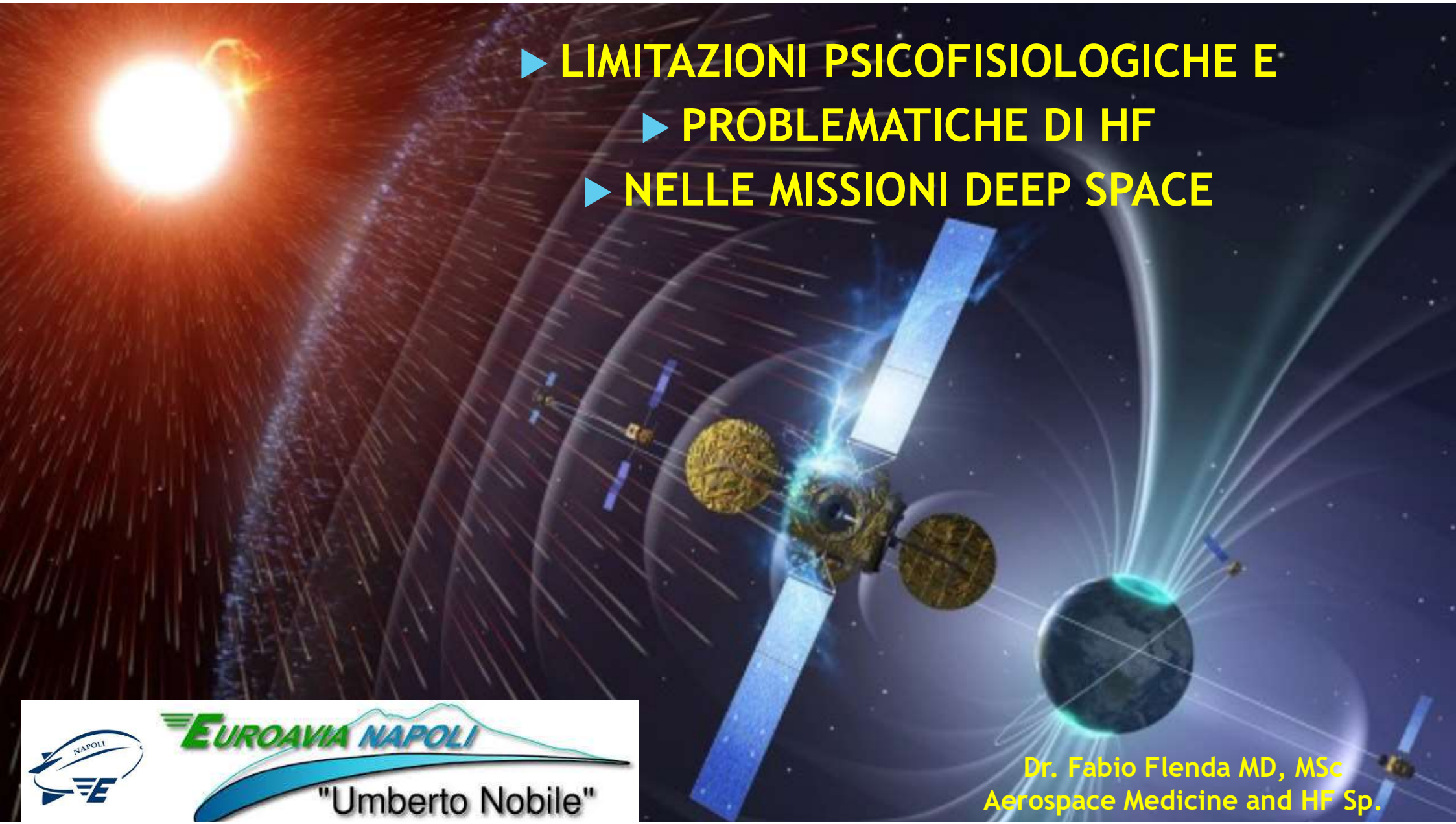
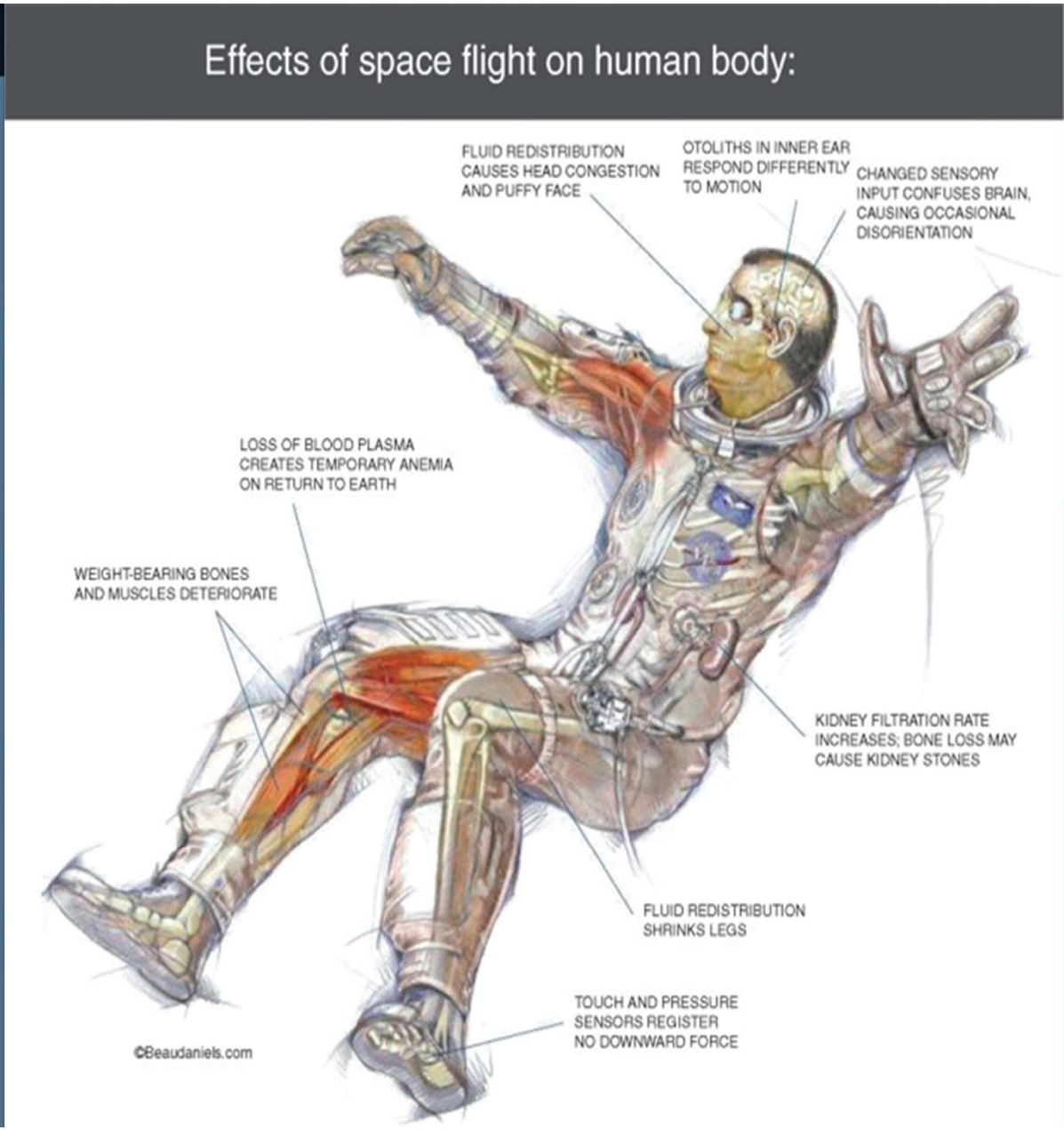


LIMITAZIONI PSICOFISIOLOGICHE E PROBLEMATICHE DI HF NELLE MISSIONI DEEP SPACE

Dr. Fabio Flenda MD, MSc
Aerospace Medicine and HF Sp.

EUROAVIA NAPOLI
"Umberto Nobile"


Short-term physiological alterations
Long-term physiological alterations
Central fluid shift (nasal and sinus congestion, headache)
Neurovestibular changes associated with motion sickness
Back pain
Anxiety
SANS
Transient orthostatic symptoms on reexposure to gravity
Bone density loss
Nephrolithiasis
Radiation-induced changes
Muscle deconditioning


