for the four runs, thus underlying the central role of heart rate in blood pressure regulation in subjects undergoing graded LBNP.

To maintain blood pressure and adequate cerebral perfusion during central hypovolemia (Mosqueda-Garcia et al., 2001) caused by HUT, LBNP or hemorrhage, reflex increases in heart rate and total peripheral resistance (el-Bedawi & Hainsworth, 1994; Hainsworth & el-Bedawi, 1994) occur. In our study, the increases in heart rate as well as the decreases in stroke volume during the LBNP phase were comparable to what has been reported by others (Convertino & Sather, 2000), and are reported elsewhere (Goswami et al., 2009c).

The major finding of this study was that physiological reproducibility in heart rate differed from the "surrogate" data across the runs. By comparing surrogate data with original ones across runs, we conclude that the correlation between runs was higher than between run and surrogate data from the run. This confirmed that physiological reproducibility in heart rate differed from the simulated "surrogate" data across the runs thus suggesting that these represented real physiological responses rather than one obtained by chance (Blaber et al., 1995).

Blood pressure data, on the other hand, showed poor correlation across runs. Furthermore, no differences, or an even higher correlation, to the corresponding surrogate data was found. This could be attributed to the close range in which the blood pressure is maintained across the entire graded LBNP stress. This is consistent with the observation that blood pressure is the primary regulated variable during stress (Julius, 1988), and therefore, operates within a narrow range.

Limitations

It is also possible that the initial HUT phase (not used in this study) of the combined HUT+LBNP could have resulted in varying levels of central volume at the beginning of the LBNP phase, which could affect the response patterns during the LBNP phase (Figure 1). For example,regulatory features might be called upon in persons with lower functional central volume reserve, induced by the HUT, to maintain blood pressure during graded LBNP. That is, such persons might more fully employ the possible range of cardiac and peripheral-vascular response patterns available in order to compensate for limited central volume reserve.

CONCLUSIONS

Young healthy males subjected to graded lower body negative, while in upright tilted position, showed only heart rate reproducibility across the four runs. This is in contrast to both heart rate and stroke volume reproducibility observed in the same subjects, when the entire HUT +LBNP protocol was used. This confirms that heart rate plays a central role in maintaining arterial blood pressure (Convertino & Sather, 2000), both under HUT (similar to everyday standing) and graded LBNP (so called "unknown stress"). Finally, surrogate data analysis is a useful tool to differentiate physiological responses from chance events in repeated runs.

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A NEW NON-INVASIVE DEVICE TO MONITOR CORE TEMPERATURE ON EARTH AND IN SPACE

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ABSTRACT

Accurate measurement of the core temperature (Tc) is fundamental to the study of human temperature regulation. As standard sites for the placement of Tc measurement sensors have been used: the rectum, the bladder, the esophagus, the nasopharynx and the acoustic meatus. Nevertheless those measurement sites exhibit limited applicability under field conditions, in rescue operations or during peri- and postoperative long-term core temperature monitoring. There is, indeed, a high demand for a reliable, non-invasive, easy to handle telemetric device. But the ideal non-invasive measurement of core temperature has to meet requirements such as i) a convenient measurement site, ii) no bias through environmental conditions, and iii) a high sensitivity of the sensor regarding time shift and absolute temperature value. Recently, together with the Draegerwerke AG we have developed a new heat flux measurement device (so-called "Double Sensor") as a non-invasive Tc sensor aiming to meet the requirements described above. Four recent studies in humans will be summarized and discussed to show the applicability of this new non-invasive method to monitor core temperature under different environmental and clinical settings on Earth and in Space.

Keywords: *non-invasive marker, core temperature, measurement, Earth, Space*

NOVA NEINVAZIVNA NAPRAVA ZA SPREMLJANJE TEMPERATURE SREDICE TELESA NA ZEMLJI IN V VESOLJU

IZVLEČEK

Natančno merjenje temperature sredice človeškega telesa (Tc) je poglavitno za preučevanje uravnavanja telesne temperature. Običajna mesta za namestitev senzorjev za merjenje Tc so rektum, mehur, požiralnik, nosni del žrela in sluhovod. Vendar pa ta mesta kažejo omejeno uporabnost v različnih pogojih, reševalnih operacijah ter med pred- ali pooperativnem dolgotrajnem spremljanju temperature sredice telesa. Tako obstaja velika potreba po zanesljivi, neinvazivni telemetrični napravi, ki bi bila enostavna za uporabo. Vendar pa mora najbolj primerno neinvazivno merjenje temperature sredice telesa ustrezati naslednjim zahtevam: i) ustrezno in priročno mesto za opravljanje meritve, ii) nepristranski pogoji v okolici in iii) visoka občutljivost senzorja glede na časovne spremembe in absolutno temperaturno vrednost. Tako smo nedavno skupaj z družbo Drägerwerk AG razvili novo merilno napravo s toplotnim pretokom (t. i. „dvojni senzor"), ki je neinvazivni senzor za merjenje Tc, ki ustreza zgoraj opisanim zahtevam. Povzeli in razpravljali bomo o štirih študijah, ki so bile nedavno izvedene na ljudeh in ki dokazujejo uporabnost te nove neinvazivne metode za spremljanje temperature sredice telesa v različnih okoljskih in kliničnih pogojih na Zemlji in v vesolju.

Ključne besede: *neinvazivni marker, temperatura jedra, merjenje, Zemlja, vesolje*

INTRODUCTION

Fundamental to the study of human temperatures regulation is the accurate measurement of deep core temperature. Under experimental conditions the core temperature is usually recorded by inserting a thermo sensor in the rectum, the bladder, the esophagus, the nasopharynx and the acoustic meatus (Gunga 2005; Wartzek et al. 2011). The relative advantages and disadvantages of these and other recording sites including the time response of the sensor have been intensively discussed ever since the first benchmark investigations by Claude Bernard in 1876 (Cooper and Kenyon, 1957; Cranston et al., 1957; Aikas et al., 1962; Nielsen and Nielsen, 1962; Saltin et al., 196; Braeuer et al., 1977; Mairiaux et al., 1983; Sawka and Wenger, 1986; Brengelmann, 1987; Deschamps et al., 1992; Moran and Mendal, 2002; McKenzie and Osgood, 2004; Easton et al., 2007; Low et al., 2007; Wartzek et al., 2011). However, none of these methods is really applicable during daily routines because the current methods are hard wired, difficult in cleaning (sanitation), not easy reusable, and uncomfortable.

There is a clear demand for an alternative method that eliminates the shortcomings of current technologies and which is applicable for multiple hours during daily activities and under clinical settings (Wartzek et al., 2011). The requirements for such a method serving to record core temperature are demanding: the new technique has to be i) non-invasive, ii) easy to handle, iii) must fulfill basic hygiene standards, iv) not influenced towards various environmental conditions, while on the other site v) changes should quantitatively reflect small temporal in core temperature, and vi) last but not least, the response time of the temperature sensors should be as short as possible (Cooper et al., 1964; Shiraki et al., 1986; Moran and Mendal, 2002; Easton et al., 2007; Lawson et al., 2007; Wartzek et al., 2011).

These requirements are essential because several terrestrial studies in humans have shown that if high environmental temperature and humidity prevail, especially in combination with heavy physical workloads and fluid loss (sweating) with inadequate re-hydration, the heat load will lead to a rapid rise in the core temperature, subsequently resulting in heat stress related injuries such as heat strokes (Shibolet et al., 1976; Wenger, 2001; Sandsund et al., 2005). Furthermore, it has been frequently hypothesized by different authors that a lack of gravity impairs in a sustained manner the natural share of convective heat transfer from the body surface. This is because gravity, as the driving force for this convective heat transfer, ceases to apply at the body surface along the body axis under microgravity conditions (Blanc et al., 2000; Kuhlmann, 2000; Yu et al., 2000; Zhang et al., 2000). This results in changes in the thermal comfort of the astronaut/cosmonaut under these specific environmental conditions (Novak et al., 1979; Novak and Genin, 1980; Novak et al., 1988; Novak, 1991; Qui et al., 1997; Qui et al., 2002), especially during extravehicular activities (EVA) (Clement, 2003). Therefore, we recently reported a new non-invasive core temperature heat flux sensor ("Double Sensor (Gunga et al. 2008) which is different from previous heat flux sensors proposed by Fox and Solman (1971) and Danielsson (1980).

In a next step we decided to use the technology at bedside during a long-term bed rest study (Berlin Bed Rest Study, BBR2) conducted by the European Space Agency (ESA) to establish whether rectal temperature recordings in humans could be replaced under those circumstances by the Double Sensor to monitor circadian core temperature changes in humans. Then we conducted a pilot study to determine whether this kind of sensor could be used also in a clinical setting during deep hypothermia (14–16°C) to monitor core temperature in the course of heart transplantation. Finally, we will show here first preliminary data of core temperature changes due to physical exercise in a single astronaut before, during and after a long-term spaceflight. Taken together, these four studies - which are partly still on-going - will be used to document the applicability of this new non-invasive method to determine core temperature in humans under different clinical and environmental setting including space.

METHODS

The Double sensor is placed at the front of the head by an adhesive tape, Further details are given in Gunga et al. (2009).

Study 1

The first study (study 1) was performed at the laboratory of occupational physiology in Trondheim (Norway). 20 male subjects (arithmetic mean ± SD) 39.5 ± 10.2 years, height 1.80 ± 0.06 m, 83.8 ± 11.0 kg) participated in the study. Thermal (rectal, nasopharyngeal, skin temperatures, Double Sensor temperatures) and cardiovascular data were collected continuously before, during and after the different experimental set-ups from 25–55% maximal intensity work load at 10, 25, and 40°C environmental temperatures. Further details are given in Gunga et al. (2008).

Study 2

The objective of the second experiment (study 2) was to establish whether rectal temperature recordings in humans could be replaced by the Double Sensor to monitor core temperatures changes due to circadian rhythms at ambient room temperatures (23.0 ± 2.0 °C). To achieve this goal, rectal and Double Sensor data were collected continuously, starting at 19:30 h in the evening until 6:30 h the following morning. The study was conducted by the Centre of Muscle and Bone Research and performed at the University Hospital Charite Campus Benjamin Franklin in Berlin during the years 2007–2008. In total 9 male subjects participated in the experiment. The anthropometrical characteristics of the subjects were as follows ((arithmetic mean ± SD) age 33.2 ± 7.9 years, body mass 80.6 ± 5.2 kg, height 1.81 ± 0.06 m, body mass index (BMI) 24.6 ± 2.3 kg/m². Further details are given in Gunga et al. (2009).

Study 3

In the third setting (study 3), which was performed in collaboration with the German Heart Institute Berlin, we determined thecore temperature by the Double Sensor technology in a single patient during a cardiac operation and compared it to a concomitantly taken vesical core temperature. The patient was cooled down to 14–16°C (deep hypothermia). After the operation was finished the patient was heated again up to the physiological temperature. In addition to the standard monitoring we recorded in this patient the skin blood flow using a Laser-Doppler-Tissue-Oxymeter (O_2C). Further details are given in Opatz et al. (2010).

Study 4

In the fourth experimental setting (study 4), the Double Sensor was used during a regular VO_2 ergometer testing (each step 25 Watt) before, several times in space on the ISS, and after spaceflight in a single male long-term astronaut. This study (called "Thermolab") is still on-going in close co-operation with NASA scientists (Exercise Lab, PI Dr Alan Moore, JSC, Houston) and will be finished in 2012. Please note, all data presented here have to be taken an preliminary and not final.

Statistics

As statistical methods descriptive statistics as well as GLM (general linear model) and paired t-Test were applied, and $P < 0.05$ was considered for statistical significance. To show the correlation between the three methods we used Lin`s Concordance Correlation Coefficient (CCC). For specific statistical methods used in the different studies, such as Bland-Altman diagrams (Bland and Altman, 1999), details are given in the specific publications mentioned above.

RESULTS

The main results of the different studies performed with the new Double Sensor technology on Earth and in space are summarized in the figures 1–4.

Study 1

The specific results of study 1 are shown in figure 1 A–C. This study revealed that i) the device under test differed between –0.16 to 0.1°C from the average of the rectal temperature and the Double Sensor, ii) showed with increasing ambient temperatures increasing concordance correlation coefficients (CCC) (10°C:0.49; 25°C:0.69; 40°C:0.75), and iii) exhibited (data not shown here) a faster temperature decrease at all resting periods at all ambient conditions as compared to rectal temperature ($P<0.01$) (Gunga et al., 2008).

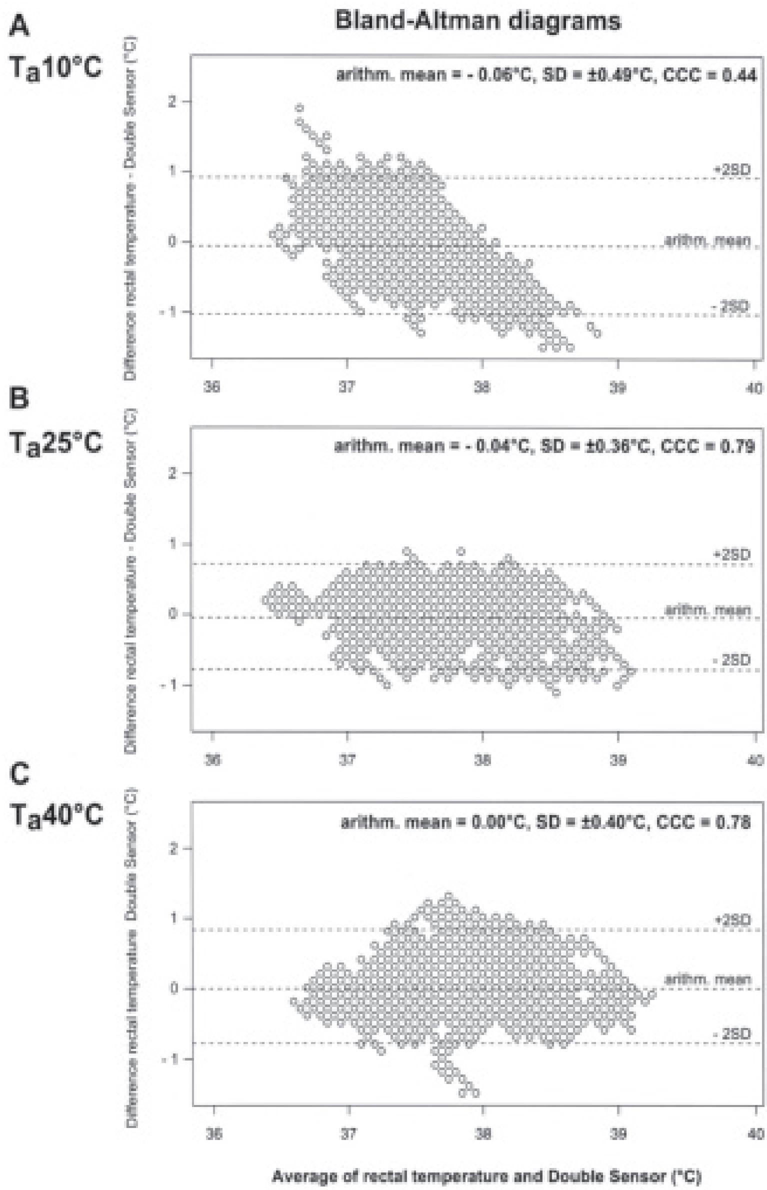


Figure 1A–C: Bland and Altman plots comparing the rectal and Double Sensor temperature during all working and resting periods at 10°C, 25°C, and 40°C ambient temperature as well as Concordance Coefficient Correlations (CCC) calculated according to formulas given by Li and Chow (2005) (adapted from Gunga et al. (2008)).

Study 2

Figure 2 shows a scatter plot and regression lines obtained from cosinor analysis for rectal (black dots, dotted line) and Double Sensor (white dots, solid line) temperature data as a function of time from a single subject. The complete group analysis showed that the individual differences between the two techniques varied between -0.72 and +0.55°C. Further details are given in Gunga et al. (2009).