Effects of space flight on human body:
FLUID REDISTRIBUTION CAUSES HEAD CONGESTION AND PUFFY FACE
OTOLITHS IN INNER EAR RESPOND DIFFERENTLY TO MOTION
CHANGED SENSORY INPUT CONFUSES BRAIN, CAUSING OCCASIONAL DISORIENTATION
LOSS OF BLOOD PLASMA CREATES TEMPORARY ANEMIA ON RETURN TO EARTH
WEIGHT-BEARING BONES AND MUSCLES DETERIORATE
KIDNEY FILTRATION RATE INCREASES; BONE LOSS MAY CAUSE KIDNEY STONES
FLUID REDISTRIBUTION SHRINKS LEGS
TOUCH AND PRESSURE SENSORS REGISTER NO DOWNWARD FORCE
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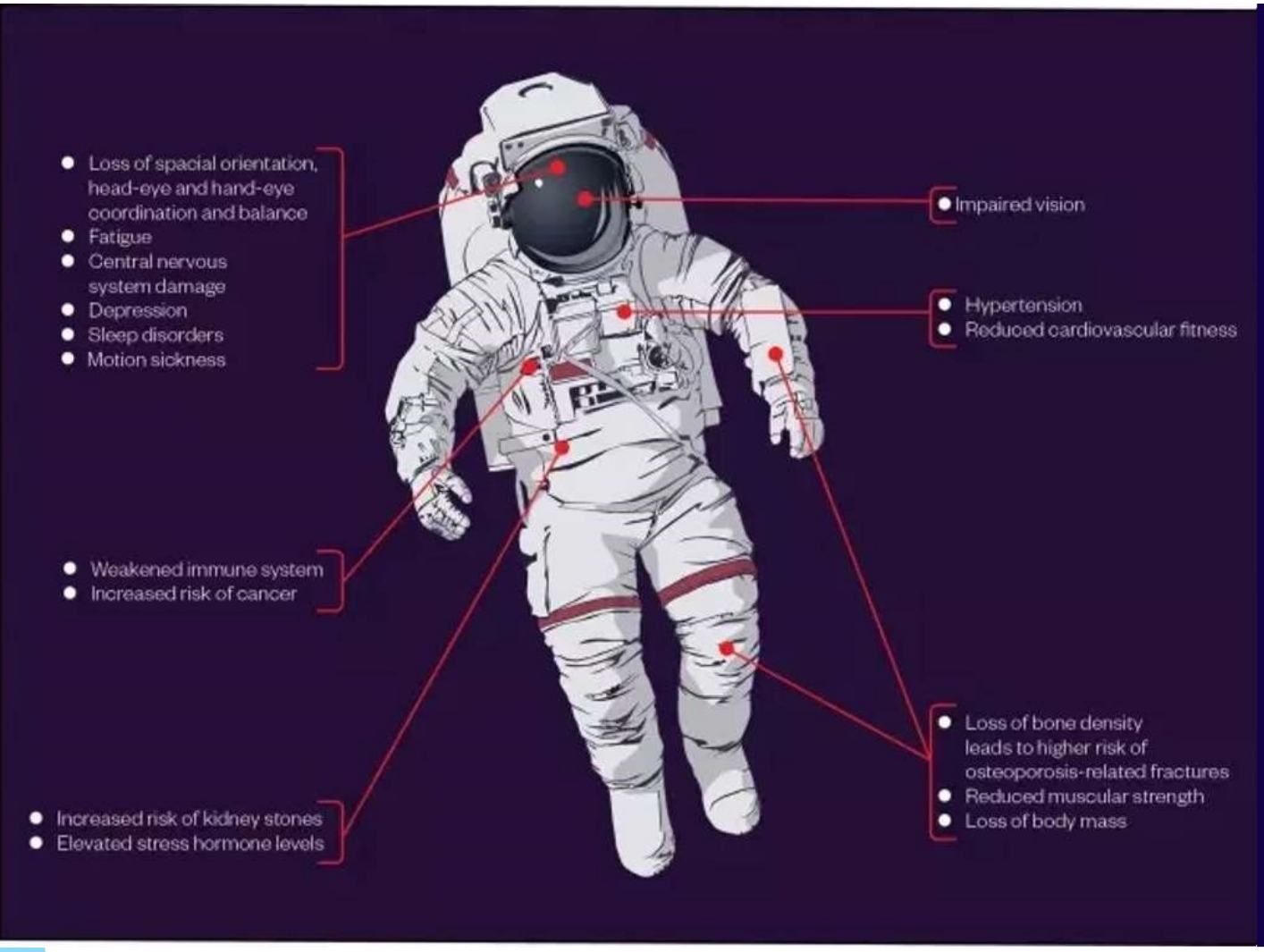
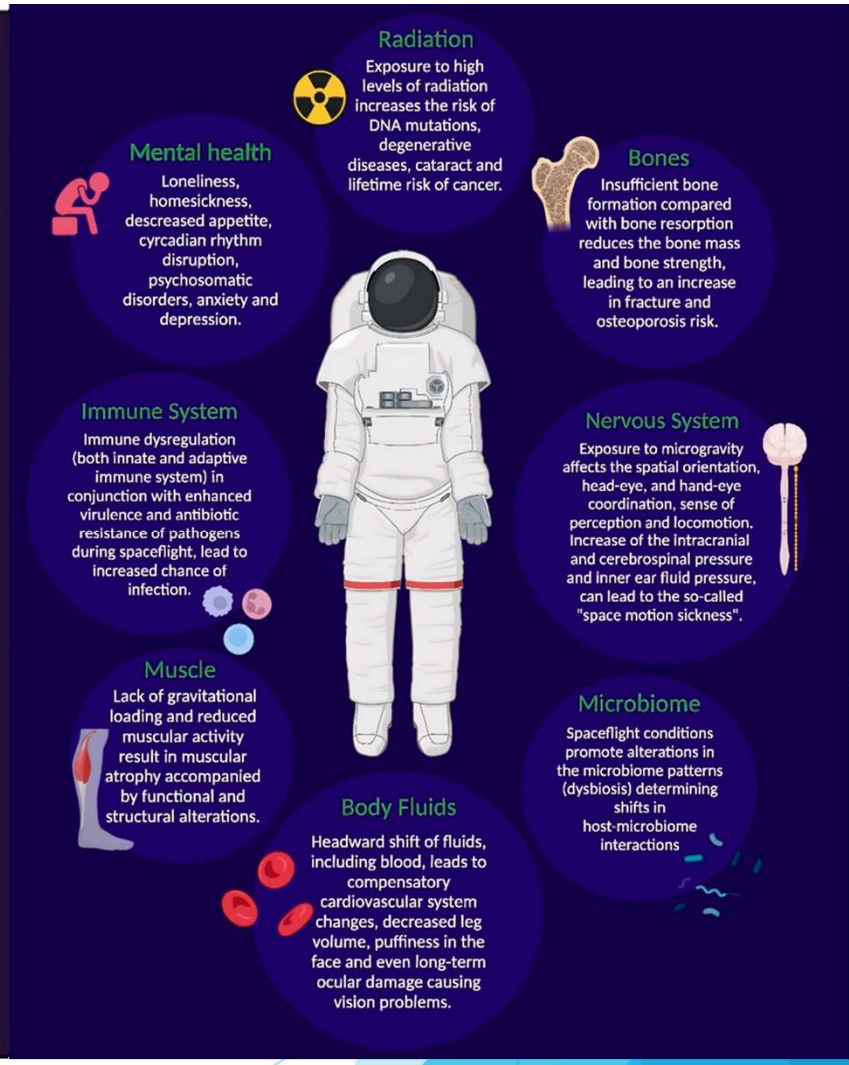

Loss of spacial orientation, head-eye and hand-eye coordination and balance
Fatigue
Central nervous system damage
Depression
Sleep disorders
Motion sickness
Impaired vision
Hypertension
Reduced cardiovascular fitness
Weakened immune system
Increased risk of cancer
Increased risk of kidney stones
Elevated stress hormone levels
Loss of bone density leads to higher risk of osteoporosis-related fractures
Reduced muscular strength
Loss of body mass


Radiation
Exposure to high levels of radiation increases the risk of DNA mutations, degenerative diseases, cataract and lifetime risk of cancer.
Mental health
Loneliness, homesickness, descreased appetite, cyrcadian rhythm disruption, psychosomatic disorders, anxiety and depression.
Bones
Insufficient bone formation compared with bone resorption reduces the bone mass and bone strength, leading to an increase in fracture and osteoporosis risk.
Immune System
Immune dysregulation (both innate and adaptive immune system) in conjunction with enhanced virulence and antibiotic resistance of pathogens during spaceflight, lead to increased chance of infection.
Nervous System
Exposure to microgravity affects the spatial orientation, head-eye, and hand-eye coordination, sense of perception and locomotion. Increase of the intracranial and cerebrospinal pressure and inner ear fluid pressure, can lead to the so-called "space motion sickness".
Muscle
Lack of gravitational loading and reduced muscular activity result in muscular atrophy accompanied by functional and structural alterations.
Microbiome
Spaceflight conditions promote alterations in the microbiome patterns (dysbiosis) determining shifts in host-microbiome interactions
Body Fluids
Headward shift of fluids, including blood, leads to compensatory cardiovascular system changes, decreased leg volume, puffiness in the face and even long-term ocular damage causing vision problems.

Problemi medici noti del Volo Spaziale per gli Astronauti:

- **Decondizionamento cardiocircolatorio, barocettivo e ridistribuzione centrale e cefalico dei fluidi (Fluid Shift) in microgravità**
- (es: «**Puffy Face**» e «**Chicken legs**», ipertensione endocranica, congestione nasale, ageusia)
- **Intolleranza ortostatica** al rientro a 1G
- **Perdita trofismo e massa muscolare con alterazioni della densità e della composizione ossea** (**Osteoporosi** e **Sarcopenia** spaziale)
- Modificazioni ematologiche: **Space Anemia**
- **Disidratazione ed ipovolemia**
- **Iperviscosità temporanea ematica con trombofilia relativa**
- **Rischio DCS ed aerombolico** per ipobarismo nelle operazioni **EVA**
- Alterazioni renali e sistema emuntorio (calcolosi renale, Nefrolitiasi)
- **Modificazioni Sistema Immunitario** anergia dell'immunità cellulo mediata e suscettibilità infezioni
- **Space Adaptation Syndrome** (Nausea, Vomito, Vertigini)
- **Alterazioni ritmo circadiano durata e qualità del sonno** (flash retinici, fosfeni)
- **Problematiche psicologiche, emotive, umorali** per il confinamento prolungato, la mancanza di stimoli e lo spazio ristretto nelle dinamiche di team e nel **CRM** (Crew Resource Management)
- **Effetti stocastici e deterministici radiazioni ionizzanti**
- **Fatica Operativa e Stress**
- **Alterazioni ormonali (Catecolamine, Cortisolo)**
- **Perdita appetito, anoressia**

Problemi medici meno noti del Volo Spaziale per gli Astronauti:

- **Rischio cardiologico e cardiocircolatorio** (DVT e aritmogenicità missioni EVA)
- Disregolazione e alterazioni neurovestibolari
- **SANS (Space Associated Neurocular Syndrome) e Space Hyperopia**
- **Ernie del disco** da microgravità
- Effetti e modifiche del **microbioma intestinale**
- **Stress ossidativo cellulare** (ROS)
- **Fertilità e sessualità**
- **Gestione del lutto, PTSD e distacco emotivo** da perdita di contatto con la Terra nelle missioni Deep Space)

Eventi medici programma Shuttle NASA

Eventi medici occorsi ad astronauti USA durante il programma Space Shuttle (STS-1 fino al STS-89, dall'Aprile 1981 al Gennaio 1998)		
Eventi Medici ed apparati coinvolti secondo le categorie ICD9*	Numero	Percentuale del totale
"Space Adaptation Syndrome" (Sindrome di Adattamento Spaziale)	788	42.2 %
Sistema nervoso ed organi di senso	318	17.0 %
Apparato digestivo	163	8.7 %
Cute e tessuto sottocutaneo	151	8.1 %
Infortuni e traumi	141	7.6 %
Apparato muscolo scheletrico e connettivo	132	7.1 %
Apparato respiratorio	83	4.4 %
Segni e sintomi comportamentali	34	1.8 %
Malattie infettive	26	1.4 %
Apparato genitourinario	23	1.2 %
Apparato cardiovascolare	6	0.3 %
Disordini endocrini, metabolici ed immunitari	2	0.1 %
***International Classification of Diseases, 9th Ed.**		