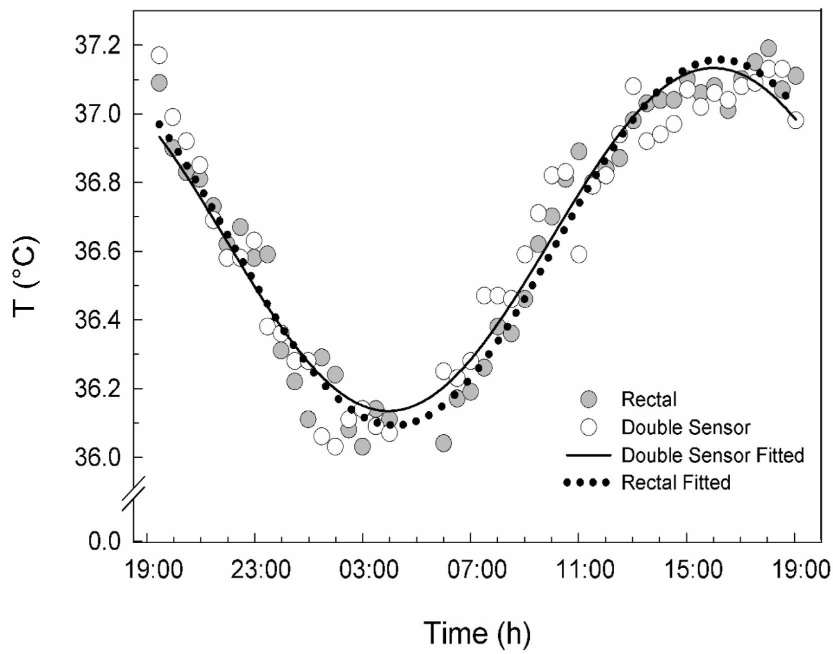


Figure 2: This graph shows a scatter plot and regression lines obtained from cosinor analysis for rectal (black dots, dotted line) and Double Sensor (white dots, solid line) temperature data as a function of time from a single, representative subject. (Adapted from Gunga et al. (2009)).

Study 3

Figure 3 shows core temperature changes (vesical and Double Sensor) changes in a clinical setting in which a patient had to be exposed to deep hypothermia (preliminary data). The measurements depicted that the Double Sensor showed great accuracy (Lin's CCC=95%). Further details are given in Opatz et al. (2010).

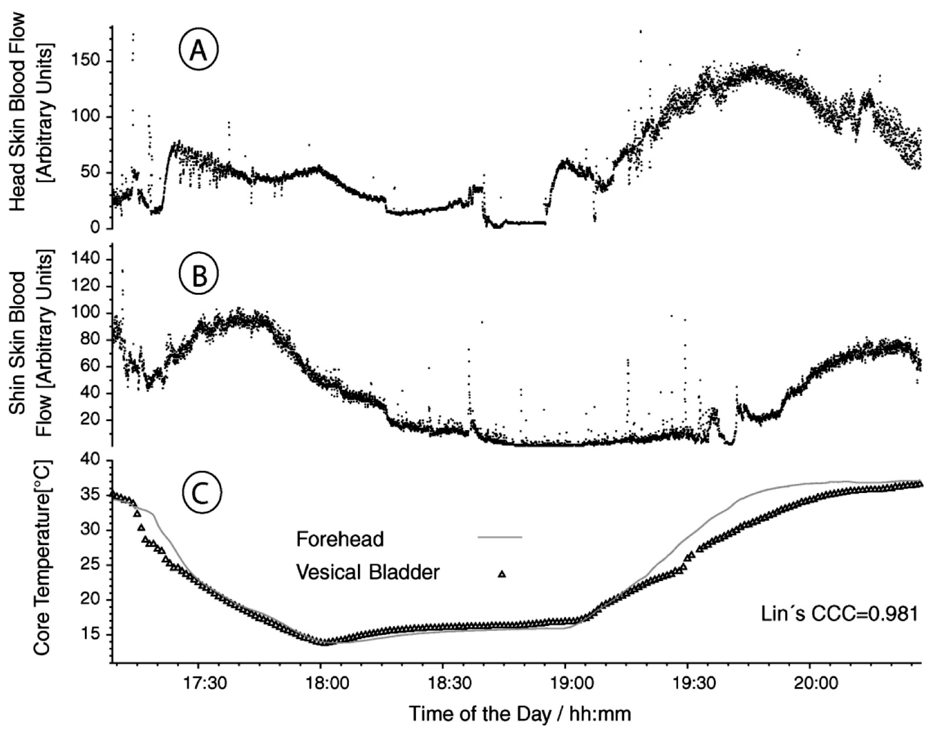
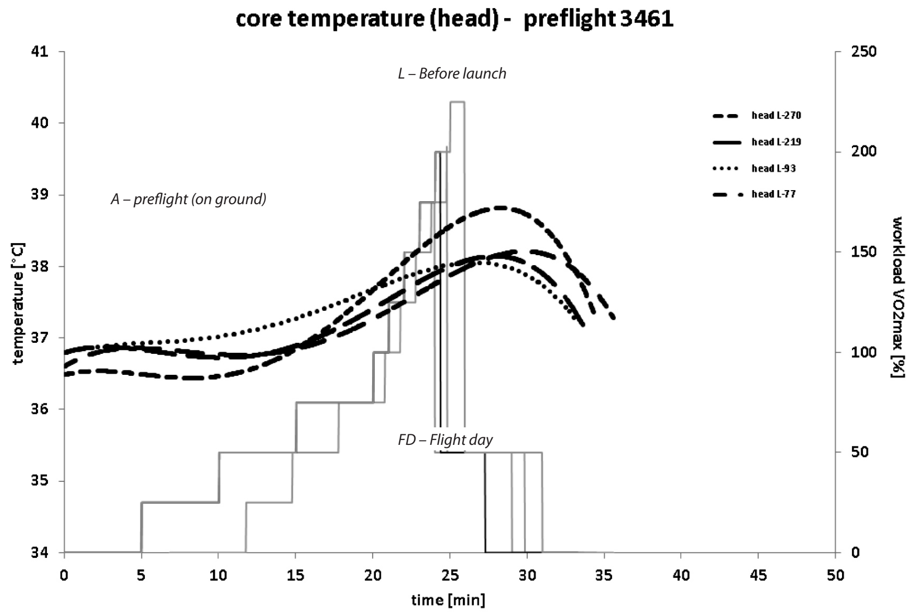
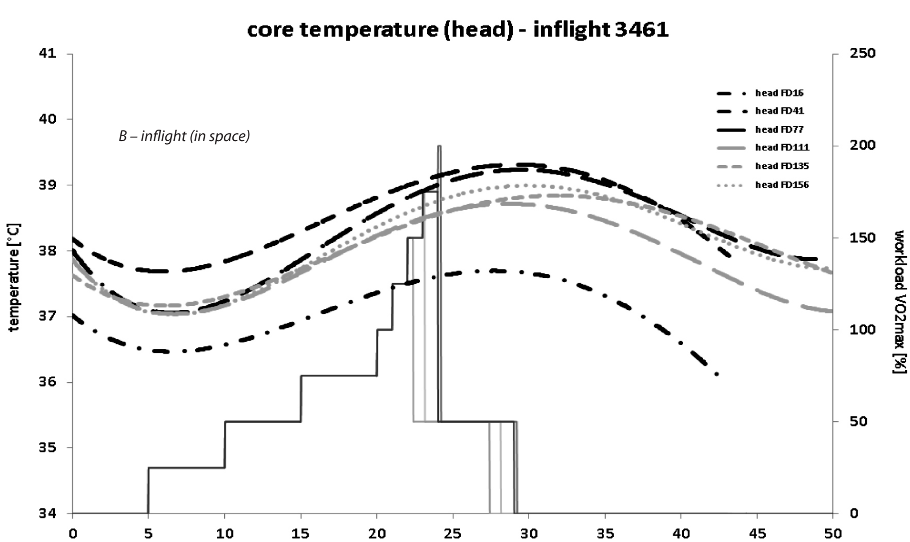


Figure 3: Core temperature changes (vesical and Double Sensor temperature) and skin blood perfusion changes during operations in a clinical setting under deep hypothermic conditions. (Adapted from Opatz et al. 2010).

Study 4

Figure 4 A–C shows core temperature changes during an exercise test before, during and after a long-term spaceflight in a single, male astronaut (preliminary data). The core temperatures were only measured at the head (front) with the Double Sensor technology. It was found i)a large scatter in core temperature profiles inflight and ii) prolonged decreases of core temperatures in the recovery phase after the exercise was finished.


core temperature (head) - preflight 3461
L – Before launch
A – preflight (on ground)
FD – Flight day
head L-270
head L-219
head L-93
head L-77
temperature [°C]
workload VO2max [%]
time [min]


core temperature (head) - inflight 3461
B – inflight (in space)
head FD16
head FD41
head FD77
head FD111
head FD135
head FD156
temperature [°C]
workload VO2max [%]
time [min]

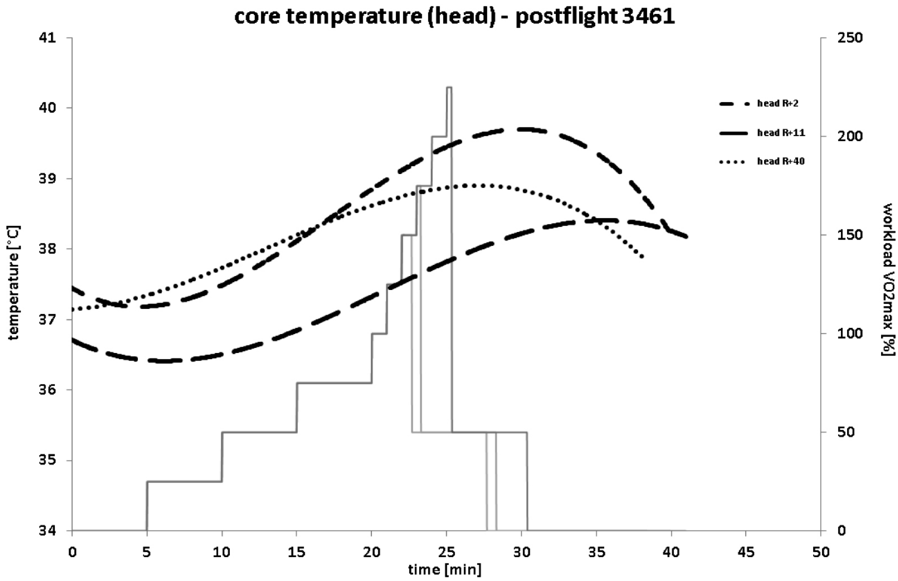


Figure 4A–C: Preliminary core temperature changes measured at the head during an exercise test during a long-term spaceflight preflight (A), inflight (B), and postflight (C) in space in a single astronaut (changing workloads during the different tests are indicated by step profiles, each step 25 Watt).

DISCUSSION

In particular study 1 revealed that for strenuous physical activity during heat exposure, the device under test appears to be a reasonably reliable method to assess core temperature and therefore might be useful as well in occupations in which individuals are exposed to thermally challenging environments. However, it is clear that this new sensor system cannot completely replace rectal or radio pill core temperature recordings under all circumstances. In the study reported here the Double Sensor system was integrated into a helmet system. As outlined and discussed earlier, lateral heat loss can also occur from the sensor, especially in cold environmental conditions below 0°C (Gunga et al., 2008). Therefore, it remains to be investigated whether this concept can be used reliably in other outdoor environmental conditions as well.

In the course of the study 2 it could be observed that the individual differences between the two techniques varied between −0.72 and +0.55°C (Gunga et al., 2009). The reasons for the differences are currently unclear. Nonetheless, when temperature data were approximated by cosinor analysis in order to compare circadian rhythm profiles between methods, it was observed that there were no significant differences between mesor, amplitude and acrophase ($P > 0.310$). It was therefore concluded that the Double Sensor technology in this specific setting is presently obviously not accurate enough for performing single individual core temperature measurements under resting conditions at normal ambient room temperature, but it seems to be a valid, non-invasive alternative for monitoring circadian rhythm profiles.

The study by Opatz et al. (2010) revealed that even during deep hypothermia (core temperature ~14–16°C) the Double Sensor technology might be applicable in such a clinical setting. Furthermore, it could be shown that heat flux measurement – as one would expect - are closely linked to skin perfusion changes as indicated by concomitantly performed near infrared spectroscopy measurements (Opatz et al., 2010). This special topic, the link between skin blood flow and heat flux measurements, has definitely to be examined in a larger group of deep hypothermic patients. Such kind of research is currently on-going and it has to be tested whether this kind of method might also applicable in the field, i.e. for example on site non-invasive core temperature measurement at the forehead in avalanche victims which, indeed, would be very helpful for a rescue team operating in the field. Finally, in this context it is interesting to note, that recently other researchers could confirm our first results on the applicability of the Double Sensor in a clinical setting to monitor peri- and post-operative core temperature in a clinical study as well (Kimberger et al., 2009).

The preliminary data of the case report in study 4 indicates that obviously under micro-g conditions heat exchange between the human body and the environment is altered in space. Especially, the time span to decrease core temperature after exercise in the recovery phase seems to be prolonged in comparison to pre- and post-flight measurements. However, it is too early to draw any definite further conclusion. The full set of experiments has to evaluated, i.e. 10 astronauts are anticipated to conduct the studies during long-term missions (6 months) to ISS until the end of 2012.

CONCLUSION

In general, the new developed heat flux sensor ("Double Sensor") seems to be a new reliable method of assessing core temperature changes under different environmental and clinical conditions, and an especially promising method to determine non-invasively circadian core temperature profiles for chronobiological research.

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PROTECTION FROM COSMIC RADIATION IN LONG-TERM MANNED SPACEFLIGHTS

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ABSTRACT

Current space programs are shifting toward planetary exploration and in particular towards human missions to the moon and Mars. Space radiation, comprised of energetic protons and heavy nuclei, has been shown to produce distinct biological damage compared to radiation on Earth, leading to large uncertainties regarding the projection of health risks. Even if uncertainties in risk assessment are reduced in the next few years, there is little doubt that appropriate countermeasures will have to be taken to reduce the exposure or the biological damage produced by cosmic radiation. In addition, it is necessary to provide effective countermeasures against solar particle events which can have acute, even life threatening effects on inadequately protected crews. Unfortunately, passive (bulk) shielding is currently unable to provide adequate protection because cosmic rays have very high energy and nuclear fragmentation in the absorbers produce light fragments. Material science could provide new materials with better shielding properties for space radiation. Active (magnetic) shielding could be an interesting alternative pending technical improvements.

Keywords: *spaceflight, space radiation, protection*

ZAŠČITA PRED KOZMIČNIM SEVANJEM MED DOLGOTRAJNIMI ČLOVEŠKIMI POLETI V VESOLJE

IZVLEČEK

Aktualni vesoljski programi se dandanes osredotočajo predvsem na raziskovanje planetov in še posebej na človeške misije na Luno in Mars. Sevanje v vesolju, ki vključuje energijske protone in težka jedra, ustvarja izrazito biološko škodo v primerjavi s sevanjem na Zemlji, kar pomeni, da obstaja kar nekaj nejasnosti glede dokazov o tveganju za zdravje. Četudi se bodo te nejasnosti na področju ocene tveganj v naslednjih letih lahko zmanjšale, obstaja dvom, da bo potrebno izvajati ustrezne protiukrepe, ki bi pomagali zmanjšati izpostavljenost oziroma biološko škodo, ki jo povzroča kozmično sevanje. Poleg tega je prav tako potrebno omogočiti učinkovite protiukrepe na področju sončnih delcev, ki imajo lahko akutne oziroma celo smrtno nevarne učinke na nezadostno zaščitene ekipe astronavtov. Na žalost pasivna (obsežna) zaščita ne omogoča zadostnega varovanja, saj imajo kozmični žarki zelo visoko energijo, nuklearna fragmentacija v blažilnikih pa ustvarja svetlobne fragmente. Stvarna znanost bi lahko ponudila nove materiale z boljšimi zaščitnimi lastnostmi, ki so potrebne na področju sevanja v vesolju. Aktivna (magnetna) zaščita bi lahko predstavljala zanimivo alternativo, ki še čaka na tehnične izboljšave.

Ključne besede: *poleti v vesolje, sevanje v vesolju, zaščita*

INTRODUCTION

When human space exploration started over 40 years ago, it was soon recognized that space radiation represented a potential hazard for the crews (Maalouf, Durante & Foray, 2011). As a matter of fact, astronauts are exposed to galactic cosmic radiation (GCR) in space at a dose rate substantially higher than on Earth. Current plans for manned space exploration require longer and longer sojourns of astronauts in space (Figure 1). For long-term interplanetary missions such as a Mars mission, doses can exceed maximum recommended limits (Cucinotta & Durante, 2006).

In deep space human beings are exposed to protons and high energy and charge (HZE) ions in the GCR, along with secondary radiation including neutrons and recoil nuclei produced by nuclear reactions in spacecraft or tissue. Practically all nuclides are present in the GCR, although elements heavier than nickel (Z=28) are so rare that they do not provide a significant risk to crews. The energy spectrum of the GCR peaks near 1 GeV/nucleon, and consequently these particles are so penetrating that shielding can only partially reduce the doses absorbed by the crew.

Figure 1: Concept of a future Mars base. Current plans of space agencies (NASA, ESA, China, and Russia) put emphasis on planetary exploration. In a permanent Mars base, crews will have access to a greenhouse for growing their own fresh vegetables. Cosmic radiation is a major hindrance to this plan, both because of the exposure during the long interplanetary travel, and of the high background rate on the planet's surface (about 100-fold the Earth's background). Image credit: NASA Glenn Research Center ImageNet.

In traveling to Mars, every cell nucleus within an astronaut would be traversed by a proton or secondary electron every few days, and an HZE ion about once per month (Cucinotta & Durante, 2006). Whole body doses of 1–2 mSv/day accumulate in interplanetary space and approximately half this value on planetary surfaces. The large ionization power of HZE ions makes them the major contributor to the risk in spite of their lower cell nucleus hit frequency than protons (Fig. 2). Iron alone (Z=26) provides approximately the same dose equivalent of the protons in deep space.

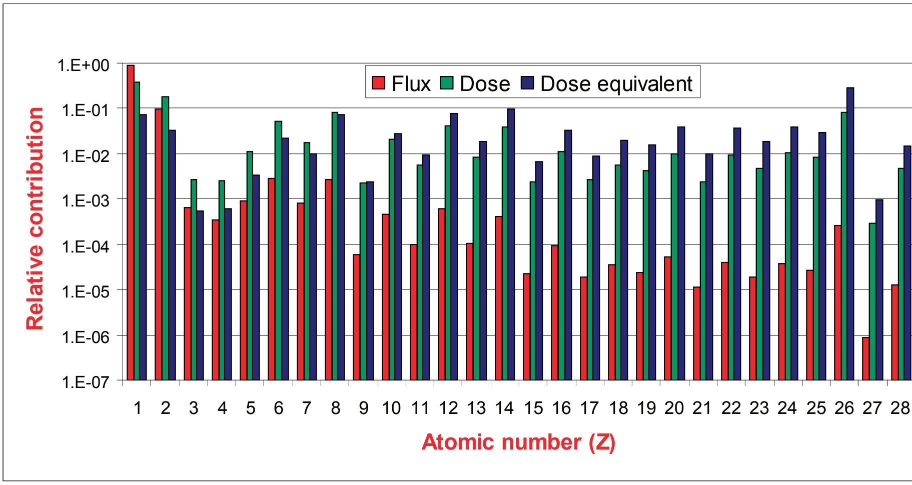

Figure 2: Relative contribution of different ions to flux, dose, and dose equivalent from galactic cosmic radiation. Nuclei heavier than nickel are very rare. Calculation by HZETRN kindly provided by Dr. Frank Cucinotta and Dr. Cay Zeitlin.

Major uncertainties on space radiation risk estimates (Durante & Cucinotta, 2008) are associated with the poor knowledge regarding the biological effects of HZE particles, with a smaller contribution coming from the characterization of space radiation field and its primary interactions (Fig. 3). The goal of the NASA Space Radiation Health Program is to reduce these uncertainties to less than ±50% within the year 2023 (NASA, 1998). This ambitious goal can be fulfilled only by an international co-operative effort in the field of radiation physics, biology, and medicine.

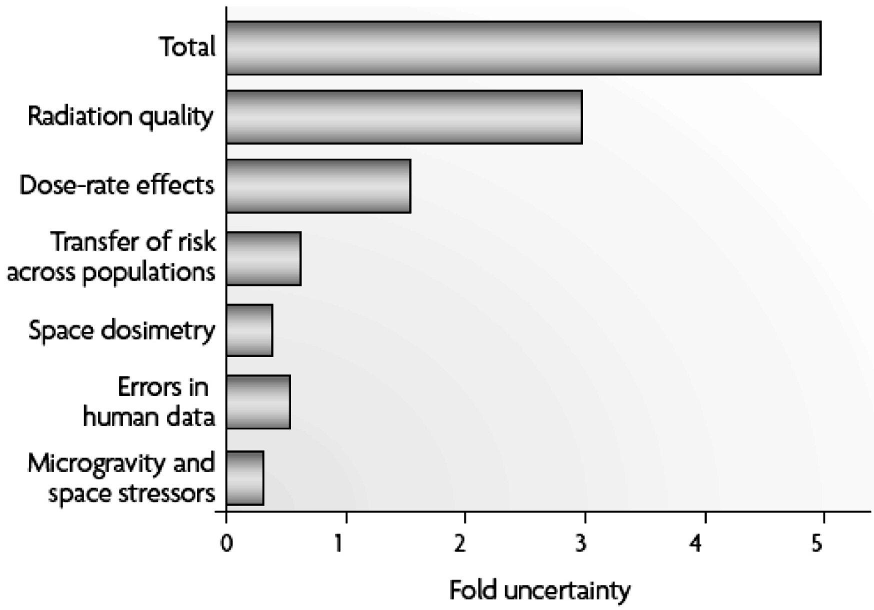

Figure 3: Estimates of uncertainties in projecting cancer risks for space and terrestrial exposures. Several factors such as radiation quality effects, space physics, and microgravity do not contribute on Earth and lead to large increases in risk projections. Predicting risks to individuals is difficult as there are very few quantitative measures of individual sensitivity. Only a select few individuals enjoy space travel and projecting risks for a few selected individuals rather than populations will be of utmost importance for space missions to Mars. The extrapolation from experimental models to humans is perhaps the greatest challenge to cancer risk assessments. Plot ***form*** *ref.[3].*

Even if risk of uncertainties will be reduced in the next few years, there is little doubt that appropriate countermeasures have to be taken to reduce the exposure or the biological damage produced by radiation. In all basic radioprotection textbooks, it is clearly stated that there are three means to reduce exposure to ionizing radiation: increasing the distance from the radiation source, reducing the exposure time, and by shielding. Distance is not an issue in space, being space radiation isotropic. Time in space should be increased rather than decreased according to the plans of exploration and colonization. Shielding remains the only feasible countermeasure. Other strategies can be effective in reducing exposure or the effects of irradiation in space. These strategies include the choice of an appropriate flight time, i.e. mission planning and ability to predict solar particle events (SPE); the administration of drugs or dietary supplements to reduce the effects of radiation and a crew selection based on genetic screening (Durante & Cucinotta, 2008).

In this paper, we will concentrate on the impact of shielding on space radiation protection. Recent reviews on risk and countermeasures are found in ref. (Cucinotta & Durante, 2006) and (Durante & Cucinotta, 2008).

SHIELDING

For terrestrial radiation workers, additional protection against radiation exposure is usually provided through increased shielding. Unfortunately, shielding in space is problematic, especially when GCR is considered. High-energy radiation is very penetrating: a thin or moderate shielding is generally efficient in reducing the equivalent dose, but as the thickness increases, shield effectiveness drops. This is the result of the production of a large number of secondary particles including neutrons caused by nuclear interactions of the GCR with the shield. These particles have generally lower energy, but can have higher quality factors than incident cosmic primary particle.

NASA is using the analytical code HZETRN coupled with NUCFRG2 (Wilson et al., 1995), developed at the Langley Research Centre, to estimate GCR doses in different shielding configurations for the International Space Station (ISS) and Mars mission. The HZETRN code calculates the straight-ahead particle transport along 512 different rays converging on the point x, and provides as output the energy spectra of the charged particles in the point x within the ISS module or the astronaut's body.

The relative attenuation of the dose equivalent H(x) produced by GCR or trapped protons at solar minimum as a function of the thickness x (in g/cm^2) of different shield materials as calculated by HZETRN is given in Figure 4 (Cucinotta, Wilson, Williams & Dicello, 2000), assuming one year exposure. Low-Z shields, including water, provide satisfactory protection for trapped protons in low-Earth orbit (LEO). However, for GCR the shield effectiveness increases slowly for thickness exceeding 10 g/cm^2. Even very thick shields of polyethylene are unable to reduce the GCR dose below approximately 50% of the unshielded value.

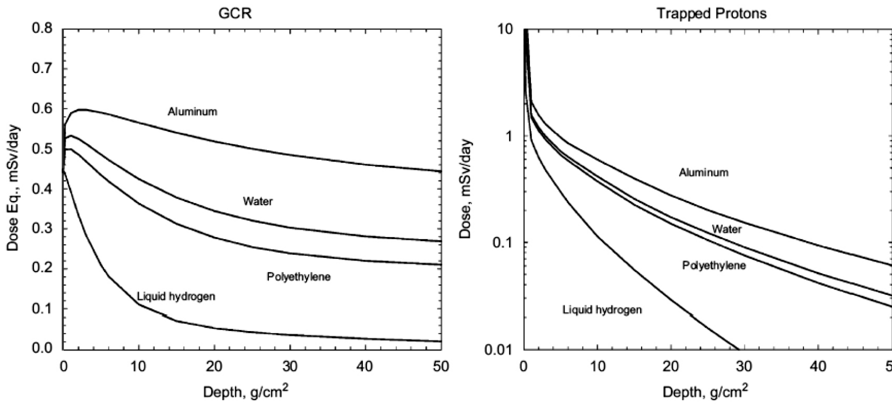

Figure 4: Dose calculations in dependence of shielding thickness for different shielding materials in the ISS orbit for solar minimum conditions. Left, galactic cosmic radiation; right, trapped protons in LEO. Shielding is effective for the low-energy trapped protons, while it is far less useful for GCR, especially when heavy materials are used. Calculations by NASA using HZETRN code, plots from reference [6].

Liquid hydrogen appears to have the maximum performance as shield material. Unfortunately, hydrogen is not a practical shield material, being a low temperature liquid. Hydrogen storage in graphite nanofibers or lithium hydride (6LiH) may have a large impact in space shield design. So far, it appears that polyethylene could be a good compromise.

Simulation of space radiation at accelerators represents a useful tool for shielding material testing. Heavy ions at energies >1 GeV/n represent in fact a reasonable proxy of the heavy-ion component in the GCR (Guetersloh et al., 2006). The attenuation in doses achieved with thin shields is in fact qualitatively and quantitatively similar to what would be expected in space, and different materials can be easily compared for their effectiveness in shielding HZE particles. The large database collected by the Lawrence Berkeley Laboratory group is summarized in reference (Zeitlin, Guetersloh, Heilbronn & Miller, 2005). Figure 5 shows recent measurements of the Bragg curves of 1 GeV/n Fe-ions in different materials: polyethylene, aluminum, Kevlar and Nextel (Lobascio et al., 2008). These latter two materials are widely used to protect human space infrastructures from meteoroids and debris impacts in low-Earth orbit, both for rigid pressurized modules (such as Columbus on the ISS) and in inflatable space modules. The initial decrease in dose is caused by projectile fragmentation, of which the cross section per unit target mass AT is approximately proportional to AT-1/3. The percentage dose reduction dD per unit thickness (in g/cm^2) can be calculated from the initial slope of the Bragg curve by extrapolation at zero depth, and this value is close to that expected for galactic HZE nuclei in space (Guetersloh et al., 2006). The data show that: i) the initial decrease in dose is more pronounced for HDPE, followed by Kevlar, Nextel, and finally Al; ii) the minimum dose before the Bragg peak is the lowest for HDPE and the highest for Al; and iii) the Bragg peak is found first in HDPE, then in Kevlar, Nextel and finally in Al (Lobascio et al., 2008).

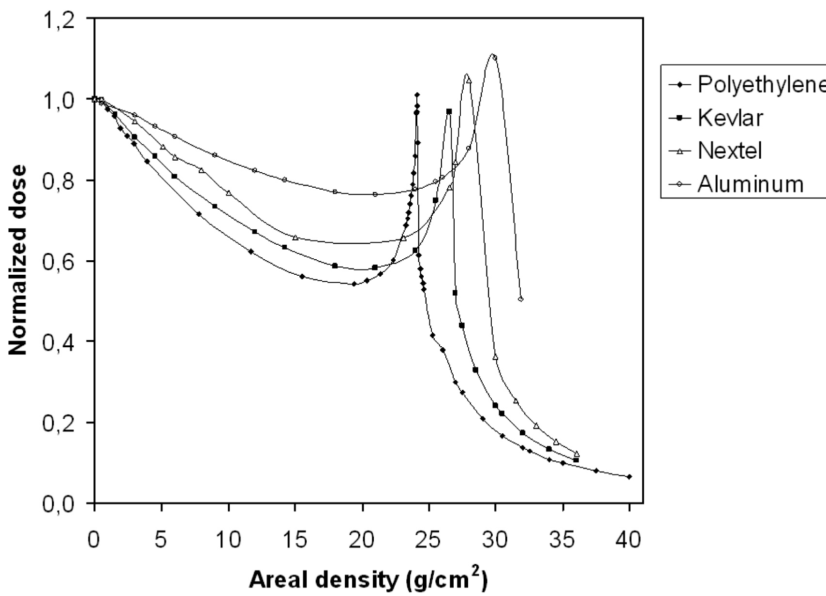

Figure 5: Bragg curves of 1 GeV/n ^{56}Fe-ions measured in polyethylene, Kevlar, Nextel, and aluminum. The beam was accelerated at the NASA Space Radiation Laboratory at the Brookhaven National Laboratory (Upton, NY, USA). Dose was measured by a egg chamber and is normalized to the value measured without shielding. Lines connect the data points. Data from ref. [9].

Accelerator-based tests are useful tools for comparing different shielding configurations to be used in space, and simulations suggest that using heavy ions at energies higher than 1 GeV/n will provide better quantitative simulations of the galactic heavy nuclei [7]. These very high energies will be available in the FAIR facility currently under construction at GSI in Germany (Durante, Reitz & Angerer, 2010).

Based on the results of tests and simulations, NASA has added polyethylene slabs in the crew sleeping quarters on ISS (Figure 6). Dose measurements were consistent with the expected dose reduction of around 20% in the shielded area (Shavers et al., 2004). In-flight tests are also under way on the ISS using the detector ALTEINO and shield blocks in polyethylene, Kevlar and Nextel (Figure 7) (Casolino et al., 2007). Research in the field of shielding is likely to have quick applications on ISS and for the mission to the moon.

Figure 6: Polyethylene panels installed in the crew sleeping quarters of ISS. Picture from NASA, Office of Biological and Physical Research.

Figure 7: The detector ALTEINO on the ISS during the ENEIDE mission in 2005. On top of the active detector it is visible a blue bag containing polyethylene, Kevlar, and Nextel shield blocks, and passive TLD detectors (ESCHILO tiles). Photo from Spillantini et al. (2007), courtesy of Dr. Marco Casolino (INFN, Rome, Italy).