Apparato cardiovascolare coinvolto 0.3% dei casi

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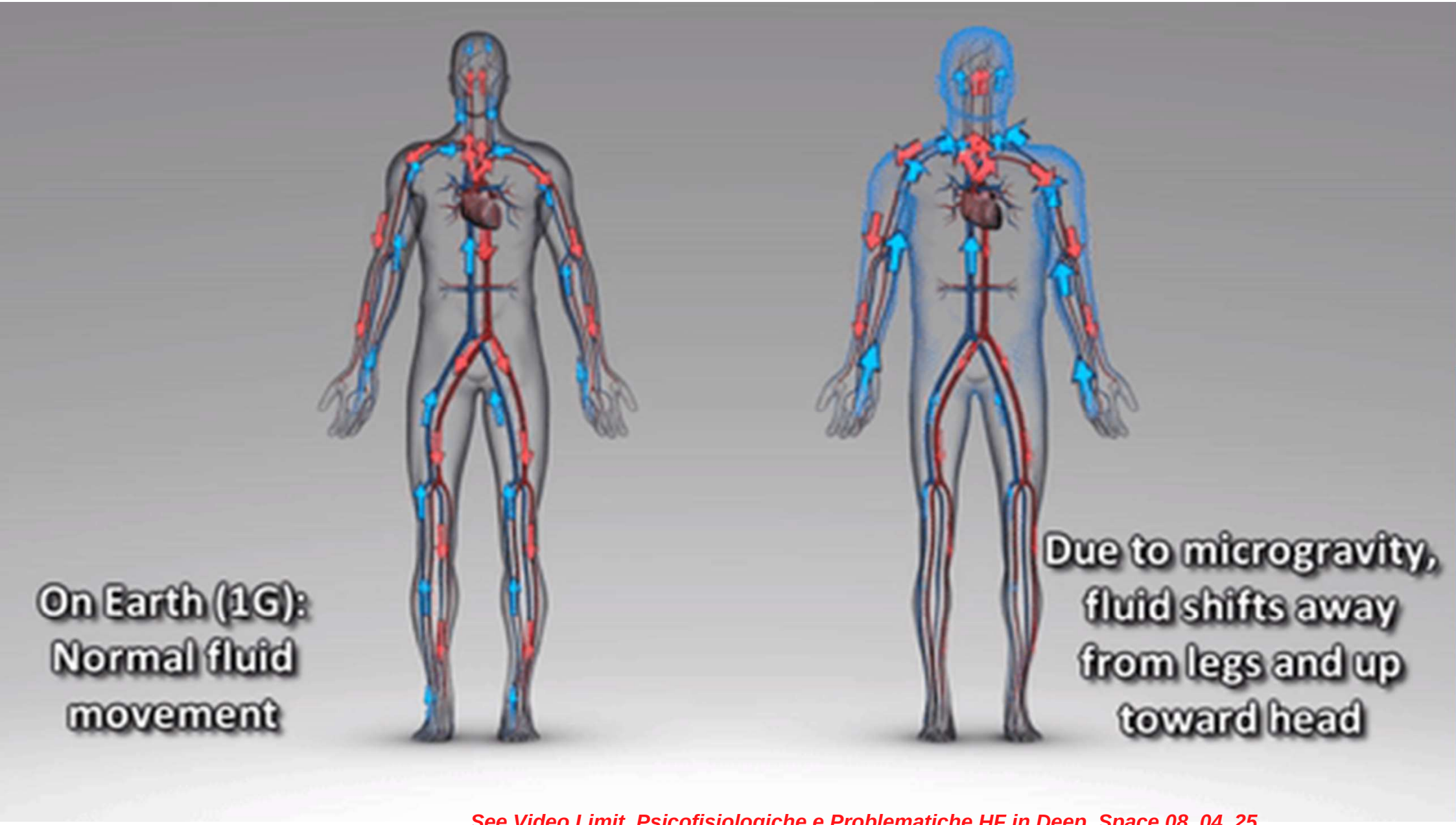
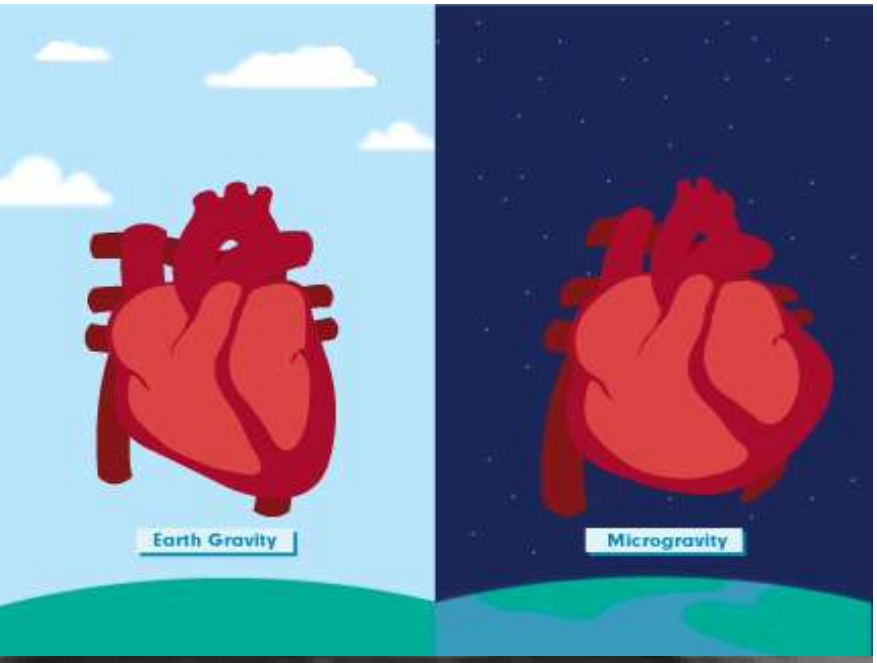
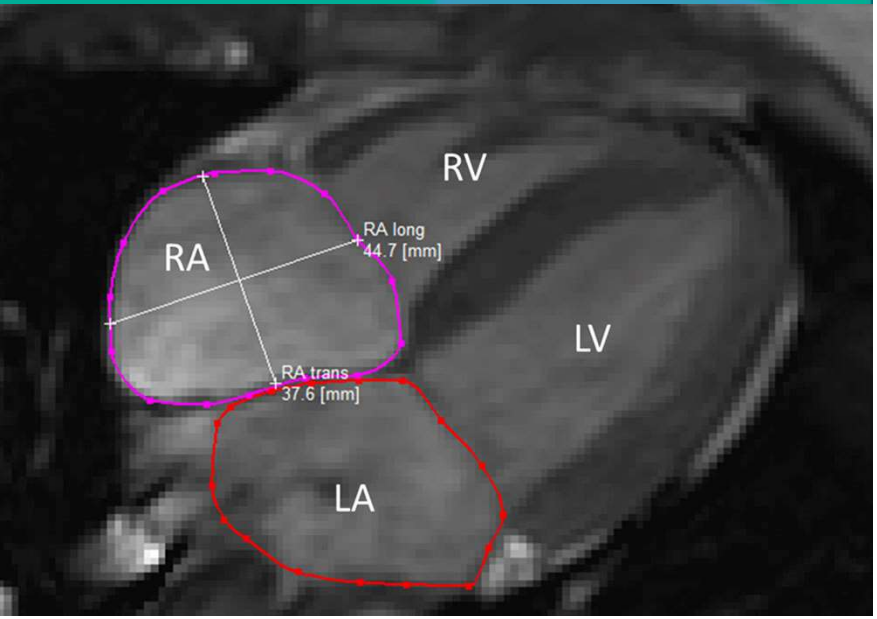
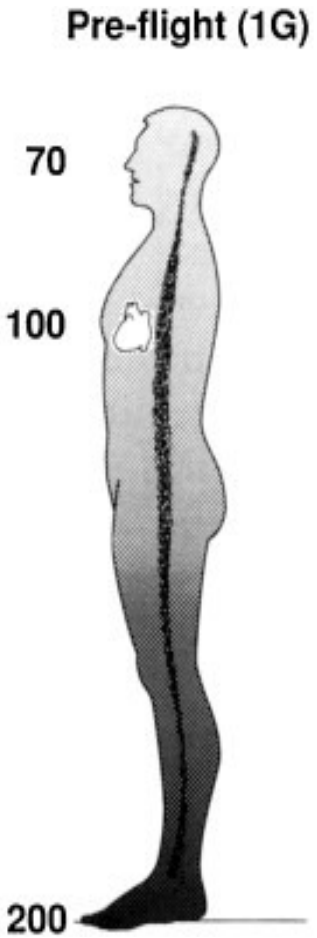
Alterazioni Cardiovascolari nel Manned Spaceflight

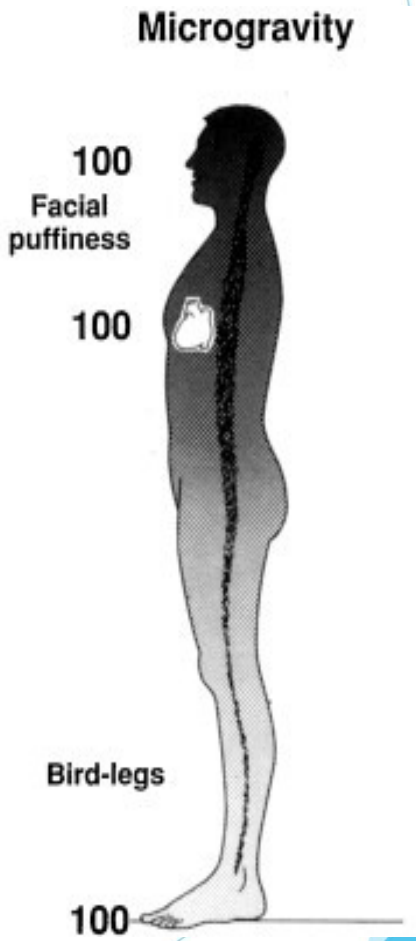


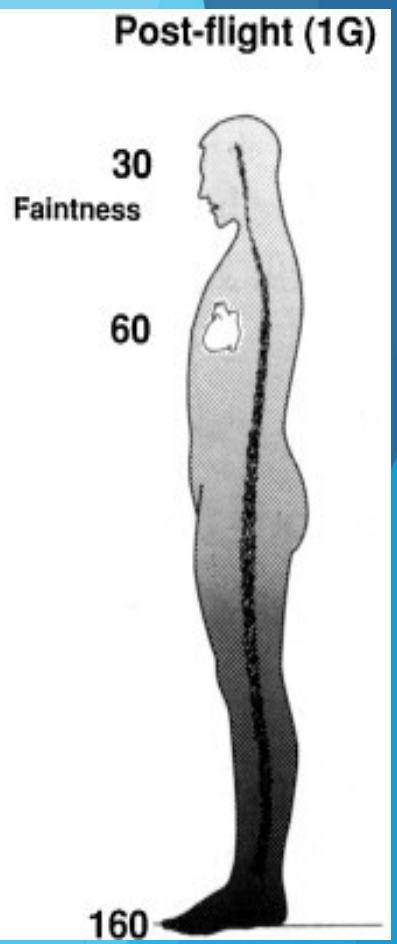
See Video Limit_Psicofisiologiche e Problematiche HF in Deep_Space 08_04_25
Slide n. 2