ACTIVE SHIELDING

An attractive alternative to passive, bulk material shielding is the use of electromagnetic fields to deflect the charged particles from the spacecraft target (Figure 8). Several investigations started in the 60's using 4 different approaches (Townsend, 2001):

I. electrostatic fields; II. plasma shielding; III. confined magnetic fields;
IV. unconfined magnetic fields.

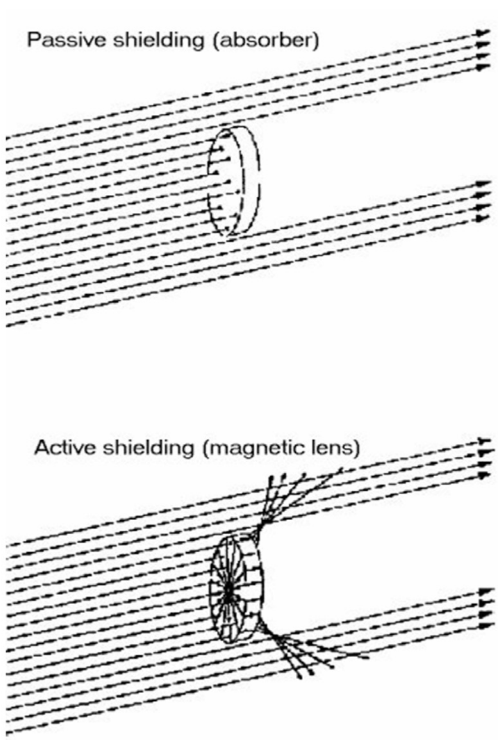

Figure 8: Protection from a directional solar particle event provided by passive shielding or defocussing magnetic lens [14]. For an equivalent Al absorber of 3,350 kg (upper part) the mass of the magnetic lens is below 1,100 kg (700 kg with 3 coils; 900 kg with 4 coils). Besides, in the passive shielding configuration, secondary fragments are unavoidably transmitted through the absorber. Image courtesy of Dr. P. Spillantini (Wilson et al. (1995)).

Most of the studies were dealing with active shielding on the shield against electrons and protons, especially in case of SPE. Active shielding against HZE particles from GCR is practically impossible by electrostatic fields. In fact, electrostatic potentials needed to deflect swift heavy ions from the GCR should be enormous, and this limitation also applies to plasma shielding that deflects positively charged particles by the electric field. Confined magnetic fields involve the use of concentric spheres and superconducting wires to obtain a strong magnetic field in a restricted volume surrounding the spacecraft. This configuration can be effective for protons up to 200 MeV, but is almost ineffective against GCR.

Unconfined magnetic field configurations typically involve a cylindrical or toroidal-shaped spacecraft having a dipole-like magnetic field, generated by an electric current through coils or the spacecraft skin. Since the Earth's magnetic field is clearly a very effective shield for solar and galactic radiation, some protection would be expected from an unconfined magnetic field against both SPE and GCR.

Protection by magnetic lenses from solar protons would be relatively easy in case of directional SPEs. However, detailed knowledge of the angular distribution of the SPE is very difficult to achieve. A non-directional active shield would be preferable, especially since it might protect against the isotropic GCR component. A solenoidal field of intensity around 2 T in a 1 m sheath around the module may provide good protection against most of the SPE, but poor protection against GCR (Spillantini et al., 2007). Perhaps the toroidal configuration has some advantages for GCR shielding, because the magnetic field reaches its maximum intensity in the internal volume, where magnetic forces can be better supported, and has smaller intensity in the outer part of the system where the large radius would require heavy structures to support the magnetic pressure of a very strong field.

As yet, magnetic shelters do not appear to be feasible for space radioprotection. However, technological progress in the field of high-temperature superconductors may provide a large impact in this field.

CONCLUSIONS

Passive or active shielding appear the best methods to protect crews of long-term space missions and humans living in the space (Durante & Cucinotta, 2011). Such countermeasures may not be necessary for a lunar base, but will likely be needed for the Mars mission, and most definitely for exploring Jupiter or Saturn's moon Titan or the nearby satellites (Durante & Cucinotta, 2008). Shielding with light, hydrogen-rich materials may substantially reduce the equivalent dose in space, but it is clear that more research in the radiobiology of heavy ions is needed to fully solve the problem. In fact, as shown in Figure 9, the shielding needed to reduce the risk to an acceptable level is controversial, because the uncertainty of the risk estimates is too high. Current radiobiology research programs sponsored by NASA at the Brookhaven National Laboratory

(USA) and by ESA at GSI (Germany) should provide the necessary knowledge for safe colonization of the Solar system.

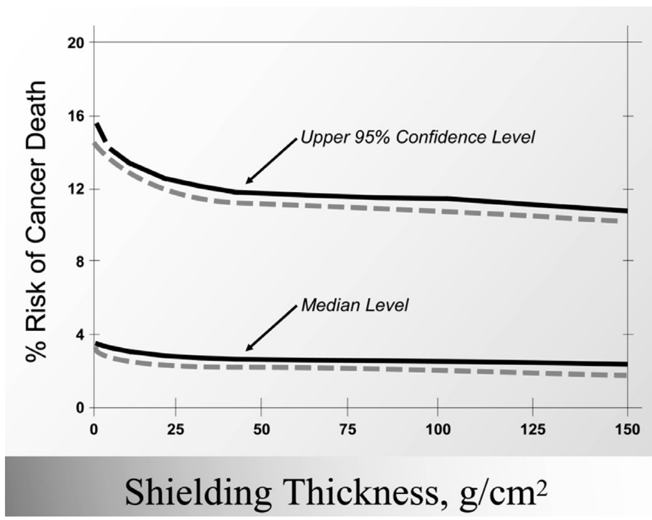

Figure 9: Cancer risk for a mission to Mars as a function of the mass thickness of shielding materials, after considering the tissue shielding of the human body. Black and red lines represent water and aluminium shield, respectively. Lower curves are median estimates, and upper curves provide the upper 95% confidence limits. This calculation shows that even very heavy shields will not be able to reduce the risk by a large factor, and the uncertainty on the risk makes it difficult to plan the shielding needed for the mission. Plot Cucinotta et al. (2000).

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PLANT GROWTH IN MICROGRAVITY FOR BLSS: GENERAL ISSUES AND THE ITALIAN CONTRIBUTION

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ABSTRACT

Plants are among the key organisms in Bioregenerative Life Support Systems (BLSS) in Space because they have a role in the regeneration of resources and in the psychological support of the crew. The design of an efficient BLSS cannot be irrespective of the profound knowledge of the functioning of the vegetal systems under the effect of Space factors. From an evolutionary perspective, reduced gravity can be considered one of the factors driving the evolution of plants in Space.

In this paper, we outline the need for plant-based BLSS to sustain exploratory-class manned missions in Space. After some evolutionary considerations about future plant development in Space, we also report a synthesis of the results of case studies performed by Italian research groups aiming to understand the effects of simulated or real microgravity on various aspects of plant growth and reproduction. We conclude by emphasizing how plant research in Space should address both the improvement of the knowledge of basic biological processes and the development of new agro-technologies. Efforts to engage in a multidisciplinary approach to understand the effects of Space factors on plant growth are needed considering that such factors affect the *biological systems contemporarily at molecular, biochemical, morphostructural and physiological levels.*

Keywords: *agrotechnology, altered gravity, plant anatomy, plant evolution, plant space biology, species selection*

RAST RASTLIN V MIKROGRAVITACIJSKEM OBMOČJU ZA BLSS: SPLOŠNA VPRAŠANJA IN PRISPEVEK ITALIJANSKIH RAZISKOVALCEV

IZVLEČEK

Rastline spadajo med ključne organizme v sistemih za bioregenerativno ohranjanje življenjskih funkcij (BLSS) v vesolju, saj skrbijo za regeneracijo virov in za psihološko podporo posadki. Oblikovanje učinkovitega sistema BLSS ne sme spregledati natančnega znanja o delovanju vegetativnih sistemov pod vplivom dejavnikov v vesolju. Iz evolucijske perspektive se zmanjšana gravitacija lahko upošteva kot eden izmed dejavnikov, ki vodijo evolucijo rastlin v vesolju.

V tem prispevku predstavljamo potrebo po sistemu BLSS, ki bi temeljil na rastlinah, da bi ohranili raziskovalne misije v vesolju. Po nekaterih evolucijskih obravnavah prihodnjega razvoja rastlin v vesolju prav tako pričamo o sintezi rezultatov študij primerov, ki so jih izvedle italijanske raziskovalne skupine, ki so želele razumeti učinke simulirane ali resnične mikrogravitacije na različne vidike rasti in razmnoževanja rastlin. Naš prispevek zaključimo s poudarkom na tem, kako bi raziskovanje rastlin v vesolju moralo upoštevati tako izboljšanje znanja o osnovnih bioloških procesih kot razvoj novih agrotehnologij. Potrebno bo vložiti veliko truda v multidisciplinarni pristop k razumevanju učinkov vesoljskih dejavnikov na rast rastlin, saj je potrebno upoštevati, da ti dejavniki vplivajo na biološke sisteme že na molekularni, biokemični, morfološko-strukturalni in fiziološki ravni.

Ključne besede: *agrotehnologija, spremenjena gravitacija, anatomija rastlin, evolucija rastlin, vesoljska biologija rastlin, vrste, selekcija*

PLANT-BASED BIOREGENERATIVE LIFE SUPPORT SYSTEMS (BLSS)

Plants are key organisms on Earth since they provide us with oxygen and occupy the first trophic level. It is therefore natural to ask why plants should be unnecessary in any environment other than Earth. The use of plants to support life in Space is not a novelty, and many studies have been carried out in the second half of the twentieth century with extensive ground-based demonstrations throughout the world (e.g. Myers, 1954; Gitelson et al., 1989; Gitelson, 1992; Tako et al., 2007; Wheeler, 2010). Such widespread interest arises from the objectives of the international Space exploration programs which include manned long duration missions. The permanence of humans in Space for long periods of space travel, onboard orbital platforms or on Lunar and Martian stations depends upon the possibility of overcoming challenges in engineering and medical research as well as in plant space biology and agro-technology (De Micco, Aronne, Colla, Fortezza, & De Pascale, 2009). Indeed, the possibility of creating an Earth-like environment where resources can be regenerated has an impact not only on the economy of space exploration, because it minimizes the need for external supply of resources, but also on the well-being of astronauts in Space. It is well accepted that plants may play a key role for the regeneration of resources in BLSS because they accomplish four main functions: a) regeneration of the atmosphere in the pressurized modules through the depletion of CO_2 and the release of O_2 by photosynthesis, b) recycling the liquid and solid wastes of the crew, c) recovering water through transpiration and d) production of edible biomass to reintegrate the astronauts' diet with fresh food (Wheeler et al., 1996). Although algae and bacteria could be used in bioregenerative systems, higher plants could certainly provide tastier and more attractive fresh food. Moreover, higher plants in Space have been demonstrated to also play a role in mitigating the stress of isolation suffered by astronauts (Williams, 2002). For these reasons there is an interest in having higher plants in closed or semi-closed support systems (also when they are designed as modular systems where chemical, physical and biological subsystems based on microorganisms are integrated). These compartmentalized systems are intended to reproduce the natural cycles occurring on Earth in a technological and reduced scale characterized by high robustness and safety (Lasseur et al., 2010).

Considering that there is common belief that plants can survive in Space, at the present the issue is to optimize plant growth to maximize the production of edible biomass, oxygen, clean water and the removal of carbon dioxide and wastes (Galston, 1992). However, ground-based experimentation cannot be irrespective of the possible growth reactions of plants due to the harsh conditions of Space characterized by different levels of environmental factors including pressure, radiation and gravity (De Micco, Arena, Pignalosa & Durante, 2011; Wheeler, Wehkamp, Stasiak, Dixon & Rygalov, 2011).

WHICH FACTORS PRIME EVOLUTION IN SPACE?

Every organism is ideally designed to fulfill precise metabolic and physiological processes in specific environmental conditions. Focusing on higher plants, there is evidence of how specific traits arose to fulfill specific needs dictated by changing environmental factors: for example, the development of complex vascular systems consisting of specialized cells with lignified walls is a means to guarantee water transport and mechanical support in organisms leaving the water environment to colonize lands (Raven, 1977). During the evolution of higher plants, the key moment when organisms moved away from the aquatic environment to colonize the land was obviously marked by the need to solve the conflict between water retention and the metabolic requirement to exchange gases with the atmosphere to accomplish photosynthesis (Niklas, 1986). Moreover, there is also evidence that many other factors, including solar radiation and gravity, may have played a fundamental role in shaping the structure and function of higher plants (Graham, 1993; Bateman et al., 1998). In a simplified model aimed at explaining the variation of gravity and radiation during higher plant evolution on Earth, we might consider that gravity has increased (because of the lack of buoyancy balancing the gravity force during submersion in water) while radiation has decreased (due to the augmentation of atmospheric oxygen and the thickness of the ozone layer) (Graham, 1993; McGinley & Weis, 2009). In the further evolution of higher plants in Space, we might expect that the plants would face again environmental conditions similar to those of remote past times at least with regards to reduced gravity and increased radiation (De Micco et al., 2009). These new levels of gravity and radiation are known to cause alterations in various aspects of plant growth. Consequently, growth reactions of plants to such factors must be taken into account in the design of space greenhouses and in the choice of species and cultivars for BLSS.

MAIN TOPICS IN PLANT SPACE BIOLOGY AND THE ITALIAN CONTRIBUTION

For organisms well-adapted to live in a given environment, any changes in biotic and abiotic factors can be perceived as stress which will likely alter growth and reproduction. Within this scenario, Space can be considered a novel environment where plants are subjected to multiple stressors which exert direct or indirect effects on developmental processes (De Micco et al., 2009). Among those factors already present on Earth, the different perception of gravity can be considered one of the main constraints to organism development in Space. Reduced levels of gravity are known to affect many processes including gene expression, cell division (affecting both vegetative growth and reproduction), gravisensing, vascular development and cell wall deposition (Brinckmann, 2007; De Micco, Aronne, Joseleau & Ruel, 2008; Paul et al., 2011).

Moreover, altered gravity can interfere with physical processes such as fluid-dynamics, thus affecting plant growth both directly (due to effects on gas diffusion) and indirectly (because of alteration of hardware functioning) (Musgrave & Kuang, 2003; Kitaya & Hirai, 2008; De Micco & Aronne, 2008a).

Over the last decades, several Italian research groups have been working on projects funded by the Italian Space Agency (ASI) and/or the European Space Agency (ESA) to address various issues of plant space biology. Three main ambitions have been pursued: a) the advancement of scientific knowledge about the effects of reduced gravity on specific biological processes, b) the choice of biological systems and species to integrate the astronauts' diet with fresh food produced onboard, and c) the development of new agro-technologies to support plant growth in Space. Experiments aiming to understand the effects of altered gravity on plant development were focused on specific processes during both vegetative growth and the reproductive cycle. Studies aimed at optimizing plant growth in Space were directed both at the identification of objective procedures for cultivar selection and to the preparation of cultivation protocols with a focus on soilless systems. (De Micco, Buonomo, Paradiso, De Pascale & Aronne, 2012; Paradiso, Buonomo, De Micco, Aronne, Palermo, Barbieri, De Pascale, 2012).

In the following paragraphs, the results from some experiments performed in simulated and real microgravity are summarized.

Studies on the effects of microgravity on seedling development.

Several experiments have been performed in Space or on Earth with the uni-axial clinostat to simulate weightlessness, albeit with the awareness that such a facility can simulate but not replicate real microgravity (Aronne et al., 2003). Most of these studies were aimed at investigating the possibility of producing sprouts in Space as highly nutritional "edible vegetal systems" that can be easily produced in few days, in a small physical volume and with low energy, to integrate fresh food into the diet of the crew (De Micco, Aronne & De Pascale, 2006a; De Micco, Aronne, Scala, Castagnolo & Fortezza, 2006b; De Micco & Aronne, 2008a, b). Although not being ideal candidates for BLSS, the production of sprouts would be desirable in Space because they are characterized by a low content of antinutritional compounds and a high content of proteins, vitamins, minerals, phenolics and other compounds having protective effects on the human body. Moreover, they can be considered "functional" foods because they seem to improve health and well-being while reducing the risk of human disease (Zieliński, Frias, Piskuła, Kozłowska & Vidal-Valverde, 2005). The choice of species might improve the beneficial effects of sprouts on the health of astronauts who are more exposed to microgravity-induced diseases such as osteoporosis and muscle atrophy. For instance, there is evidence that specific compounds absorbed through a soy-based diet can protect bones from osteoporosis (Taku, Melby, Nishi, Omori & Kurzer, 2011). Moreover, it has been proven that rats fed with soy protein isolate are less exposed to muscle atrophy when subjected to weightlessness (Tada & Yokogoshi, 2002).