Earth Gravity
Microgravity


RV
RA
RA long
44.7 [mm]
LV
RA trans
37.6 [mm]
LA

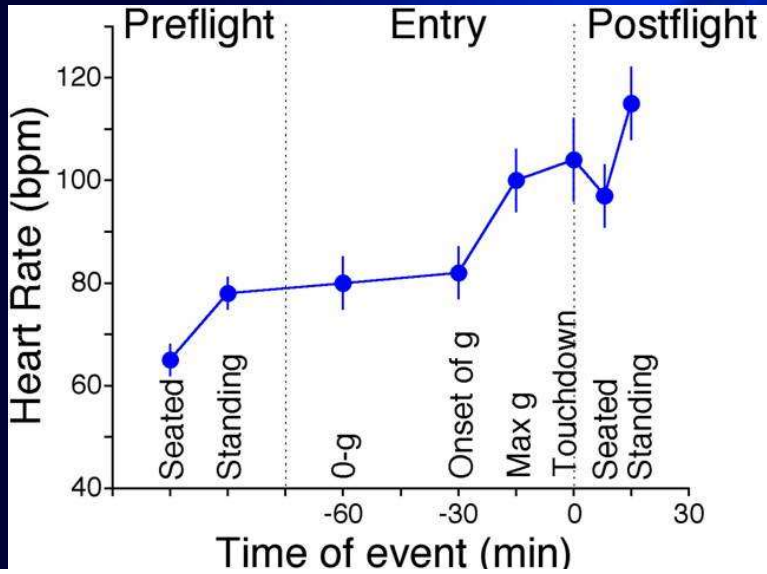

Pre-flight (1G)
70
100
200

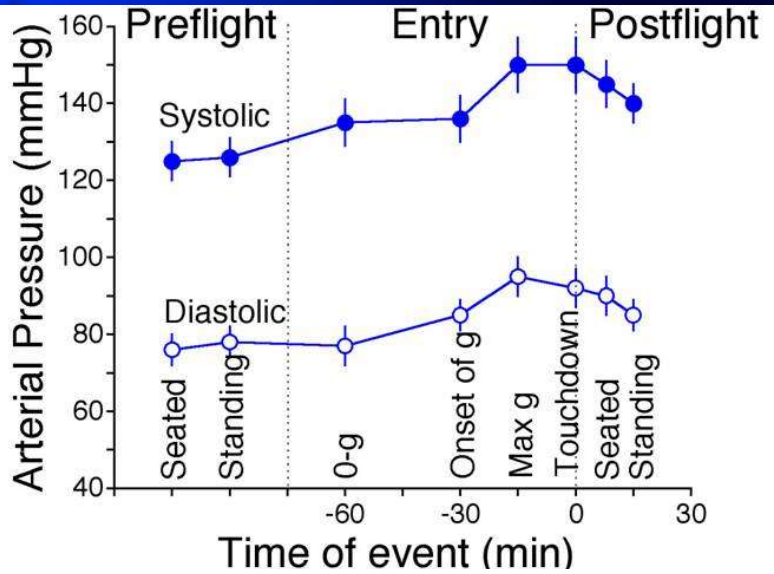

Microgravity
100
Facial
puffiness
100
Bird-legs
100


Post-flight (1G)
30
Faintness
60
160

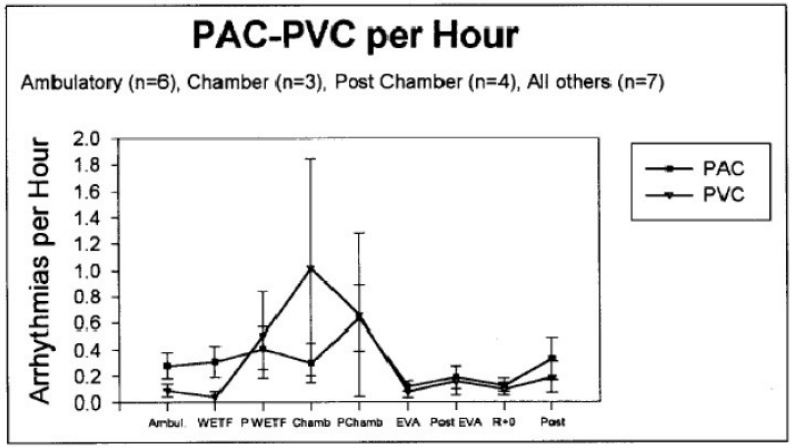
Post-flight orthostatic intolerance

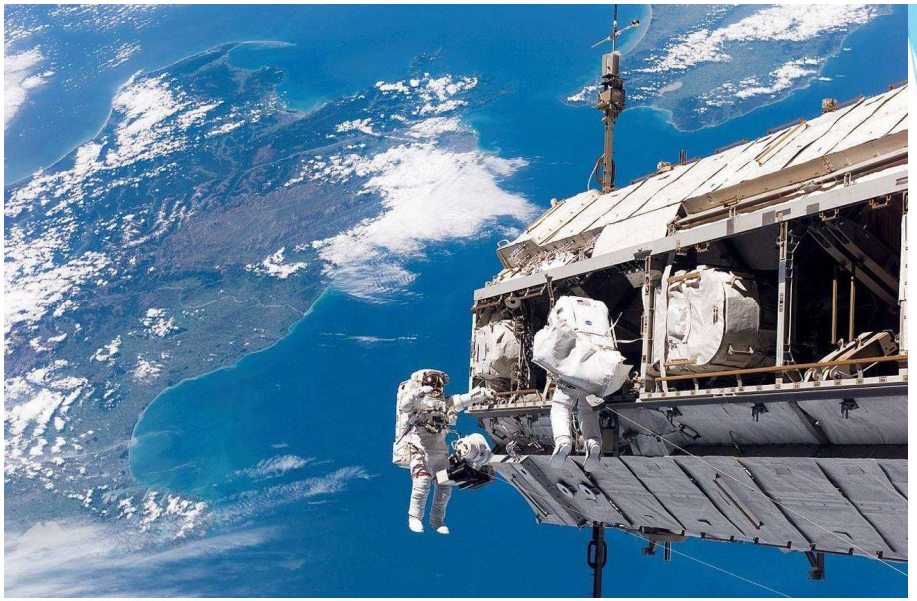
- 27% after Shuttle flights did not complete 10min. stand test (64 % after long flights – 6mo);
- variable symptoms and muvement effect (activation of the muscle pump)

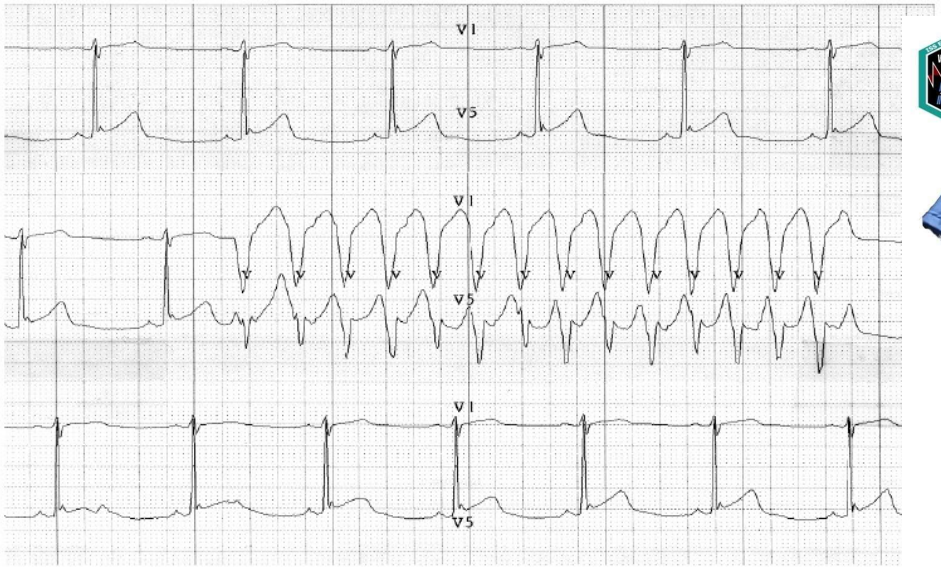




Caso I Aritmia in EVA







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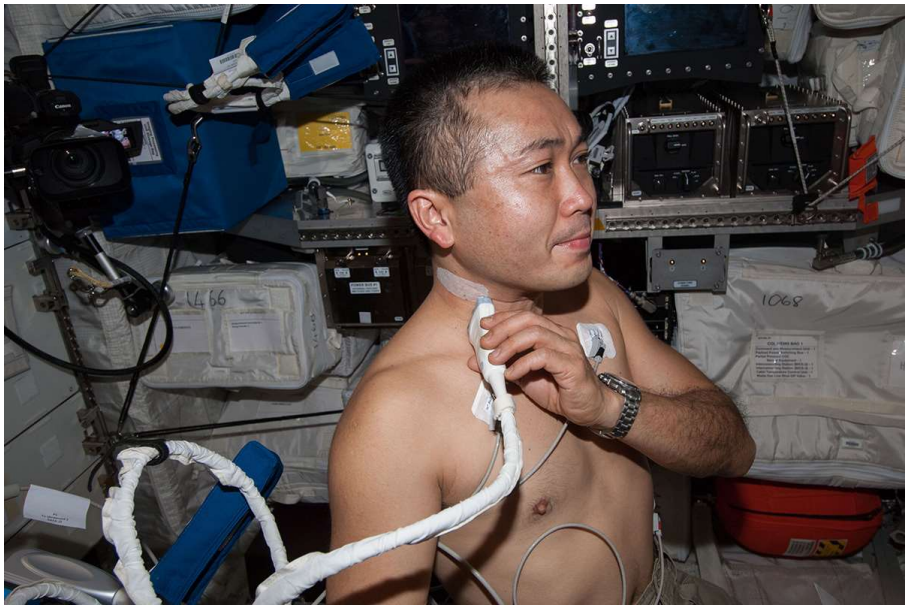
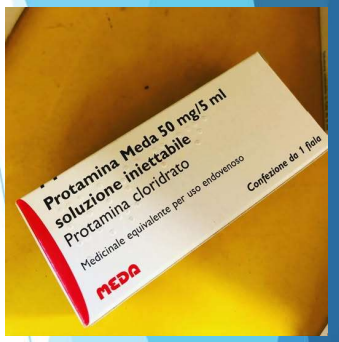
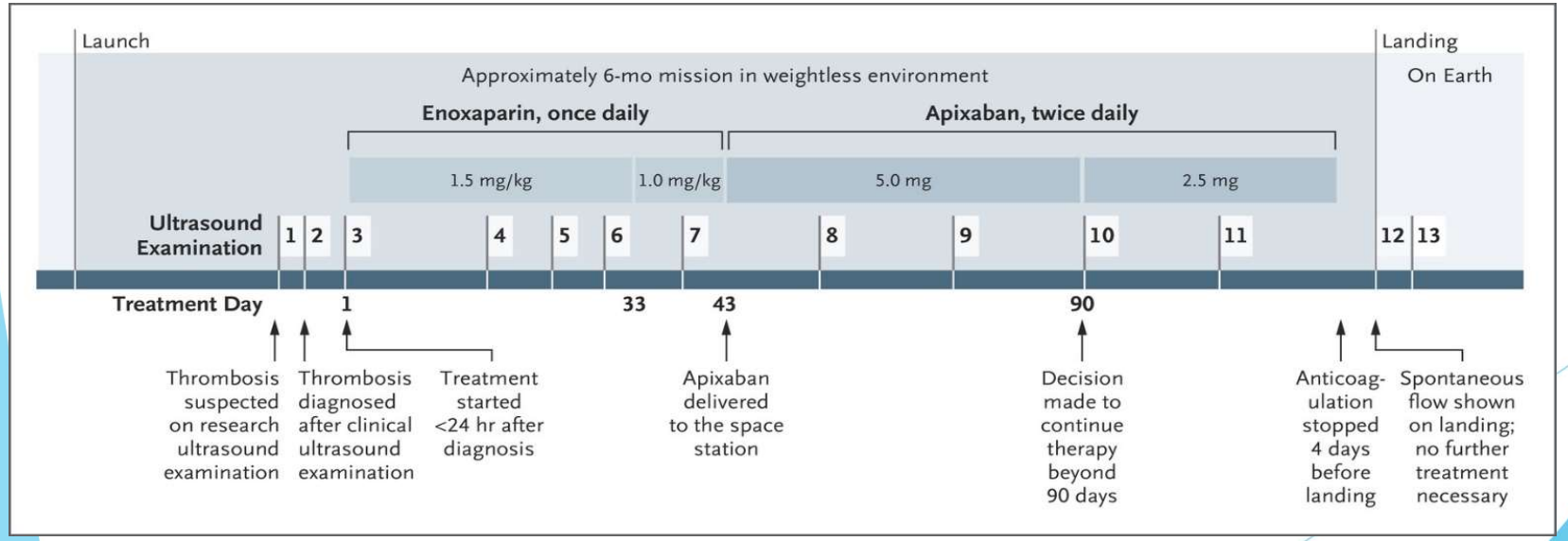