Several experiments were carried out with the aim of studying the morpho-anatomical development of bean and soy seedlings under simulated microgravity (ASI project "Morphological and Physiological response of seedlings to a low-gravity environment") and in Space (ESA – SAYSOY project, Foton-M2 mission) (Aronne et al., 2003; De Micco & Aronne, 2008a, b). Specific attenion was paid to root gravitropism, vascular development, cell wall deposition and lignification, accumulation of phenolic compounds and starch metabolism (both in statoliths and in storage organelles). Observations by means of light, epi-fluorescence and transmission electron microscopy, combined with digital image analysis, allowed quantifying anatomical and cytological parameters. Experiments on bean germinating on the clinostat showed that prolonged clinorotation determines modifications during root development including a loss of orientation of the statocytes in the columella, a decrease in the starch content and changes in cell size in various regions of the root (Figure 1) (Aronne et al., 2003).

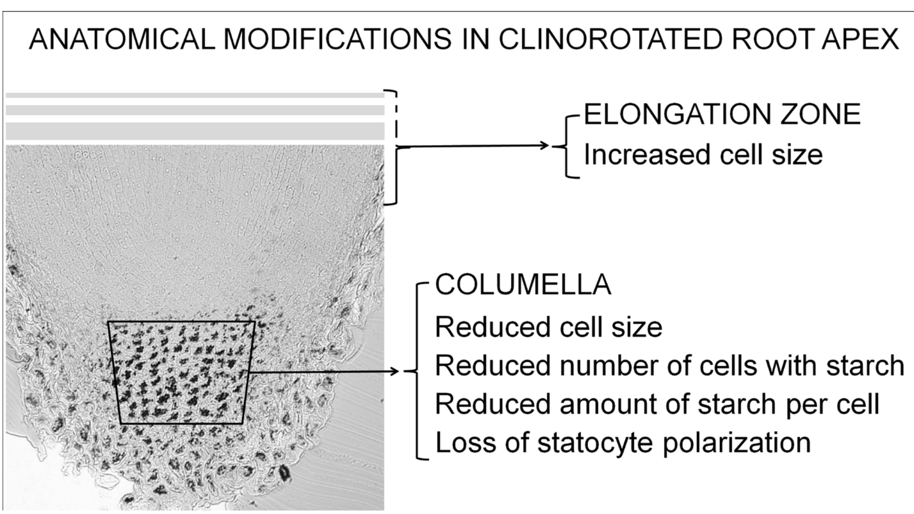

Figure 1: Graphic representation of the modifications happening in clinorotated roots of Phaseolus vulgaris L.

At the vascular level, perturbations have been found in soy seedlings developed both on Earth under clinorotation and in real microgravity in Space (De Micco & Aronne 2006a; De Micco et al., 2006a, 2008). At the ultrastructural level, alterations in the deposition of cellulose microfibrils were evidenced in the cell walls of soy seedlings growing in Space. These alterations are in agreement with the broadened view of the microtubule/microfibril paradigm which links the ordering principles of the deposition of cellulose microfibrils with the orientation of cytoskeleton microtubules. However, these perturbations were evident only in primary cell walls at early stages of development, while ordering principles seemed to be restored during the deposition of secondary wall layers (De Micco et al., 2008). The delay in the deposition of compact cell walls might be responsible for the delay in morphological development in Space and for the development of larger cells due to the lack of mechanical constraints ascribed to cell walls at the beginning of cell enlargement.

Morpho-anatomical modifications due to microgravity have been demonstrated to be dependent also on interactions with other environmental factors: for example, sub-optimal temperatures were responsible for more evident alterations of the morphological development in clinorotated soy seedlings (De Micco et al., 2006a). Such a sensitive interaction between gravity and other environmental factors, as well as other sources of variability (e.g. the use of different hardware, protocols, biological sources), might be responsible for the contrasting results often reported in the literature.

Studies on the effects of microgravity on pollen germination.

Several experiments have been performed to understand the effects of simulated microgravity on pollen germination and pollen tube development in many herbaceous and woody crops (ASI project "Morphological and Physiological response of seedlings to a low-gravity environment"). These experiments were characterized by a double approach: a) to evaluate the possible influence of microgravity-induced alterations on the completion of the reproductive cycle and b) to investigate the possibility of applying methods for gametophyte selection in Space (Figure 2). Results of these experiments showed that reduced gravity can alter nuclei formation and migration during pollen tube development; moreover, the lack of coordination between the formation of callose plugs and nuclei migration might impede nuclei to reach tube tip thus preventing fertilization. These modifications might be the consequence of alterations of cytoskeleton organization. However, it is clear that these perturbations were strictly dependent on the species (De Micco, Scala, & Aronne, 2006c, d).

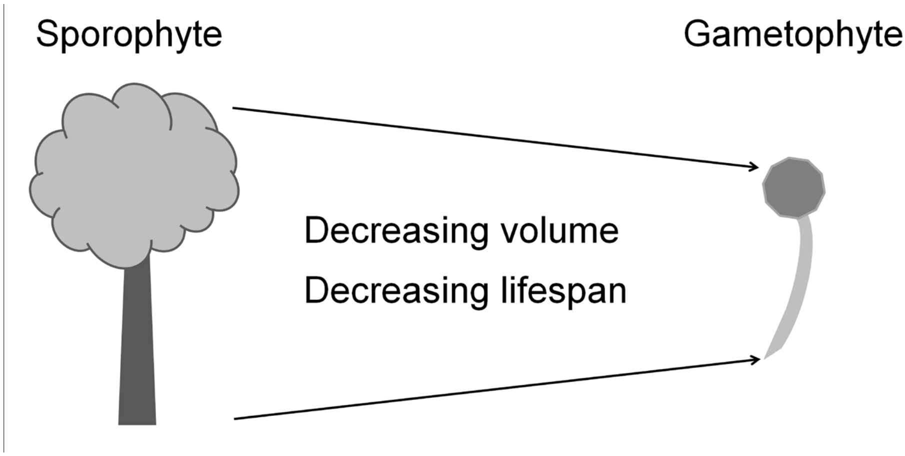

Figure 2: Sporophyte (diploid mother plant) versus male gametophyte (aploid germinated pollen): during the evolution of higher plants, gametophyte has diminished in terms of both size and longevity compared to the sporophytic generation. The selection among genotypes can be done by screening the pollen produced by mother plants (male gametophyte selection) with advantages in terms of time and volume which are two main constraints in Space.

FURTHER PERSPECTIVES

The leitmotiv of the studies on the response of biological systems to microgravity mentioned in this paper was the focus on those biological processes that not only affect the normal course of plant growth, but have also an importance on the properties of fresh food. For instance, vascular development and lignification processes affect the palatability of the fresh food due to their influence on tissue softness. On the other hand, changes in the content of phenolics, which is a common phenomenon in stressful conditions such as those experienced in Space or Space-like environments (Figure 3), affect the nutritional value of seedlings because such compounds have antioxidant properties and some of them confer a bitter taste to the food. Results from these studies open up interesting perspectives in the vision of space explorations in which the astronauts' diet can be supported with fresh food produced onboard in BLSS or in simple automatic hardware, such as the SAYSOY hardware designed and built within an ESA-Education Project (SAYSOY – Space Apparatus to Yield SOYsprouts) (De Micco & Aronne, 2008b).

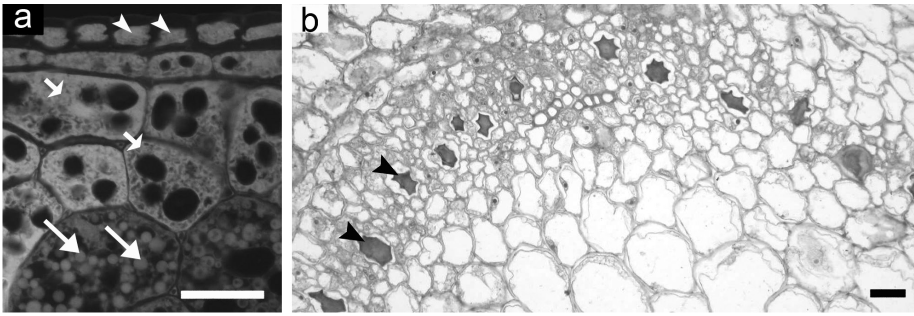

Figure 3: Epi-fluorescence (a) and light (b) microscopy views of soybean cotyledons (a) and hypocotyl (b) grown in Space. Phenolic compounds are present in epidermal cells (a, arrowheads), subepidermal cell layers (a, short arrows) and in parenchyma cells (a, long arrows) of cotyledons. Phenolic bodies are around the stele in hypocotyl (b, arrowheads). Microgravity determines increased content of phenolic compounds in both cotyledons and hypocotyls (De Micco & Aronne, 2008a). Bars = 50 microns.

Further studies aimed at fulfilling the requirements for the productivity and quality of biological systems subjected to Space factors are needed to produce the ideal BLSS which can be considered a stable Space platform where all vegetal organism needs are supplied with optimal water, light, temperature and microgravity ranges, according to the space environmental conditions. In the future perspectives, the study of the effect of microgravity on photosynthesis is needed because it is a key process for the building of an efficient BLSS. Although deriving from limited spaceflight experiments, information on the effects of microgravity on photosynthesis suggest that photosynthetic machinery can be altered at different steps (Stutte, Monje, Goins & Tripathy, 2005). Studies conducted onboard the International Space Station on wheat have demonstrated that the response of plants to microgravity in terms of net photosynthesis, water use efficiency and electron transport activity depend on light intensities experienced during the experiment (Monje, Stutte & Chapman, 2005; Stutte et al., 2005). Moreover, changes in stomatal resistance and gas exchanges due to altered fluid-dynamics in microgravity might be taken into account (Kirkham, 2008).

It is worth highlighting that based on available knowledge, we are beyond plant survival in Space: future goals will be to module plant systems and agrotechnologies to reach high efficiency in BLSS. The latter can be achieved only through tight cooperation between the various disciplines within plant biology, agronomy and technology. Plant biologist in Space have to consider that microgravity and other environmental factors deeply influence organism growth at molecular, biochemical, morphostructural and physiological levels with interactions that can be considered additive, antagonistic or synergic. Finally, considering that experiments in Space and in simulated space conditions are costly and constrained by opportunities, there is a need to dedicate experiments starting from a well-selected biological source (species/cultivar), focusing on specific developmental processes that affect the optimal growth of plants, but have also influence on the nutritional quality of the fresh food.

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BIOREGENERATIVE LIFE SUPPORT SYSTEMS IN SPACE (BLSS): THE EFFECTS OF RADIATION ON PLANTS

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ABSTRACT

The growth of plants in Space is a fundamental issue for Space exploration. Plants play an important role in the Bioregenerative Life Support Systems (BLSS) needed to sustain human permanence in extraterrestrial environments. From this perspective, plants are basic elements for oxygen and fresh food production, air regeneration as well as providing psychological support to the crew. The potential of plant survival and reproduction in space is limited by the same factors that act on Earth (e.g. light, temperature and relative humidity) and by additional factors such as altered gravity and ionizing radiation.

This paper analyzes plant response to space radiation, which is recognized as a powerful mutagen for photosynthetic organisms thus being responsible for morpho-structural, physiological and genetic alterations. Until now, many studies have shown evidence as to how the response to ionizing radiation is influenced by several factors associated both with plant characteristics (e.g. cultivar, species, developmental stage, tissue structure) and/or radiation features (e.g. dose, quality and exposure time). The photosynthetic machinery is particularly sensitive to ionizing radiation. The severity of the damage induced by ionizing radiation on plant cell and tissues may depend on *the capability of plants to adopt protective mechanisms and/or repair strategies. In this paper, a selection of results from studies on the effects of ionizing radiation on plants at the anatomical and eco-physiological level is reported and some aspects related to radioresistance are explored.*

Keywords: *Bioregerative Life Support System (BLSS), higher plants, ionizing radiation, photosynthesis, radioresistance*

SISTEM ZA BIOREGENERATIVNO PODPORO ŽIVLJENJU (BLSS): VPLIVI SEVANJA NA RASTLINE

IZVLEČEK

Rastlinska rast v vesolju je temeljno vprašanje na področju raziskovanja vesolja. Rastline igrajo pomembno vlogo v sistemih za bioregenerativno podporo življenju (»Bioregenerative Life Support Systems« ali BLSS), ki so potrebni za ohranjanje človeškega bivanja v nezemeljskih okoljih. S tega vidika so rastline osnovni elementi za nastajanje kisika in sveže hrane, obnavljanje zraka, prav tako pa nudijo psihološko podporo posadki. Možnosti preživetja rastlin in razmnoževanja v vesolju so omejene z enakimi dejavniki, ki so prisotni na zemlji (npr. svetloba, temperatura in relativna vlažnost), ter še z dodatnimi dejavniki, kot sta spremenjena gravitacija in ionizirajoče sevanje.

V tem prispevku analiziramo odzive rastlin na sevanje v vesolju, ki pa se smatra kot močan mutagen za fotosintezne organizme ter je tako odgovorno za morfološko strukturne, psihološke in genetske spremembe. Do danes so rezultati mnogih študij pokazali, kako mnogi dejavniki, ki so povezani tako z značilnostmi rastlin (npr. kultivar, vrsta, razvojna faza, struktura tkiv) in/ali z značilnostmi sevanja (npr. količina, kakovost in čas izpostavljenosti), vplivajo na odzivnost na ionizirajoče sevanje. Fotosintezni mehanizem je še posebej občutljiv za ionizirajoče sevanje. Stopnja škode, ki jo ionizirajoče sevanje povzroči na rastlinskih celicah in tkivih, je lahko odvisna od zmožnosti rastlin, da vzpostavijo zaščitne mehanizme in/ali strategije odprave škode. V tem prispevku je opisan izbor rezultatov študij o učinkih ionizirajočega sevanja na rastline na anatomski in eko-fiziološki stopnji, prav tako so predstavljeni tudi nekateri vidiki, povezani z odpornostjo na sevanje.

Ključne besede: *sistem za bioregenerativno podporo življenju (BLSS), višje rastline, ionizirajoče sevanje, fotosinteza, odpornost na sevanje*

INTRODUCTION

The possibility of growing plants in Space is an important topic within plans for space exploration from the point of view of future long-duration manned missions. All scenarios for the long-term habitation of space platforms and planetary stations involve plants as a fundamental part of Bioregenerative Life Support Systems (BLSS) to support the crew (Salisbury, 1999; Salisbury et al., 2002; Drysdale et al., 2003). Indeed, humans and plants are ideal space traveling companions: plants consume carbon dioxide, purify water and release oxygen, humans consume oxygen and release carbon dioxide; moreover humans can use the edible parts of plants for nourishment, while human waste and inedible plant matter can provide nutrients for plant growth after the digestion processes mediated by microbes in bioreactors (Wheeler, 2003). The sole input needed to keep such a system going is light energy. The most important characteristics of a BLSS is "self-sufficiency" since it can be considered a "miniature ecosystem" where each element supports and is supported by each of the others. In terrestrial ecosystems, most energy entering the biosphere comes in via photosynthesis by plants (producers) and is transferred along the many steps in a food chain to the consumers (herbivores, carnivores). This process is responsible for most of the organic carbon in the biological world. At the death of living organisms, detritivores and decomposers (bacteria and fungi) collectively account for the use of all such "waste" and, through the processes called decomposition and mineralization, allow the recycling of the organic matter and the return of nutrient to plants. In Figure 1 the analogies between a natural ecosystem and a BLSS are shown.

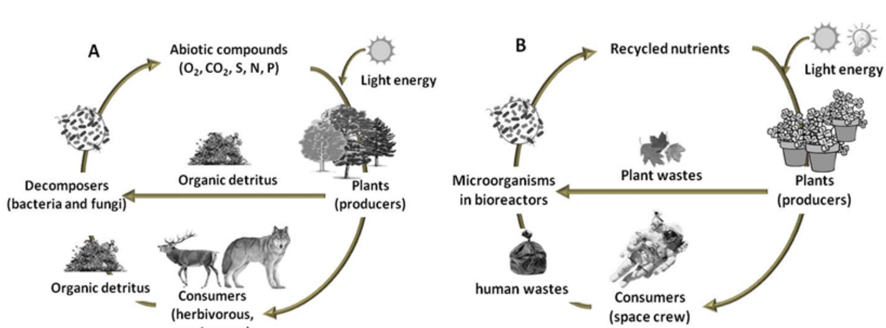

Figure 1: The analogies between a natural ecosystem (A) and a Biological Life Support System, BLSS, (B).