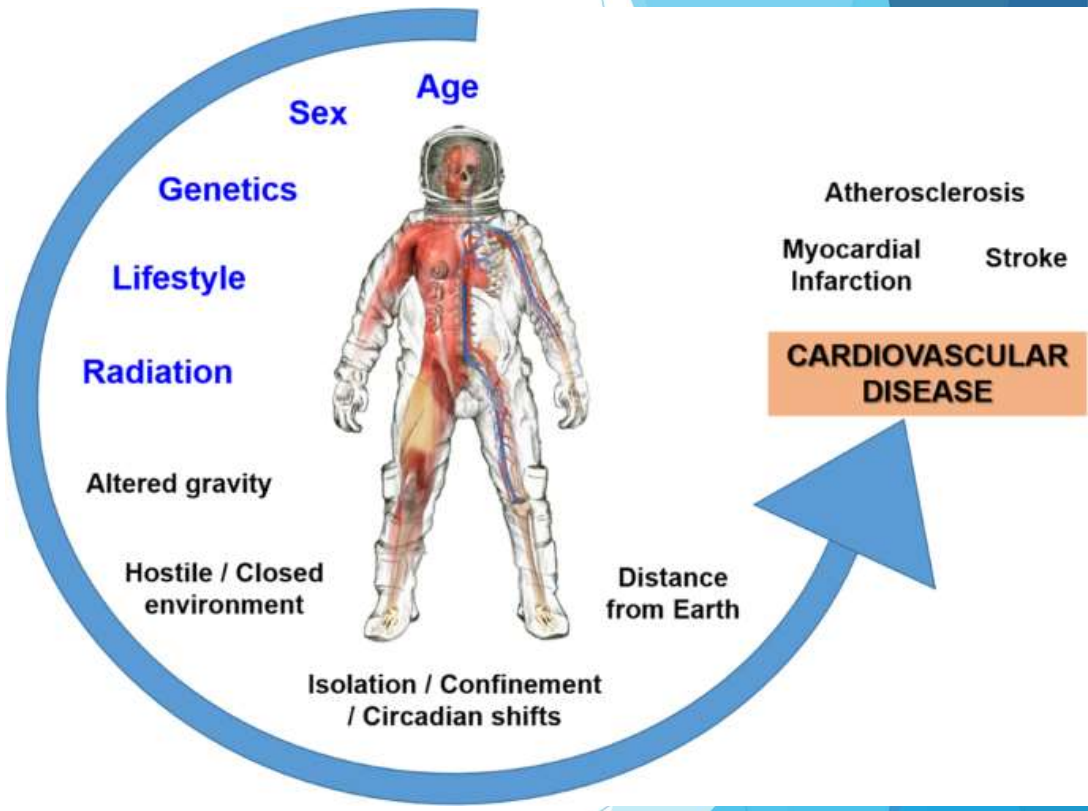


Caso II DVT (Deep Venous Thrombosis)

Sintomi della DVT spaziale

- Totalmente asintomatico riscontro causale durante ecodoppler TSA
- Assenza della cefalea da iperafflusso e congestion faciale limitata (“Puffy face”)
- Cordone trombotico iugulare alla palpazione

- Fluid Shift
- Puffy face e Chicken legs
- Decondizionamento barocettori e miocardio
- Variazioni morfologiche ed anatomiche VS e AD
- Perdita di volume plasmatico ed ipovolemia (-10/20%)
- Variazioni PA e MAP (ca 100 mmHg in tutti i distretti)
- Minor GC (CO)-1.5 lt/min
- Minor introito liquidi
- Minor introito calorico
- Perdita massa muscolare ed ossea
- Minor resistenza fatica
- Disidratazione relativa
- Iperviscosità ematica
- Space Anemia
- Ipotensione ortostatica (Stand Test post volo)
- Iperincrezione catecolamine (fatica, stress)
- Aumento dello stress ossidativo (ROS)
- Danno da radiazioni
- Trombofilia



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ARRESTO CARDIOCIRCOLATORIO (ACC) PER:

- Trauma
- Emorragia (in ipovolemia e space anemia)
- Sepsi
- Avvelenamento, inalazione tossici, farmaci
- Iper/ipotermia
- DCS, ipobarismo, iperventilazione
- Folgorazione, elettrocuzione
- Aritmia fatale (condizioni aritmogene in geneticamente predisposti o misconosciute)
- TEP (Trombo Embolia Polmonare) per DVT, aeroembolismo

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Problemi CPR/BLS/ALS in microgravità:

- Necessità di vincolarsi al paziente o vincolare il paziente al CMRS
- Somministrazione di farmaci?
- Defibrillare DAE?
- Intubazione?
- Aspirazione?
- Parametri?
- ROSC?
- Durata?
- Stress?

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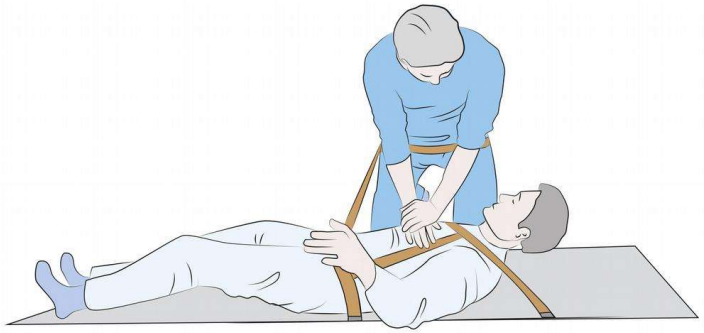

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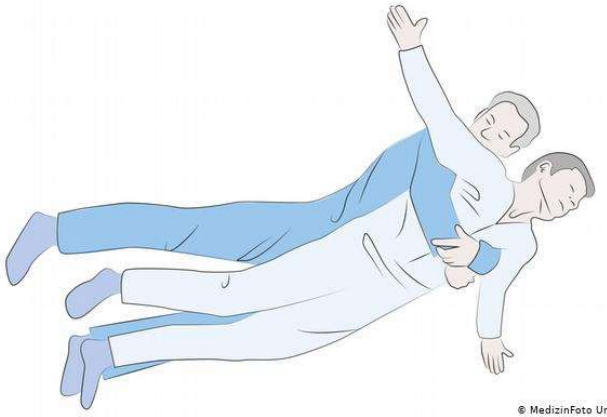

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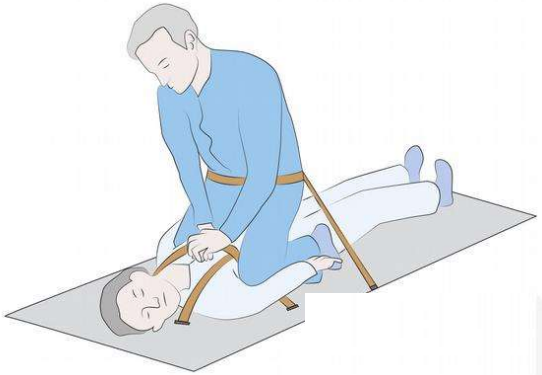

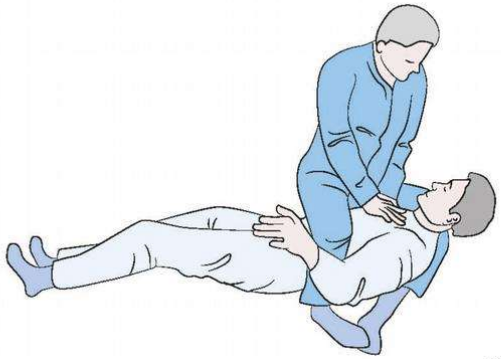

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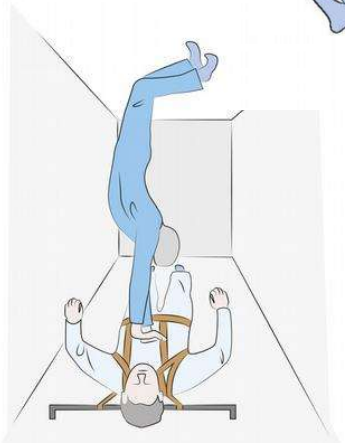

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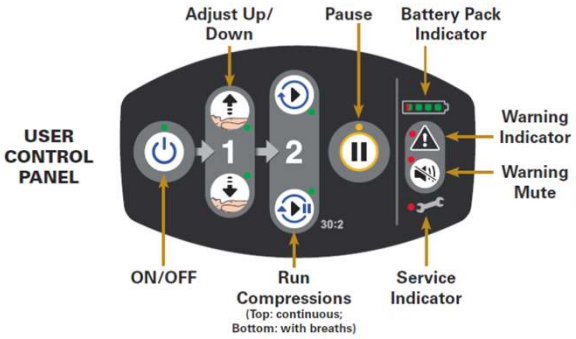

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Problemi non risolti:

- Gestione del **ROSC** (trombolisi, PTCA, emodinamica, ECMO)
- Emoderivati, polimeri di emoglobina o carrier Hb, utilizzo ALS
- Mancanza di **UTI** o **ICU** in una medical facility (Luna? Marte?)
- Chirurgia?
- **Quando terminare CPR chi decide? CMO? Commander? MCC?**
- **Problemi etici, emotivi, affettivi, culturali, religiosi**
- **Stress coping supporto psichiatrico, self care PC, psicofarmaci?**
- **Comunicazioni T/B/T (46') gestione cadavere**
- **Evacuare? Come?**
- **Missioni senza ritorno?**