Another important aspect of plant cultivation in space is related to the human psychological implications of having plants present in a confined living space: there is evidence to support the benefits of working with plants and consuming fresh foods (as opposed to stored foods) on long-duration missions (Flagler & Poincelot, 1994; Waters et al., 2002).

In the long term, to reduce the need for resupplying life support materials for extended missions, it is interesting to evaluate the potential of plant survival and reproduction in extraterrestrial environments. Actually, the presence of plants on Earth is the result of an evolution process which started millions of years ago and can be considered the consequence of the continuous process of plant adaptation to specific ecological factors such as light, temperature, water and nutrient availability. The complexity of these factors and their synergistic effects have determined the characteristics of the higher plants now living on the Earth and their success in the colonization of such an environment. Similarly, the cultivation in space is strictly dependent on the scientific knowledge of the effects of space factors on plant growth processes. In space, plant growth can be altered not only by factors like those on Earth but also by the action of new environmental factors such as microgravity and ionizing radiation. On Earth, radiation has influenced the colonization of lands by early higher plants which evolved a number of adaptations such as the synthesis of pigments and antioxidants as well as gene-repair mechanisms (Hessen, 2008). It has to be expected that in space where radiations of different qualities and levels of intensity (Rozema et al., 1997) occur, plant life might be severely constrained by this factor.

THE EFFECTS OF IONIZING RADIATION ON PLANTS

The effect of radiation on plants has been the object of extensive research in the past, with different aims concerning several fields of research. From the beginning of the nineteen-sixties until now, low doses of low- and high-LET (Linear Energy Transfer) ionizing radiation have been widely used for agricultural interests such as the development of new decontamination methods (alternative to heating and chemical sterilization) (Farkas, 1988), or in breeding programs for the selection of new cultivars, especially cereals, legumes and vegetables with improved yields in crops (Maity et al., 2005; Yu, 2005), enhanced resistance to diseases and semi-dwarf growth (Mei et al., 1994; Li et al., 2007).

A second area of application is radioecology, namely the study of the effects of radiation pollutants in ecosystems. This topic was widely considered after the Chernobyl accident (Real et al., 2004; Fesenko et al., 2006) and has sparked renewed interest after the recent Fukushima disaster. As a result of the Chernobyl accident, tens of thousands of hectares of forests experienced massive radioactive contamination, offering a unique opportunity to study in situ the effects of acute and chronic exposure of plants to ionizing radiation. These studies were mainly concerning conifers (Scotch pine), but also herbaceous plants and grasses (Sidorov, 1994; Real et al., 2004).

The third area of interest on radiation concerns space-oriented experiments focused on the cultivation of plants under space conditions, being plants an essential component of Bioregenerative Life Support Systems (BLSSs). These studies explore the response of seeds, higher plants and photosynthetic microorganisms to low-LET (γ- and X-rays) and high-LET (heavy ions) ionizing radiation. Generally, ionizing radiation may have different effects on plant metabolism, growth and reproduction depending on the dose: positive effects at very low doses, detrimental consequences at intermediate levels and pronounced damage at high doses are expected (Figure 2). Besides the dose, it is widely documented that the severity of the effects is dependent upon other factors such as species, cultivars, plant developmental stage, physiological and morphological traits as well as genetic characteristics (Holst & Nagel, 1997; De Micco et al., 2011). At the same dose, high-LET are more dangerous than low-LET radiation because heavy ions have been shown to cause a higher induction of mutation in the genome (Shikazono et al., 2002; Wei et al., 2006).

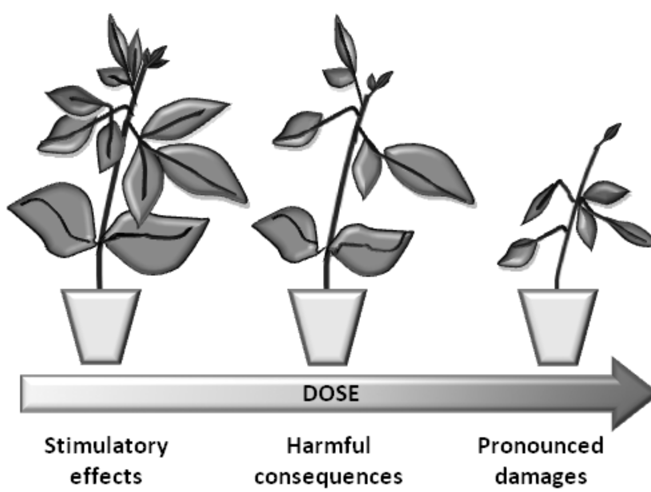

Figure 2: The effects of ionizing radiation on plants depend on dose: generally the effects are positive at very low doses, detrimental at intermediate doses and pronounced at high doses.

Consequences for plant growth

Ionizing radiation may have several impacts on different plant organs and tissues. Generally, more complex tissue architecture is less sensitive to damage. The alteration in morphological traits can be positive or negative depending not only on the species but also on the dose. Generally the exposure to ionizing radiation increases embryo lethality, induces dwarf architecture and modification of floral elements (Mei et al., 1998; Shikazono et al., 2002). However, radiation has also been reported to increase growth (e.g. taller plants), yields, reproductive success (e.g. formed seeds) and increase the ability to endure water shortage (Zaka et al., 2002; Maity et al. 2005; Yu et al., 2007).

At the anatomical and cytological level, there is evidence that irradiation with cosmic- and γ-rays affects cell wall traits (Bayonove et al., 1984; Kovàcs et al., 1997). Irradiation increases the activity of enzymes responsible for the degradation of pectins, the dissolution of middle lamellae and the separation of cells. Irradiation would also stimulate the autolysis of polysaccharides, also determining the dissolution of matrix material which results in alterations during the arrangement of cellulose microfibrils with a loss in firmness (Kovàcs et al., 1997).

Implications for photosynthetic machinery

The growth and reproduction of an individual plant and ultimately, the survival of the species, depend upon photosynthesis, the key process for the conversion of solar radiation into stored biomass energy. The photosynthesis of higher plants is considered one of the most critical biological processes of plant-based BLSSs (Wheeler et al., 2003). Light energy harvested by photosystems drives all the subsequent reactions leading to the production of ATP and NADPH utilized for the reduction of CO_2 in the carbon reduction cycle. Many studies have been performed on photosynthetic microorganisms and higher plants in order to elucidate the consequences of radiation exposure (De Micco et al., 2011). It is clear that the photosynthetic process may be altered at any step by ionizing radiation: electron transport carriers, light-harvesting pigment-protein complexes and enzymes of the carbon reduction cycle (Figure 3).

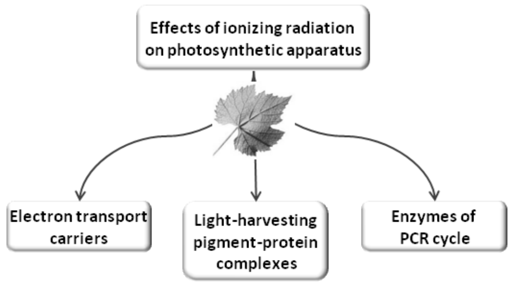

Figure 3: Ionizing radiation affects several steps of the photosynthetic apparatus: carriers of the photosynthetic electron transport chain, light-harvesting complexes, enzymes of photosynthetic reduction cycle (PCR).

The carriers of photosynthetic electron transport chain (i.e photosystems and cytochromes) seem to be specific targets of the damaging effect of γ- radiation. Experiments conducted on cyanobacteria by means of stratospheric balloons and spaceflights have shown evidence that photosystem II (PSII), one of the pigment–protein complex in the chloroplast, is particularly sensitive (Angelini et al., 2001; Rea et al., 2008). The damage on PSII is mainly localized at the D1 protein level where the electron transfer between the primary electron donor and the secondary plastoquinone acceptor happens. The degree of PSII damage is influenced by the level of light, being more pronounced at high light conditions which favour the photoinhibition of the photosynthetic apparatus (Giardi et al., 1997; Esposito et al., 2006).

The components of the photosynthetic electron transport are vulnerable also in higher plants where the exposure to both acute and chronic doses of γ-radiation induces the oxidative damage by the over-production of reactive oxygen species (ROS) (Zaka et al., 2002). The increase of ROS affects not only the photosynthetic apparatus but also the whole cell, being responsible for membrane lipid peroxidation and protein modifications (Foyer & Mullineaux, 1994).

The light harvesting complexes are also injured by low- and high-LET ionizing radiation. Irradiation of plants with γ- and heavy ions may determine the dilation between thylakoid membranes and the incidence of defective chloroplasts with chlorophyll mutations (Cheng & Chandlle, 1999; Abe et al., 2002). The consequence of chlorophyll depletion is a reduced absorbance spectrum pattern and a loss of functionality of the whole antenna complexes (Palamine et al., 2005).

Radioresistance

An interesting issue related to plant exposure to ionizing radiation is the induction of radioresistance. The occurrence of radioresistance has been observed mainly in plants growing in the radioactively contaminated areas of Chernobyl and neighboring regions (Zaka et al., 2002). After the Chernobyl accident, due to the impossibility of leaving the polluted zone, plants experienced both acute and chronic doses of radiation. It has been observed that radioresistance depends on the species (Real et al., 2004). Generally herbaceous species are less sensitive to irradiation than woody species because the latter experience cumulative detrimental effects of radiation (Holst & Nagel, 1997).

The ability to develop protection mechanisms and the capability of repairing damage are the basis for the radioresistance of a given species. However, it is clear that long-term exposure to γ-radiation generates the potential for irreversible consequences due to the accumulation of unrepaired damages. The acquisition of radioresistance may be ascribed to both biochemical and molecular mechanisms (Esnault et al., 2010). It is ascertained that the exposure of plants to ionizing radiation triggers an overproduction of ROS. However, even if ROS production is deleterious to the photosynthetic machinery, it has to be remarked that the rise of radicals in the plant cell can act as a signal for the activation of protective response and defense pathways (Foyer & Noctor, 2005). In this context, the overproduction of scavenger enzymes as well as the over-activation of poly(ADPR)polymerases enzymes (PARPs), represent essential mechanisms to counteract the cell oxidative damage and enhance stress tolerance in plants (Alscher et al., 1997; Doucet-Chabeaud et al., 2001; Esnault et al., 2010). More specifically, PARPs recognize the damaged DNA acting as a stress signal; the PARP over-activation produces the formation of PAR polymers that work as effectors recruiting on damaged DNA site the enzymatic machinery for the repair (Amor et al., 1998).

The acquisition of radioresistance may be considered an adaptive response of plants to the changing environment and may represent a valuable benefit in the sight of the plant growth in BLSSs.

AN IDEAL CANDIDATE PLANT FOR BLSSs

One of the main concerns of plant space biology is which species should be considered an ideal plant candidate for life support in Space. Until now, many research groups have been involved in the identification of the most suitable plant species for BLSSs (Mitchell et al., 1996; Salisbury & Clark, 1996; Tibbitts & Henninger, 1997). The criteria for the selection of such species include high photosynthetic rates, nutritional value and the ratio edible dry mass/total dry mass, as well as dwarf growth that is a desirable property in reduced volumes (Hoff et al., 1982; Salisbury, 1997; Tibbitts & Henninger, 1997). The high photosynthetic yield is essential because despite the crop harvest, a fraction of the biomass should always remain photosynthetically active in order to provide continuous O_2 production, CO_2 removal and water recycling (Stutte et al., 1999). In addition, the suitable crops should respond to specific dietary requirements (i.e. carbohydrate, protein and fat content), providing also vitamins and minerals, while being free from anti-nutritional compounds. Apart from resistance to diseases, another important aspect for an ideal candidate plant for BLSS is radioresistance, useful to mitigate the higher level of ionizing radiation in space. Studies from both ground-based and space-oriented experiments have demonstrated that radioresistance is an important characteristic that makes species less sensitive to the detrimental effects of radiation (Doucet-Chabeaud et al., 2001).

In light of these considerations, it is clear that identifying a species having all the desirable characteristics is very difficult. The needs of space crews (including the complete diet requirements) might be fulfilled more efficiently through a combined cultivation of various species (Hoff et al., 1982; Wheeler et al., 1996).

CONCLUSIONS

Future human exploration of space will be centered on biological life support systems which utilize compartments supported by plants and microorganisms. However, the use of plants as the basis for biological life support systems presents limitations due not only to the lack of knowledge about the impact of new environmental factors on plant growth but also to challenges in technology. Many experiments, both space-oriented and ground-based, have identified several deleterious factors of spaceflight in restraining plant physiological performance, in particular microgravity and ionizing radiation. With regards to radiation, results are often contrasting and not easily comparable because plant response depends on many factors including type and dose of radiation, plant species and plant developmental stage. Generally the damage increases with increasing doses. Furthermore, at same dose, high-LET radiations are more dangerous than low-LET ones in inducing genetic mutations (Shikazono et al., 2002). Even if plant response to ionizing radiation is not yet fully understood, it is clear that some species exhibit an intrinsic radioresistance due to molecular and biochemical mechanisms (Esnault et al., 2010).

At present, although many experiments have been performed, a comprehensive understanding of plant response to irradiation in space is still far off and its achievement is further complicated by other source of perturbations such as microgravity. Within this scenario, further experimentation is needed before the efficient cultivation of higher plants in ecologically closed support systems for life in Space can become a reality.

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THE CHALLENGING DREAM OF PLANTS IN SPACE

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ABSTRACT

Plants are essential components of Bioregenerative Life Support Systems (BLSS) because they provide fresh food, produce oxygen, uptake CO_2 *from air and purify waste water via the leaf transpiration processes. In the consideration of long-duration human space missions, the issue of food production is becoming increasingly important. Therefore the possibility of growing plants in space represents the challenge for human space missions on the Moon and Mars and is related to the development of appropriate BLSS. Key issues include food production, nutritional needs, hydroponic techniques, horticultural requirements, waste processing and engineering systems.*

Keywords: *bioregenerative life support system, space plant growth, food production, space constraints*

NOV IZZIV – SANJE O RASTLINAH V VESOLJU

IZVLEČEK

Rastline predstavljajo poglaviten element Sistemov za bioregenerativno podporo življenju (Bioregenerative Life Support Systems ali BLSS), saj nudijo svežo hrano, proizvajajo kisik, absorbirajo ogljikov dioksid iz zraka in čistijo odpadno vodo s pomočjo izhlapevanja skozi liste. Pri obravnavanju dolgotrajnih človeških misij v vesolje, področje proizvajanja hrane postaja vedno pomembnejše. Zato možnost gojenja rastlin v vesolju predstavlja izziv za človeške misije na Luno in Mars, prav tako pa je povezana z razvojem ustreznih sistemov BLSS. Ključna vprašanja se nanašajo na proizvajanje hrane, hranilne potrebe, hidroponične tehnike, hortikulturne zahteve, obdelavo odpadkov in tehnične sisteme.

Ključne besede: *sistem za bioregenerativno podporo življenju, gojenje rastlin v vesolju, proizvodnja hrane, omejitve v vesolju*

INTRODUCTION

During the second part of the last century, space became the so-called last frontier and space exploration started to be seen as a very exclusive research opportunity over the entire world. The scientific community has always auspicated the possibility of growing plants in space because, as photosynthetic organisms, they can play an essential role in the bio-regenerative systems. The initial interest in growing plants in space was mainly focused on air regeneration (O_2 production and CO_2 removal). As the consideration of long-duration space missions increased, the importance of food production became more and more a crucial need for the crew. Since the beginning of this inquiry, all the possible scenarios for long-term space missions and other extraterrestrial structures have involved plants as a human supporting environment. In 1986, Edwards and Pickard proposed for the first time that plants could actually detect and transduce external physical stimuli (Walter, 1987). That substantial evidence gave rise to a series of other experiments aimed at finding out the possible consequences of an alien life for plants. Subsequently, all the European, Asiatic and American space agencies have been putting their effort in involving seeds or previously grown plants in their spaceflights. In fact, even if specific growth facilities have been hypothesized and crafted by different research groups, the actual physiological effects of space environment on plants can only be identified in a weightless environment. Nowadays, the growth of plants in space remains a priority for plans concerning the long-term habitation of space and the media has helped to spread the idea of a possible space farm in the near future. Recently, millions of basil seeds have been put on board the International Space Station (ISS) for a project called Photosynthesis Experiment System Testing and

Operations (PESTO). A certain amount of those seeds will be brought back to Earth and here analyzed and planted in soil; the rest will be kept on board and the crew will try to complete the entire life cycle of the plants from seed to seed. By this time, plants are proper features of the space stations.