ROSC: Return of Spontaneous Circulation
PTCA: Percutaneous transluminal coronary angioplasty (**Angioplastica percutanea**)
ECMO: Extracorporeal Membrane Oxygenation

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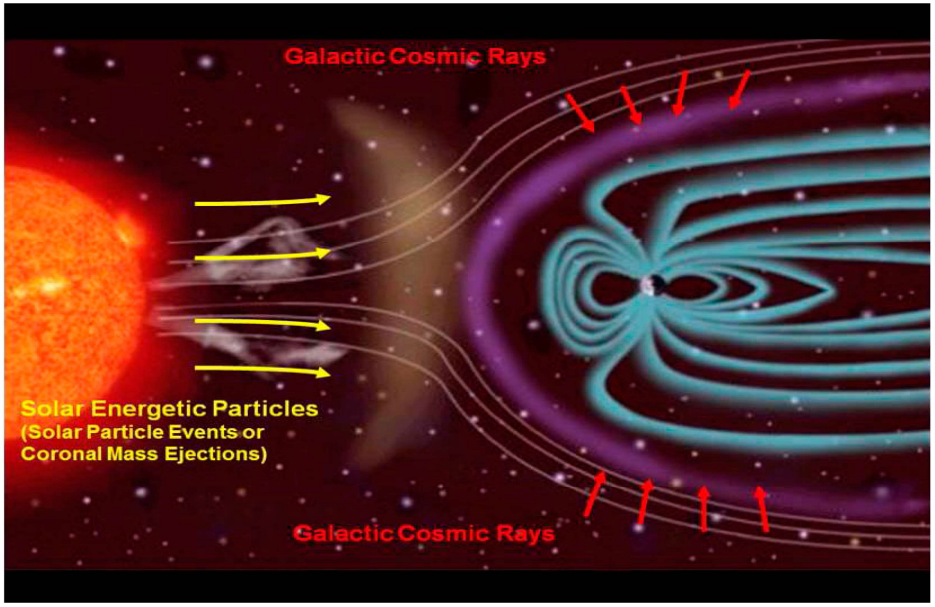

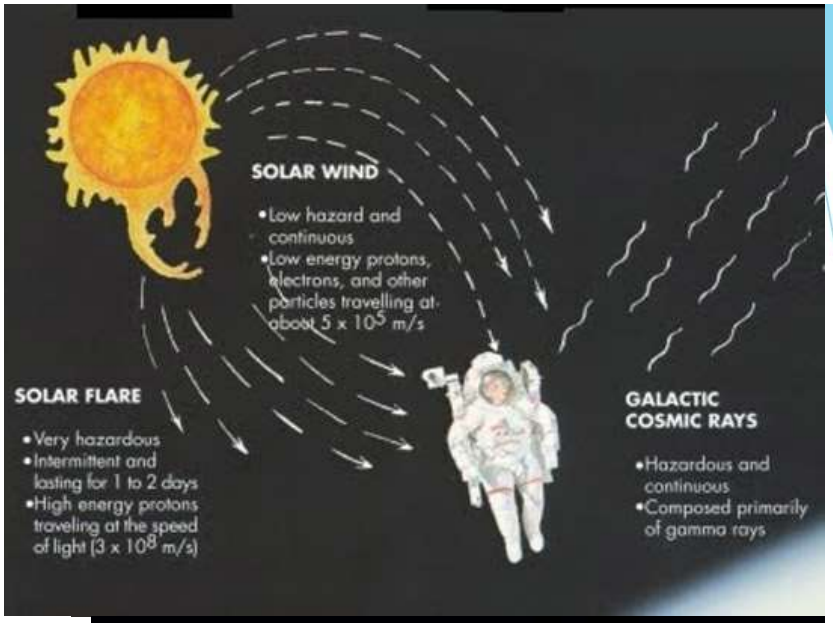

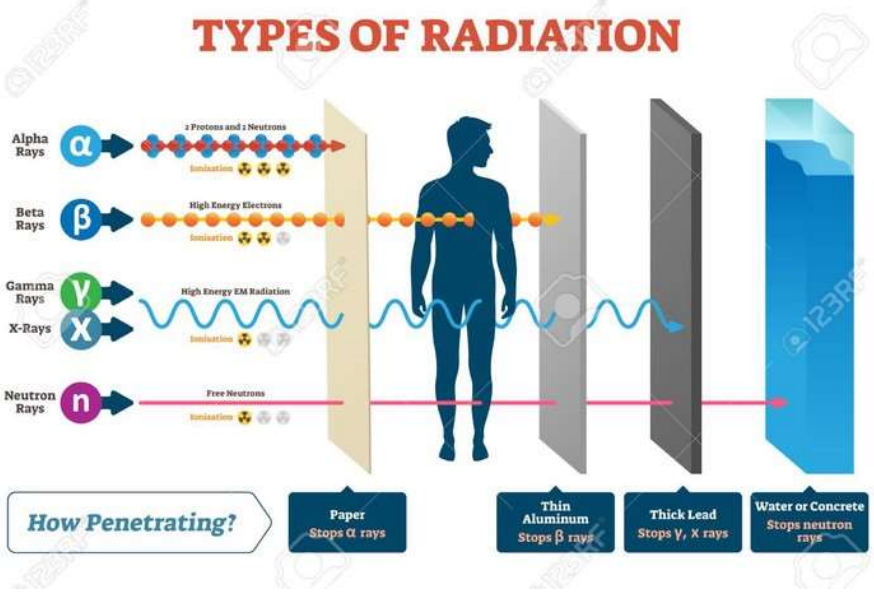

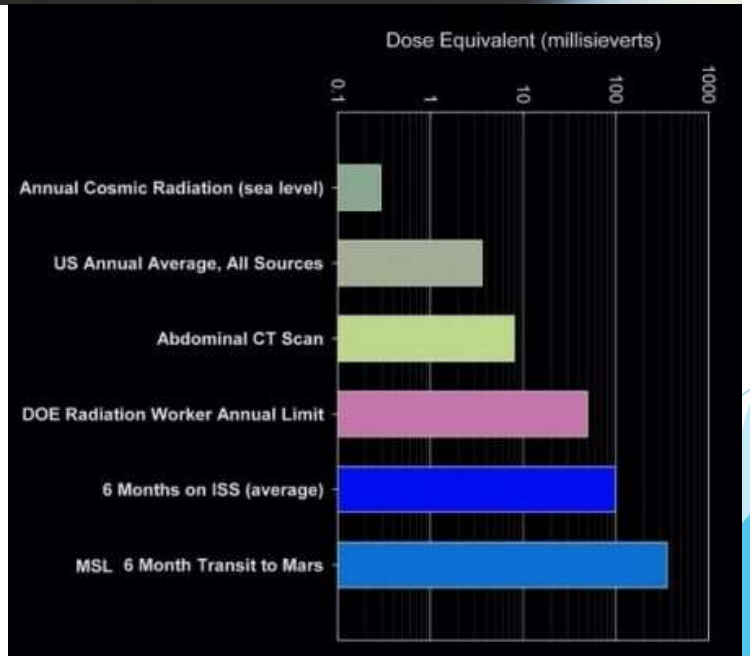

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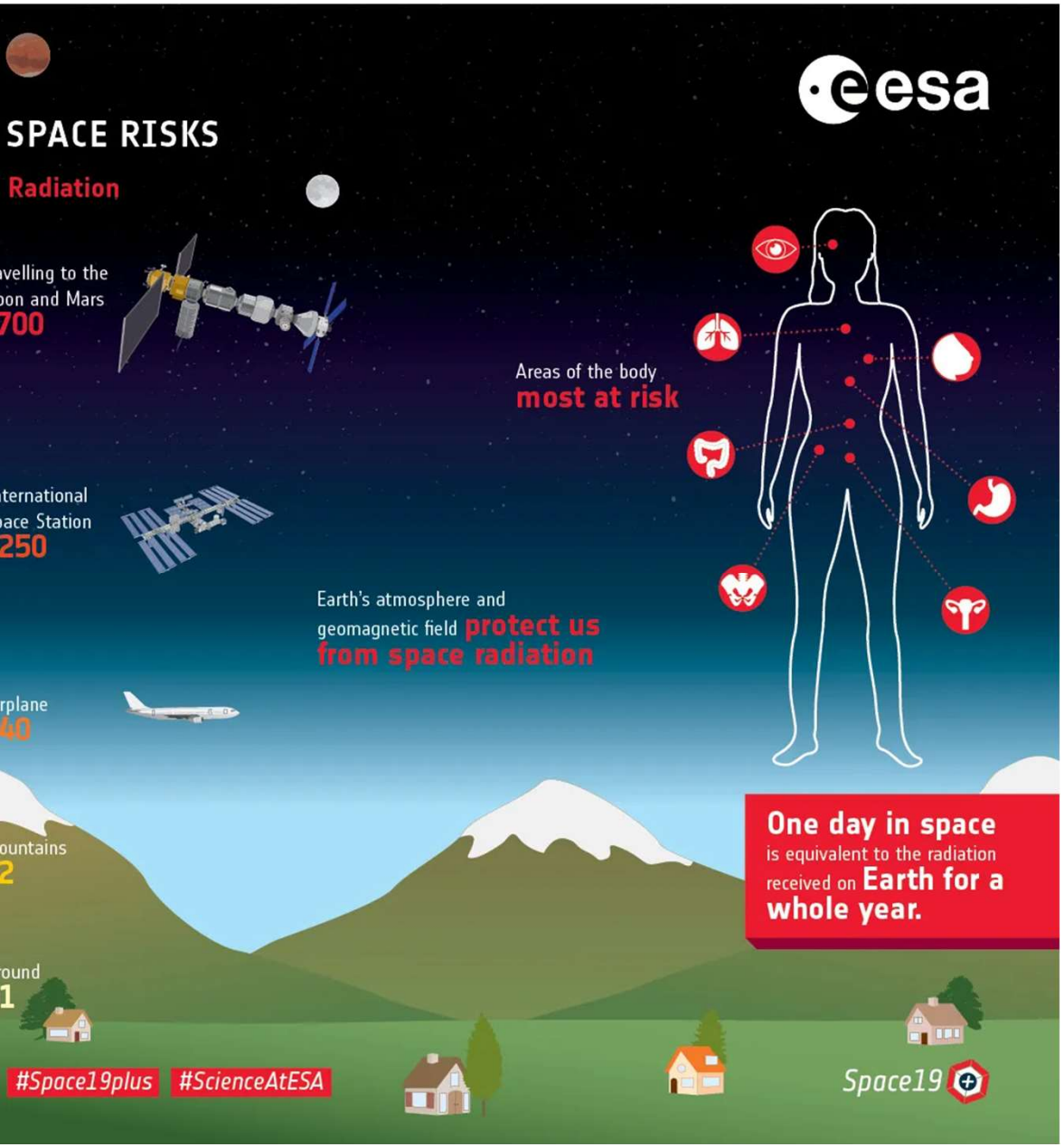
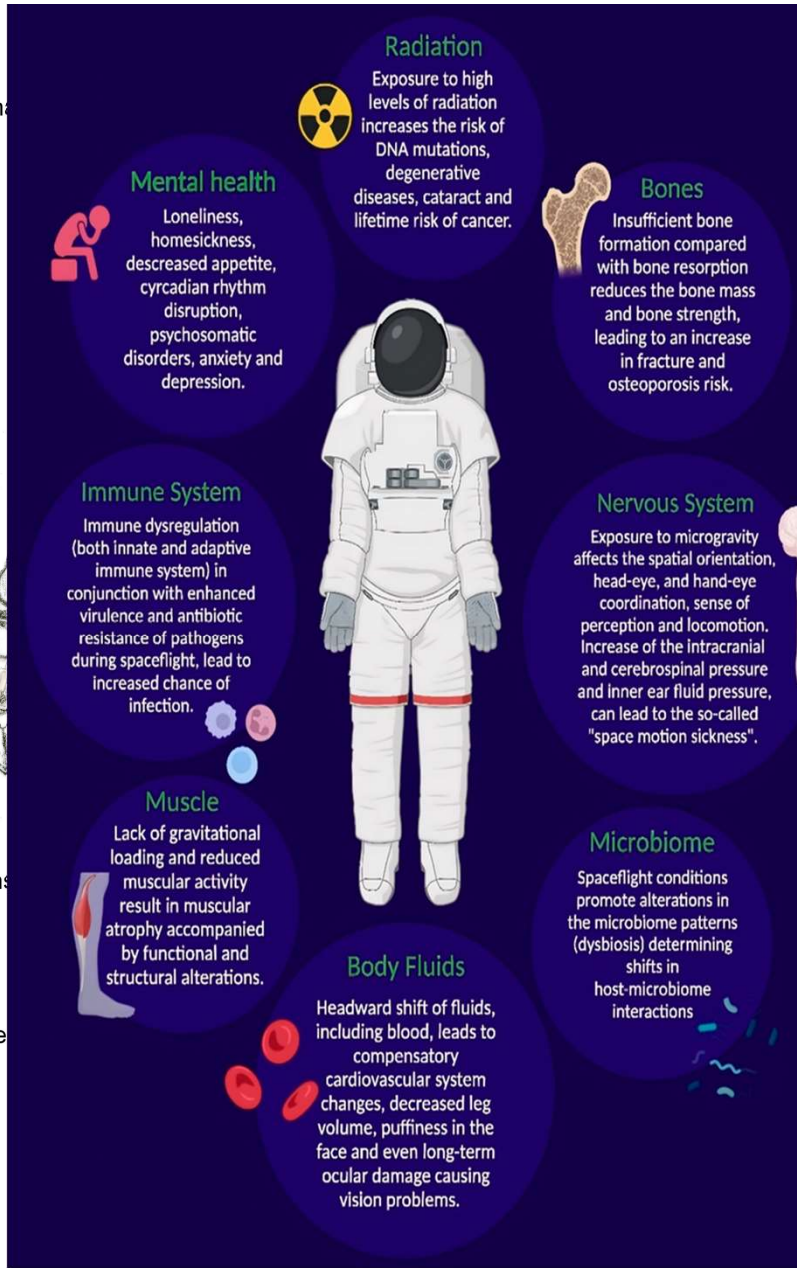


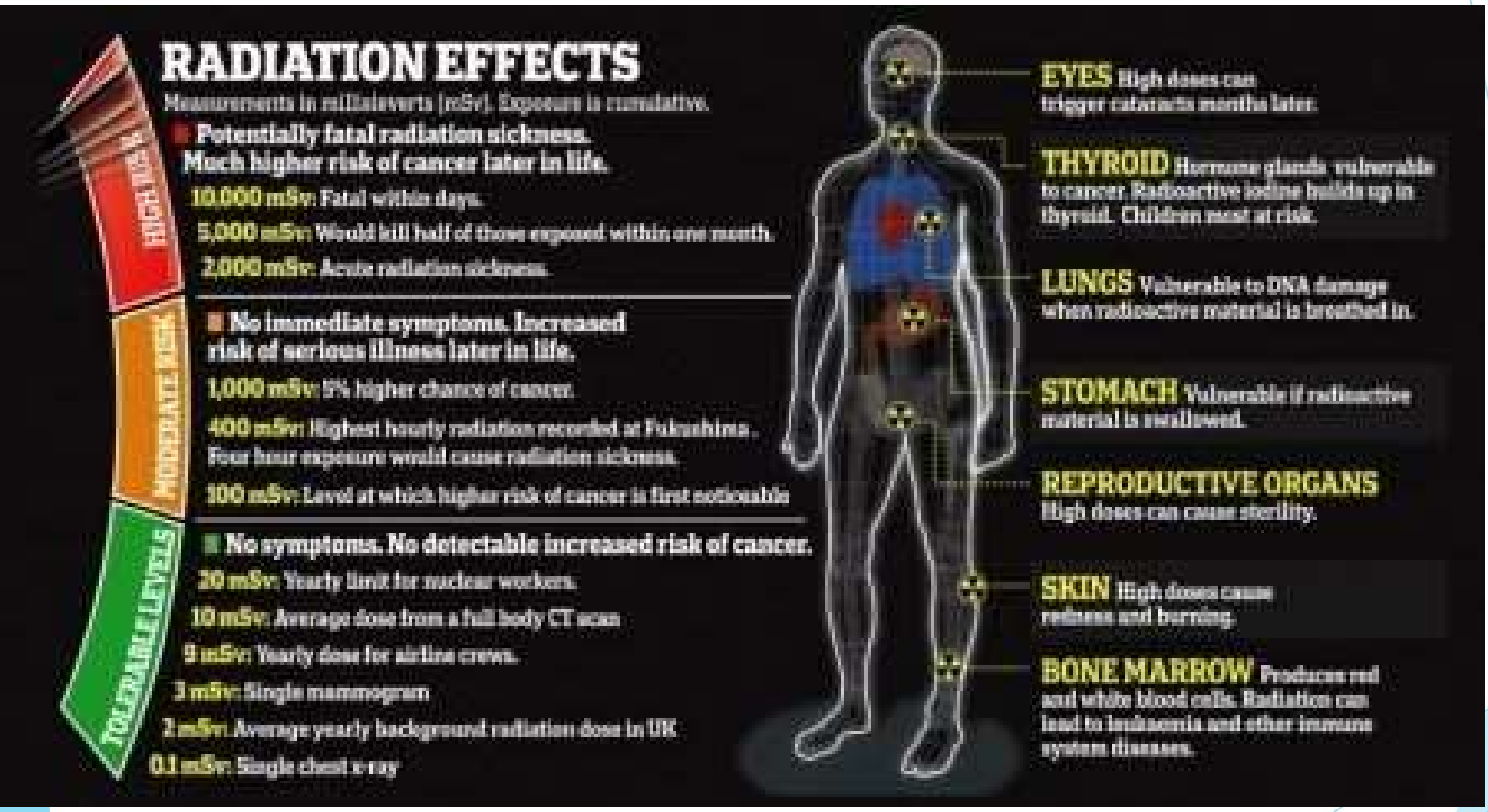
Cataract forma

Increased cancer risk

Skin burns

Changes to bone, muscle and cartilage microarchitecture




RADIATION EFFECTS
Measurements in millisieverts (mSv). Exposure is cumulative.
HIGH RISK
Potentially fatal radiation sickness. Much higher risk of cancer later in life.
10,000 mSv: Fatal within days.
5,000 mSv: Would kill half of those exposed within one month.
2,000 mSv: Acute radiation sickness.
MODERATE RISK
No immediate symptoms. Increased risk of serious illness later in life.
1,000 mSv: 5% higher chance of cancer.
400 mSv: Highest hourly radiation recorded at Fukushima. Four hour exposure would cause radiation sickness.
100 mSv: Level at which higher risk of cancer is first noticeable
TOLERABLE LEVELS
No symptoms. No detectable increased risk of cancer.
20 mSv: Yearly limit for nuclear workers.
10 mSv: Average dose from a full body CT scan
9 mSv: Yearly dose for airline crews.
3 mSv: Single mammogram
2 mSv: Average yearly background radiation dose in UK
0.1 mSv: Single chest x-ray
EYES High doses can trigger cataracts months later.
THYROID Hormone glands vulnerable to cancer. Radioactive iodine builds up in thyroid. Children most at risk.
LUNGS Vulnerable to DNA damage when radioactive material is breathed in.
STOMACH Vulnerable if radioactive material is swallowed.
REPRODUCTIVE ORGANS High doses can cause sterility.
SKIN High doses cause redness and burning.
BONE MARROW Produces red and white blood cells. Radiation can lead to leukaemia and other immune system diseases.

Age in Years	Dose Limit-Male Astronauts (Average Life-Loss Per Death in Years)	Dose Limit-Female Astronauts (Average Life-Loss Per Death in Years)
25	520 mSv (15.7)	370 mSv (15.9)
30	620 mSv (15.4)	470 mSv (15.7)
35	720 mSv (15.0)	550 mSv (15.3)
40	800 mSv (14.2)	620 mSv (14.7)
45	950 mSv (13.5)	750 mSv (14.0)
50	1150 mSv (12.5)	920 mSv (13.2)
55	1470 mSv (11.5)	1120 mSv (12.2)

NASA career effective dose limits (Sv) for a one year mission

Gender	Age at first exposure			
	30	40	50	60
Female	0.60	0.70	0.82	0.98
Male	0.78	0.88	1.00	1.17

NSCR Example Realistic Case

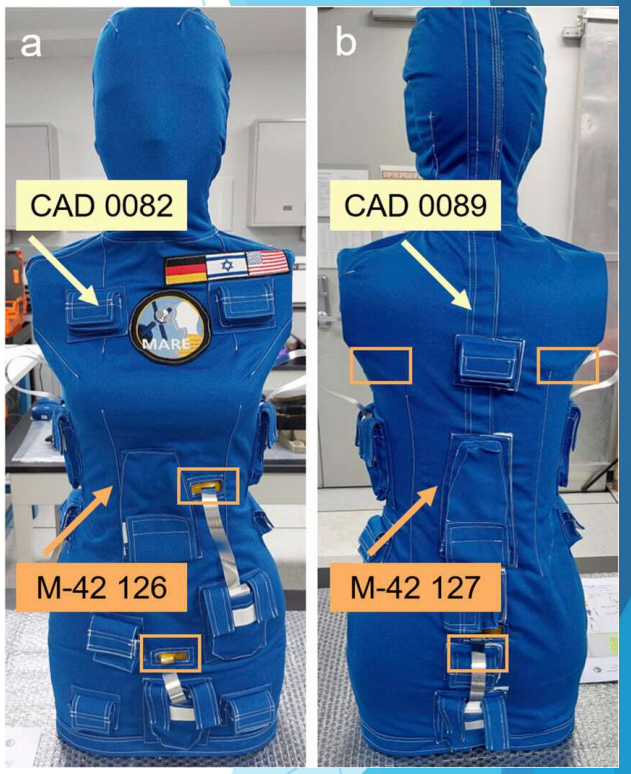
Results for first mission and Permissible Mission Duration (PMD) for a 2nd mission assignment

	Mission Duration [d]	Crew Dosimeter [mGy]	Effective Dose [mSv]	REIC P97.5% [%]	REID P97.5% [%]	Remaining PMD [d]
Male age 44y	320	135	210	3.9	1.9	211
Female age 44y	320	135	214	5.1	2.7	43

For the first ISS mission, the radiation exposure is less than the NASA SPEL (career limit for cancer is 3 percent REID evaluated at the upper 95th percent confidence interval).