Roles of plants in space

For the first space researchers one of the first matters was to provide life support during space missions. The easiest and most used solution is an initial launch mass with periodic resupplies of consumables. Unfortunately, since from the beginning it was quite clear that it could become very expensive and wasteful on a long time scale as the stowage increases linearly as mission duration or distance from the Earth. In the late 80s, the idea of a Bioregenerative Life Support Systems (BLSS) for providing sustained life support during space missions was raised for the first time (Olson et al., 1988). In this prospective, vegetal systems play an important role for sustenance, producing food for the crew (Figure 1). Moreover, plants regenerate the air by removing CO_2 and producing O_2, and they purify water through transpiration. Another important aspect to be underlined is the psychological support that living organisms can give to the astronauts (Wheeler et al. 1996; De Micco et al. 2009). In regards to the food production, the human diet seems to require about 15 species of plants which must be grown on each space mission to ensure a complete, balanced diet (Olson et al., 1988). The ideal space-plant would have short stalks to save room, would have few inedible parts, would grow well in low light, and would be resistant to microbial diseases. The most efficient designs of regenerative life support systems combine both physicochemical and plant-based systems. In this case, food and waste processing, and temperature control can be accomplished with physicochemical systems beside the use of plants. Early studies of bioregenerative life support focused on algal systems, but converting the algae to useful and palatable food proved difficult (MacElroy and Bredt, 1984). Some algae are very rich in protein and are not appropriate for a balanced diet, moreover they may contains indigestible cell wall materials. Several studies focused on what crops might be the best candidate for the BLSS taking into consideration the nutritional needs and also the best harvest index (ratio of edible to total biomass). Research was aimed at choosing varieties of wheat, rice, lettuce, potatoes and other plants that meet these criteria. Many studies have highlighted growing more conventional crops using hydroponics to eliminate water and nutrient stress (Resh, 1989). Soilless culture has many advantages in cultivation of plants in space, such as no use of soil, reuse of water in the plant system, best control of nutrient levels and reduced risk of weeds. Moreover because the candidate crops are all C3 photosynthetic type elevated carbon dioxide concentrations and high light levels were applied to enhance growth rates and yields (Bugbee and Salisbury, 1988; Wheeler and Tibbitts, 1997). On ground extensive experiments were conducted to test crop responses to mineral nutrition, humidity, temperature, humidity, photoperiod and even light spectral quality. Currently, the possibility of growing plants in space is a requirement for the realization of long-duration manned missions.

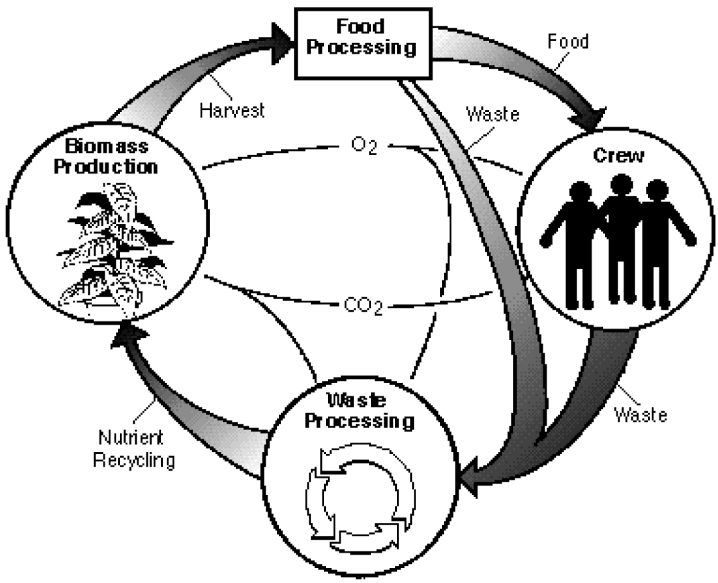

Figure 1: The fundamental relationships among plants, animals and humans within Bioregenerative Life Support Systems. A continuous supply of food, oxygen and clean water is available for the crew, while products of waste processing and CO_2 are reutilized by plants.

Space constraints for plants

The space environment that includes such factors as altered gravity and cosmic rays may affect plant growth and fitness in various aspects, but even today, there are few answers to these questions. The efficient development of plants in space is constrained by: a) the same environmental factors as the Earth, such as temperature and light (Zimmermann et al. 1996); b) the new space factors such as microgravity and ionizing radiation; c) the interaction of usual and new factors that modify the availability of resources. Our knowledge on plant growth response to the microgravity environment of low Earth orbit comes from experiments performed mainly aboard Space Shuttles, Mir and the International Space Station. The challenge of using plants as bioregenerative life support systems in space is the management of water, nutrient and light delivery. Nutrient delivery and water recycling will be most difficult in systems operated in microgravity. Technological advances are promising areas for enhancements in long-term space research. Improvements in lighting efficiency and the genetic engineering of crops that are better suited to a spaceflight environment such as dwarf crops, or of plants with high light harvesting indexes that can grow in artificial light or elevated CO_2 conditions, have been the aims of space researchers during the last years. The light system is one of the most important and critical components for growth of plants in a BLSS. The requirement to reduce power needs have brought to use lamps with narrow spectra (blue and red light) or light emitted diodes (LEDs). Some BLSS researches include the developments of a particular plant growth unit to be used on the surface of the Moon or Mars, such as an inflatable greenhouse that relies on direct photosynthetically active radiation (PAR) to irradiate crops. In this case transparent films would be required to withstand large external temperature gradients, strong cosmic-galactic and UV radiation, micrometeorite impacts and low atmospheric pressure.

Moreover, to investigate plant behavior in space, the effects of ionizing radiations have been studied since last century. For this purpose, ground-based experiments have been performed with particles of different charge and energy (as X- or γ-rays) (Durante and Cucinotta 2008). The aim of this space research is not only to identify qualitatively and quantitatively the effects of ionizing radiations but also to define countermeasures to mitigate these effects.

Studies on space effects on plants

A comparison of various studies has clarified how space effects are deeply influenced by plant characteristics (e.g. species, cultivar, stage of development, tissue architecture and genome organization) (Holst and Nagel 1997). In relatively short-term space-flight experiments, it has been pointed out the space environment causes chromosome aberration and changes in the cell cycle of plant cells. This may be due to either microgravity or increased cosmic rays in space or resulting from unfavorable growing conditions in the plant growing unit. Structural and functional changes in the DNA molecule are responsible for most of the damage expressed after exposure to ionizing radiations, at both the cellular and the systemic levels. DNA modifications range from single base alterations, base substitutions, base deletions, chromosomal aberrations to epigenetic modifications. In general, radiation exposure can induce both negative and positive effects on plants, and the mutations at the base of these effects can also be transmitted to the progeny (Mei et al. 1998; Yu et al. 2007). Apart from reduced germination, among the detrimental effects, there is often reference to embryo lethality, dwarf architecture, modification of floral morphology with altered occurrence of fertile floral elements (Kranz 1986; Sah et al. 1996). On the other hand, stress conditions, like the exposure to ionizing radiations, can have stimulatory effects on specific morphological parameters and can increase the yield of the plants in terms of growth, reproductive success and ability to withstand water shortage (Maity et al. 2005; Yu et al. 2007; Melki and Dahmani 2009). A few space-flight experiments have attempted to test the effects of the space environment on plant reproduction. For instance, *Arabidopsis thaliana* and wheat plants were grown in space for different durations (Mashinsky et al., 1994; Salisbury et al., 1995).

They were found to produce and develop flowers, but the flowers produced more sterile seeds than did ground control plants. These experiments could not specify the cause for such failure in seed production.

CONCLUSIONS

For space research, it is mandatory to understand how our planet supports all of us, and somehow replicate the parts that are necessary so that we can have affordable and even doable long-term space missions. A bioregenerative life support system will probably never fully replace the mechanical one on the International Space Station but with the help of plants and microbes, future space stations will truly become worlds unto their own.

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A LARGE HUMAN CENTRIFUGE FOR EXPLORATION AND EXPLOITATION RESEARCH

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ABSTRACT

This paper addresses concepts regarding the development of an Altered Gravity Platform (AGP) that will serve as a research platform for human space exploration. Space flight causes a multitude of physiological problems, many of which are due to gravity level transitions. Going from Earth's gravity to microgravity generates fluid shifts, space motion sickness, cardiovascular deconditioning among other changes, and returning to a gravity environment again puts the astronauts under similar stressors. A prolonged stay in microgravity provokes additional deleterious changes such as bone loss, muscle atrophy and loss of coordination or specific psychological stresses. To prepare for future manned space exploration missions, a ground-based research test bed for validating countermeasures against the deleterious effects of g-level transitions is needed. The proposed AGP is a large rotating facility (diameter > 150 m), where gravity levels ranging from 1.1 to 1.5g are generated, covering short episodes or during prolonged stays of weeks or even months. On this platform, facilities are built where a crew of 6 to 8 humans can live autonomously. Adaptation from 1g to higher g levels can be studied extensively and monitored continuously. Similarly, re-adaptation back to 1g, after a prolonged period of altered g can also be investigated. Study of the physiological and psychological adaptation to changing g-levels will provide instrumental and predictive knowledge to better define the ultimate countermeasures that are needed for future successful manned space exploration missions to the Moon, Mars and elsewhere. The AGP initiative will allow scientific experts in Europe and worldwide to investigate the necessary scientific, operational, and engineering inputs required for such space missions. Because so many different physiological systems are involved in adaptation to gravity levels, a multidisciplinary approach is crucial. One of the final and crucial steps is to verify the AGP concept through a large scientific community through feedback from various scientific societies. This facility will also serve clinical research on Earth, because a multitude of health problems such as osteoporosis, frailty of the elderly, inactivity, sarcopenia, obesity, insulin resistance and diabetes, cardiovascular problems, connective tissue ageing and immune deficiency, among others stand to benefit from the fundamental insights into the effects of our ever-present terrestrial gravity gained with such a novel research platform.

Keywords: *hypergravity, artificial gravity, microgravity, weightlessness, human exploration, human hypergravity habitat*

VELIKA ČLOVEŠKA CENTRIFUGA ZA RAZISKOVANJE IN IZKORIŠČANJE

IZVLEČEK

Ta prispevek opisuje koncepte na področju razvoja platforme za spreminjanje gravitacije (Altered Gravity Platform ali AGP), ki bo služila kot raziskovalna platforma za človeško raziskovanje vesolja. Polet v vesolje povzroči številne fiziološke težave, izmed katerih se mnoge pojavijo zaradi sprememb gravitacije. Prehod iz Zemljine gravitacije v mikrogravitacijo ustvarja redistribucijo tekočin, slabost, slabšanje srčno-žilnega sistema, vrnitev v okolje gravitacije pa astronavte postavi pod podobne stresne pogoje. Daljše zadrževanje v mikrogravitaciji sproži dodatne škodljive spremembe kot so zmanjšanje kostne mase, mišična atrofija, izguba koordinacije ali specifične psihološke strese. Z namenom, da bi se lahko pripravili na prihodnje človeške misije v vesolje, je potrebna raziskava za odkrivanje ustreznih protiukrepov na področju škodljivih učinkov, ki jih sprožijo spremembe gravitacije, raziskava pa bi se izvajala na Zemlji. Predlagana AGP je dejansko velik rotirajoči objekt (v premeru > 150 m), kjer ravni gravitacije segajo od 1,1 do 1,5 g, in kjer se lahko izvajajo krajši preskusi ali celo preskusi v daljših obdobjih, na primer tednih ali mesecih. Na tej platformi bodo zgrajeni objekti, kjer bo lahko samostojno živela ekipa s 6 do 8 osebami. Tako se lahko neprekinjeno preučuje in spremlja prilagajanje človeka gravitaciji 1 g ali višji gravitaciji. Podobno se lahko preiskuje tudi ponovna prilagoditev na gravitacijo 1 g po daljšem obdobju bivanja v spremenjenih težnostnih pogojih. Preučevanje fizičnega in psihološkega prilagajanja spreminjajočim ravnem gravitacije bo tako omogočilo instrumentalno in napovedno znanje, ki bo lažje določilo najboljše protiukrepe, ki so potrebni za prihodnje človeške misije na Luno, Mars in drugam. Pobuda za AGP bo vrhunskim znanstvenikom v Evropi in po svetu omogočila, da raziskujejo vse potrebne znanstvene, operativne in tehnične vložke, ki so potrebni za takšne misije v vesolje. Ker so v prilagajanje na različne ravni gravitacije vključeni različni fiziološki sistemi, je poglaviten več-disciplinaren pristop. Eden izmed zadnjih in poglavitnih korakov je, da koncept AGP preveri širša znanstvena javnost s pomočjo povratnih informacij s strani različnih znanstvenih skupnosti. Ta platforma bo prav tako služila kliničnim raziskavam na Zemlji, saj bi lahko preučevali tudi učinke zemeljske gravitacije v primerih različnih zdravstvenih težav kot so osteoporoza, slabotnost starejših, nedejavnost, sarkopenija, debelost, odpornost za inzulin in sladkorna bolezen, srčno-žilne težave, staranje veznega tkiva in slabljenje imunskega sistema.

***Ključne besede:** hipergravitacija, umetna gravitacija, mikrogravitacija, breztežnost, človeško raziskovanje, človeški življenjski prostor v hipergravitaciji*

INTRODUCTION

Space flight research makes use of the unique microgravity environment, where the gravitation is compensated by the fact that spacecrafts are in free fall, to learn about the effects of weight on the human physiology and psychology. When we consider a physical entity like weight (accelerated mass) acting upon a system, researching weight is basically not any different from exploring *e.g.* temperature (Aschoff & Wever, 1958; Brink & Werber 1994) or pressure (Foster & Butler, 2009). In order to understand how a physiological and psychological system responds to an environmental variable we need to modulate it. For many systems it is therefore as relevant to look at responses to hypergravity (larger than Earth 1g) as it is to consider hypogravity or even near weightlessness. Since humankind developed the capability of going into space, numerous space flight experiments, some of significant duration, have been performed, initially on board the Soviet Salyut (Grigoriev et al., 1994), later on the American Skylab (Johnston et al., 1977) in the early nineteen seventies, on Mir mainly during the 1990s and currently on the International Space Station, ISS. Some cosmonauts / astronauts were under near weightless conditions for several months and longer. In sharp contrast, most hypergravity studies have been performed using short exposure times. If one is interested in the long-term effects of gravity on human physiology we also need to expose humans to hyper-gravity for periods of days, weeks or even months. In his flying career the Russian cosmonaut Sergei Krikalev has been exposed to hypo-gravity conditions on board orbital space stations for more than 800 days in total. There has never been a single person exposed to more than 1.0 g for a period of time anywhere near to these 800 days, despite the fact that a hyper-gravity facility is far less complex than a micro-gravity platform. In fact, the longest period to which humans have been exposed to hypergravity was for a few weeks during pilot studies performed in Downey (California, USA) and Pensacola (Florida, USA) in the 1960s but only few publicly accessible reports have been released from these studies.

Concept and Objectives

Humans in space experience problems at many different levels. Microgravity and gravity transitions both have enormous impacts on the human physiology, behavior, psychology as well as operations and well-being (Schmidt et al., 2009). g-Level transitions are acutely problematic for various physiological systems such as the neuro-vestibular, cardiovascular and fluid regulation system, whereas prolonged microgravity causes undesirable adaptations in *e.g.* muscle, bone and the immune system. Such drastic changes in the physiological system, and especially those in the nervous system, in turn affect both individual psychology (cognition, emotion, motivation, activity levels and cycles, etc.) and psychosocial factors such as social perception and interaction. Going from an Earth gravity level into microgravity puts significant stress on all these systems, but the reverse is also true, *i.e.* moving from a microgravity (μ-g) into a gravity environment. Going from μ-g (hypo-gravity) to 1g is equivalent to going from

1g to hyper-gravity, although the effects might be different in magnitude.

Human spaceflight is one of the few areas of research where all these physiological and psychological changes take place in the same subject (Kanas & Manzey, 2008; NASA, 2005 Williams et al., 2009). In essence, during spaceflight we see many physiological changes similar to those typical of ageing (Asher, 1947; Biolo et al., 2003; Blottner et al., 2006; Corcoran, 1991; Gannon et al., 2009; Narici et al., 2002; Vernikos et al., 2010). One can regard spaceflight as an extremely accelerated 'ageing' process. Therefore, the need for countermeasures that tackle these deleterious effects drives many research efforts in different institutes throughout the world.

In contrast to typical clinical studies, the number of astronauts is usually extremely limited, *i.e.*, at most a dozen of astronauts can take part in one experiment. However, results from space experiments drive other ground-based research projects where larger groups of subjects can be included (Clemets, 2011). To date only two ground-based simulations of the effects of long duration spaceflight are used; 'bed-rest' (Armbrecht et al., 2011; Arbeille et al., 2008, Pavy-Le Traon et al., 2007) and 'dry immersion' (Iwase et al., 2000; Moukhina et al., 2004; Navasiolava et al., 2011). During bed-rest studies healthy subjects continuously stay for a period of weeks to months, in a bed that is tilted 6 degrees head down. Dry immersion is a model where healthy subjects are immersed for typically one week in a bath, without making contact with the water by means of a sealing cloth. Both experimental models generate comparable physiological effects as microgravity, mainly for the muscular (Moriggi et al., 2010), bone (Belavý et al. 2011) and cardiovascular systems (Perhonen et al., 2001; van Duijnhoven et al., 2010). However, for the neuro-vestibular system, neither of these ground-based models seems appropriate because the subjects are still exposed to 1g. In this regard it is important to note that in recent years more compelling evidence is emerging on the role of the neuro-vestibular system on other physiological systems such as muscle, bone or circadian rhythms (Levasseur et al., 2004), suggesting that simulations that fail to include neuro-vestibular changes may be lacking important components.

Spaceflight-induced effects are not entirely due to microgravity. It is known that g-level transitions also cause several physiological changes (Paloski et al., 2008). Going from one g on Earth to micro- g in space, provokes problems, but the reverse transition does as well, *i.e.* upon return of the astronauts from space to Earth, while for systems such as the skeleton, the time needed to recover is longer than the mission duration (Vico et al., 2000). Whereas on Earth, medical support is omnipresent during the days and weeks after return, this will not be the case when landing on the Moon, let alone on Mars. To increase the success of the human exploration program, understanding the changes that take place during gravity-level transitions and during prolonged altered gravity is fundamental. Such research protocols help to define countermeasures in order to mitigate the deleterious effects emerging from these challenging conditions.

Post-flight scientific evidence shows that the inner ear utricular nerve-afferent sensitivity is strongly regulated by exposure to even a short duration in microgravity experienced during orbital missions, requiring hours to days to recover after the return to Earth (Boyle *et al.*, 2001). Transition from hyper-g to normal gravity resembles the transfer from 1g to microgravity, and might be used as a valid analog ground-based model. Human studies have also shown that when astronauts were exposed for one hour to 3 times the force of gravity, they experienced after this centrifugation session comparable symptoms of space motion sickness as they experienced on board the Space Shuttle (Ockels et al., 1990; Bles et al., 1997). Thus the transition from 3g to 1g was similar in the broad sense to the transition from 1g to microgravity. However, only the neuro-vestibular responses were investigated in these studies leaving open the questions related to other organ systems.

During the last two decades, many studies have presented evidence of alterations in molecular mechanisms and signal transduction processes in cells of the immune system as a direct result of reduced gravity (Cogoli et al., 1984; Boonyaratanakornkit et al., 2005). Together with clinical observations, these studies raise serious concerns as to whether spaceflight-associated immune system weakening ultimately precludes exposure to long-duration space flight (Crucian et al., 2009). Therefore, it is a fundamental question whether a gravity continuum exists for the signal pathways of immune system cells, which might support the use of hypergravity as a countermeasure treatment on immunity. It might be argued that hypergravity could be applied as a possible therapeutic strategy to strengthen the human immune system on Earth.

Since several-crew members will live and work on board the AGP, this facility could also be used for psychological studies. The AGP could be complementary to other space flight related analogs such as pressurized modules, isolation chambers, underwater habitats, submarines, as well as Arctic and Antarctic stations or the Mars-500 study (Angener, 2012; Harrison et al., 1991; Inst. of Medicine, 2002; Kanas & Manzey, 2008; Olsen, 2002).

Another of the technological capabilities of such a hyper-gravity platform would be for testing new life support systems (Czupalla et al., 2005; Hendrickx et al., 2006) or as a low pressure (hypoxic) environment such as foreseen for the Moon and Mars bases (Lieberman et al., 2005). In addition, the crew could be used for testing new training methods for flight-like space operations. While human experiments are running, parallel studies using animals and plants can also be performed. Given the size of the AGP, a further application of the system is in geophysical fluid mechanical studies, where a large-scale Coriolis force is required to properly simulate planetary phenomena (Orr et al., 2008).

Rather than mimicking the effects of microgravity, hypergravity can be used to study how the different physiological systems react to changing gravity, in particular going from 1g to more than 1g, and vice versa. Such studies are complementary to the research conducted on board the ISS, and contribute to the space exploration program from a completely novel and different angle of attack. Directly related to this knowledge are medical issues in e.g. the ageing population. Diseases associated with the contemporary life style such as osteoporosis, sarcopenia, cardiovascular diseases and obesity can be addressed using the AGP (Trappe, 2009; Vernicos & Schneider, 2010). The outcome of these multidisciplinary studies will provide us with the best possible and collaboratively conceived arguments to actually develop such a facility, taking into account the input from all involved scientific, engineering, and operational disciplines.

The Altered Gravity Platform (AGP)

To study the effect of altered gravity conditions, we propose the use of a ground based research platform, to be called the Altered Gravity Platform, AGP, that as a baseline consists of a habitat for 6 or more subjects, and where the adaptations to altered gravity can be studied during prolonged experiments. Human behavior and adaptation will be studied when subjects are subjected to different g-levels along the gravity continuum. If we consider this paradigm of a gravity continuum, *e.g.* that physiological processes scale with the magnitude of applied acceleration (Tou et al., 2002; van Loon et al., 2005; Wade, 2005) one may learn about the long-term adaptation of the body to different g loads. How fast does the human body adapt to a hyper-g load, but also how fast does the body respond when returning to 1g after long duration centrifugation?

The concept of the AGP was initiated in a Topical Team of the European Space Agency (ESA) (van Loon et al., 2009a, 2009b). This concept is also supported by the United States, Japanese and Canadian space agencies; NASA, JAXA and CSA, respectively. The Topical Team members have discussed the gravity levels and angular velocities for which the human body could be safely exposed to for extended periods of time. Also, experimental protocols addressing the countermeasures as well as basic human physiological and psychological research were proposed. Issues such as ethics, safety, as well as the required technology were addressed. The outcome of these discussions will be shared with scientists, engineers and operators to provide profoundly conceived arguments for designing and building such a facility, taking into account the input from all involved scientific, engineering and operational disciplines.

The AGP consists of a rotating platform within a weather-protected shell. The Topical Team's scientific requirements regarding acceptable rotation rates suggest a reference radius in the order of 75 m. The nominal test range will be 2 g at the outer rim, which is achieved by a rotation at 4.5 rpm, hence a tangential speed of 35.7 m/s or some 128.5 km/h. These values are considered as baseline at this point, and may change according to the requirements emerging from future, more detailed, analysis from scientists and operational experts.

A modular habitat is installed along the 75 m radius, to accommodate various scientific requirements and operational functions. A 75 m radius allows for the installation of up to 47 units of 10 m each along a 471 m perimeter. In such a maximum configuration and considering a baseline habitat-width of 3.75 m, this will add up to a total of 1,762 m², including 1400m² of usable space. The modules will include functions such as living and working accommodation, labs, life support systems, and storage. The 'gravinauts' will be subjected to altered gravity confined in the Gz direction; this is realized with a variable tilting system that positions the floor between 0° (no rotation) and 60° (2g level) to compensate for the radial acceleration imposed on the modules. The large platform surface allows testing stations at various distances from the AGP rotation axis, thus providing various gravity levels at the same revolutions. The platform is internally balanced with a system of counterweights ensuring rotational stability.

In nominal operations the start and stop of the AGP will be below vestibular threshold, *i.e.* it will take up to several hours for reaching full speed or stopping the rotation. This is to avoid acute motion sickness or cardiovascular events, and to take into account the energy efficiency and the inertia of the platform. Constant rotation can last from hours up to six months without stopping the facility.

Although the platform and habitat have ample space for the storage of spare parts, food and water, a flexible resupply system is foreseen to permit the wide range of planned studies. Here a transition unit can be loaded with supplies while in the static center of the platform and then rotated up to speed to synchronize with the main platform. At that point a “radial transition unit” transports items from the system center to the outer radius. This design allows the resupply of the modules without stopping the system, and importantly provides the possibility for bringing in or evacuating individuals during operations.

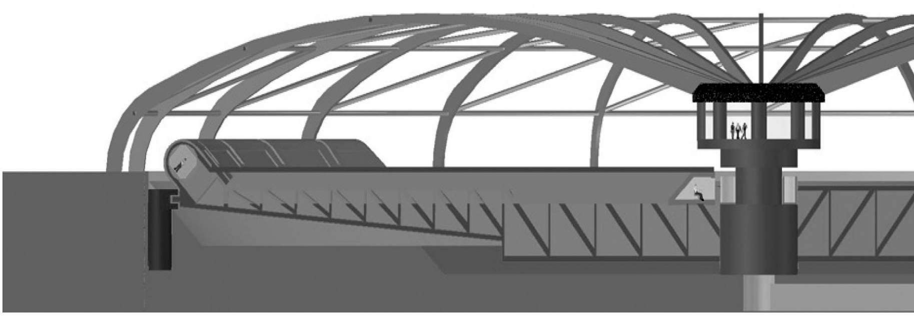

*Figure 1: Concept drawing for the AGP. The habitat (shown on the left with a standing subject) is located eccentric to the platform center to subject the subjects and module contents to centrifugal force up to 2 times the gravity normally experienced on Earth. The motor drives (*in red*) are placed along the platform‘s perimeter. In the center (right side of cartoon) the rotating and radial transition units can be seen. Note human figures standing in the center of the AGP, while a subject is located in a 45° tilted cabin while the AGP is running with a total load to the subject of √2g.*

?? In the current configuration the platform has a design mass of about 1000 metric tons. The rotating the structure is foreseen by means of electric linear motors located at the perimeter, a system based on existing MAGLEV technology (Gieras et al., 2012). The absence of mechanical wear ensures the required autonomy for long-duration studies. The location of the active components on the non-moving part (around the platform) allows for easy access for maintenance and repair during rotation.

The static center area will be safely accessible for goods and people by means of an underground tunnel. This center area could also host a visitor center with an observation deck that will be used for public outreach and educational purposes. Around and level with the rotating platform an area will give direct access to the platform when it is stationary. This area will be used for technical work on the system and for emergency exits. Evacuation from the platform could also be done towards the center by using the resupply unit during rotation or by stepped corridors in the platform structure during non-rotation.

The platform is weather protected by means of a dome-shaped roof structure. This guarantees stable conditions inside and gives full control of the aerodynamic aspects of the rotating structures. Technical installations will be in the non-rotating center, around, and under the rotating platform. A Mission Control Center will include facilities for preparing experiments and technical, operational, and maintenance areas. The large unobstructed roof surface could accommodate a field of solar photovoltaic panels to reduce the running cost of the facility. The objective is to construct a low energy building using passive solar gains and cogeneration principles, thus making the best use of waste energy and heat dissipation of its technical systems to further reduce the energy demand. Furthermore, the building will require a medical facility in order to guarantee the safety and medical follow-up of test subjects. A location near an existing hospital is recommended.

Scope of the AGP project

After 50 years of bioastronautics research, human space flight has entered a new phase of exploration towards the Moon, Mars, and asteroids. In that context, the primary objective of the next bioastronautics research program is to extend our knowledge of the effects of long-duration space flight on crew health and performance, further develop efficient countermeasures, and facilitate post-flight re-adaptation to the terrestrial gravitational environment (NASA, 2005). Such basic research is a prerequisite activity aimed at improving the capability for interplanetary travel and life on other planet surfaces, as the current countermeasures regarding the physiological and psychological changes associated with long-duration missions in orbit are far from being fully adequate.

The classical approach used so far in space research, which consisted of investigating adaptations to microgravity as per organ functions, needs to evolve toward a strong integrated model of the physio-pathological adaptation of multiple organ systems. Understanding the mechanisms of the adaptation of the human body as a whole to altered gravity conditions, including hypergravity, requires investigations from the molecular level up to integrated systems levels. Long-duration studies in the AGP, combining results obtained in a large population of both male and female subjects, together with a suite of contemporary instrumentation for human research, would significantly contribute to this knowledge.

Human missions to the Moon and Mars include long transit time in microgravity and stay in reduced gravity, as well as transitions in gravity levels during launch and re-entry. A better understanding of these transitions is essential to develop adequate countermeasures.

For decades, clinicians, physiologists and pshychologists have worked separately without taking full advantage of potential strong common interests and "cross-fertilization". This is also true for ground-based research, for example the research on ageing and chronic diseases. In our search for the environmental factors that fuel the pandemic of chronic diseases, we face a paradox. We know that our modern western societies have adopted a sedentary lifestyle. Such a lifestyle has been associated with an increased risk of numerous burdensome chronic diseases such as musculoskeletal, cardiovascular and coronary diseases, stroke, cancer, obesity and type 2 diabetes. Physical inactivity annually results in more than two million deaths worldwide and combined with a poor diet, is classified as one of the major causes of mortality (Agostini et al., 2010, Fogelholm, 2010; Thijssen et al., 2010). However, the causal relationships between sedentary behaviors and obesity and its related metabolic disorders are essentially based on observational epidemiological studies. We know from paired controlled animal studies where rats (Moran et al. 2001), hamster, rat, guinea pig, and rabbit (Katovich, 1978; Pace et al., 1985) or chickens (Smith et al., 1963) have been exposed to long duration chronic accelerations that fat mass decreases while bone density and cardiac capacity increases. Such observations deserve appropriate hypergravity human studies to see if these effects translate to humans.

Figure 2: Left: Human centrifuge, Karolinska Institute, Stockholm, Sweden. Right: DESDEMONA facility at TNO-Soesterberg, The Netherlands.

In the process of establishing more detailed design requirements for the AGP, two series of pilot experiments are foreseen, one in Stockholm (Sweden) in the Karolinska Institute (Petersson J., 2006) where a 7.25 m radius centrifuge is operating, and one pilot study at TNO Soesterberg (the Netherlands) with the DESDEMONA facility (Bles et al., 2009) (See Figure 2).

A major issue regarding the use of centrifuges concerns spatial disorientation and vertigo caused by Coriolis forces and cross coupling angular accelerations, when a subject moves in a rotating environment (Dizio et al., 2001; Elias et al., 2008; Eyeson-Annan et al., 1996; Muth, 2000). The pilot experiments mainly aim at determining levels of threshold and susceptibility for spatial disorientation, sensorimotor coordination and motion sickness in groups of healthy volunteers and results from such studies will inform the final AGP design.

CONCLUSIONS AND FUTURE DIRECTIONS

After many decades, in which the main task for progress in medicine was to collect the "parts catalogue" of the human body and uncover molecular regulatory mechanisms, the challenge for the first decades of the 21st century in medicine is to unify the respective knowledge and enable a more integrative and individualized medicine. Space biology and medicine integrate complex studies on humans and are therefore well suited to this challenge. The AGP offers great potential for successful steps in this endeavor.

The transition of gravity research from physiological functions to a more integrated approach requires a focused, competitive research strategy for solving targeted risks of human health and individual and group performance. Reaching these goals and measures will not only provide the basis for critical, high quality health care for crews on orbit, but also result in a wealth of novel physiological and psychological data to investigate. Studies performed in the AGP will undoubtedly yield solutions for the medical challenges for long-term space missions. The lessons learned will provide the basis for evidence-based decisions of issues such as immunology, mineral metabolism, protein synthesis, chronobiology, cardiology, and nutrition in space taken as a whole. The AGP will also provide the basis for the design and testing of new countermeasures to be used both in space and on Earth in ageing, rehabilitation, or training.

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