For the astronaut's second ISS mission 3 years later (age 47y, same altitude but lower rates of radiation exposure):

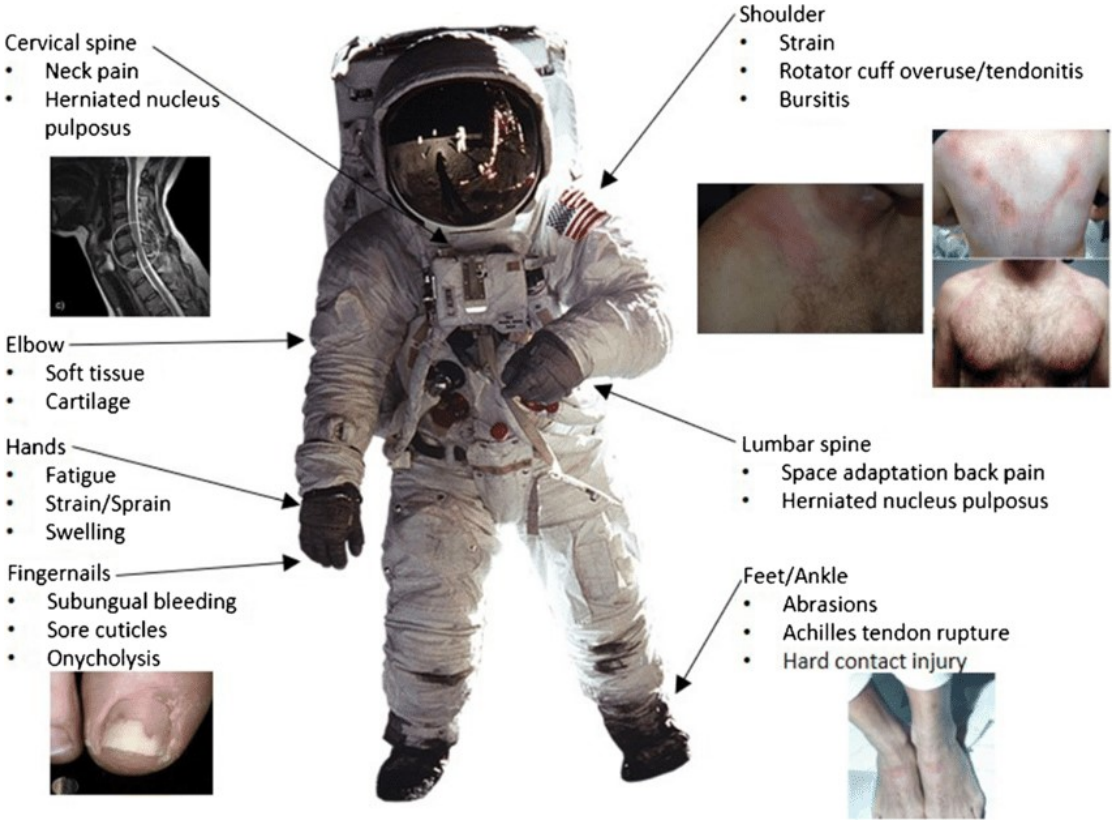
The male's career exposure would meet the SPEL for a planned ISS mission duration of 211 days.
The female's career exposure would meet the SPEL for a planned ISS mission duration of 43 days.



Under **NASA's** current approach, a 30-year-old female would be limited **to ~180 millisieverts (mSv)** of radiation exposure in space, whereas a **60-year-old male would be limited to ~700 mSv.**
For reference, a **180-day mission to the ISS would expose an astronaut to 50-120 mSv.**

Metodo:

1. Analisi retrospettiva delle **patologie di IVDD di 321 astronauti NASA ed ESA**
2. Studio prospettico longitudinale in vivo ed in vitro di 6 astronauti volontari e modelli animali **in 6 mesi di missione sull'ISS**
3. Confronto con popolazione del territorio di 1636 pazienti di cui 181 con LBP da IVDD



*Dati ufficiali estratti dai medical post mission reports degli Space Surgeons del Health and Medical Technical Authority (HMTA) della NASA e dell'ESA

Dati missione ISS su studio prosepettico longitudinale su 6 astronauti volontari (6 mesi) e dati animali su cavie murine e conigli missioni: COSMOS 2044, biosatellite Cosmos 1887 e STS-131 (Bailey et al., 2018)

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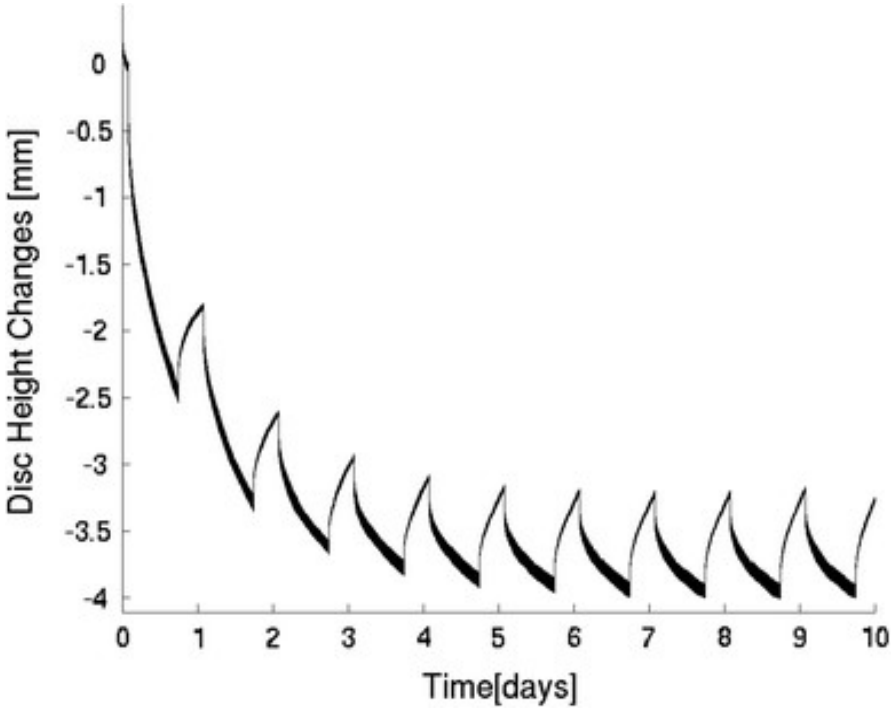

Riduzione altezza Disco Intervertebrale (IVD)
nei giorni dopo il rientro sulla Terra

Dr. Fabio Flenda

Evidenze: la microgravità e il volo spaziale agiscono come una macchina del tempo causando un aging rapidissimo

IN VIVO:

-Decondizionamento ipotrofia riduzione massa muscolare e perdita fibre della muscolatura paravertebrale anti gravitaria (multifidus)

-**Osteopenia e osteoporosi avanzata con assottigliamento dei somi vertebrali** ed erniazioni dei dischi intervertebrali (**alterazioni Modic** e **ernie intraspongiose di Schmorl**)

-Fissurazioni AF e lacerazioni della parte inserzionale dell'IVD, che appare ipertrofico con iperidratazione del NP con **neo innervazioni** della parte fibrosa legamentosa ed **ipervascolarizzazione reattiva**

-Aumento statura seduta ed in ortostatismo ma maggiore rigidità articolare

IN VITRO:

-Degenerazione matrice: perdita proteoglicani e GAG , alterazione strutturale collagene tipo I e II, alterazione rapporto collagene/GAG.

-Aumento attività metalloproteinasi che degenerano la matrice e attivazione cellule infiammazione, LT, macrofagi, PMN.

-Iperalgesia e **Allodinia** per rilascio nella matrice **TNF, IL1, IL6, NGF, BDGF**.

Può generarsi «tolleranza immunitaria» per i detriti discali e l'ernia.

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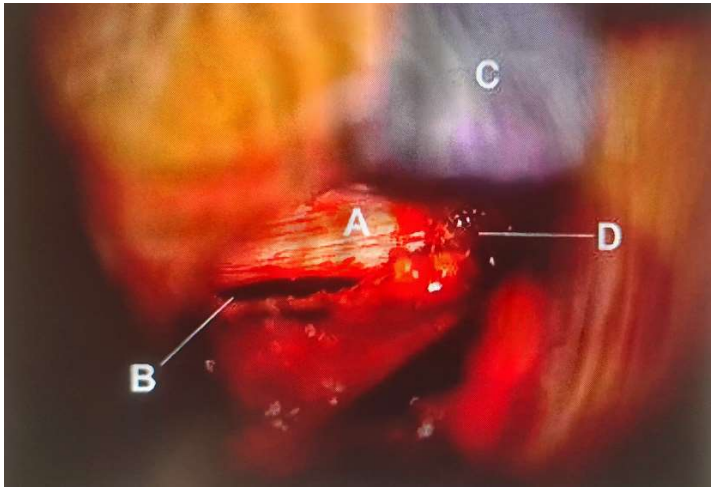
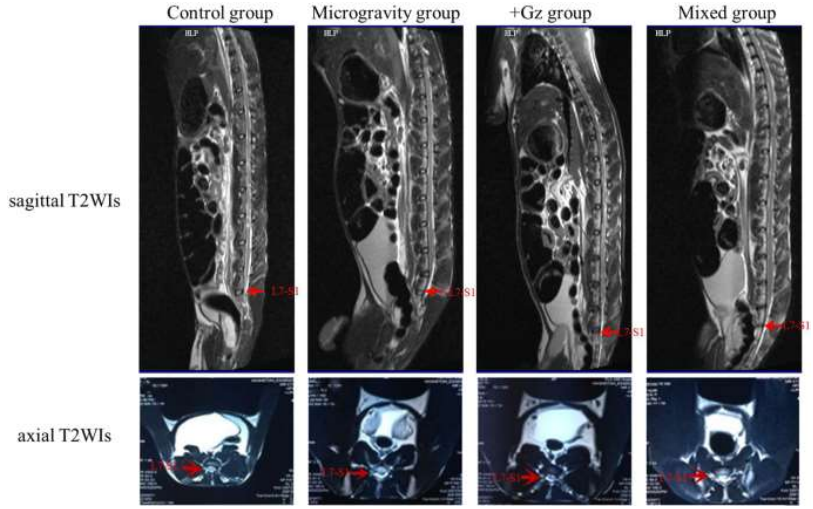
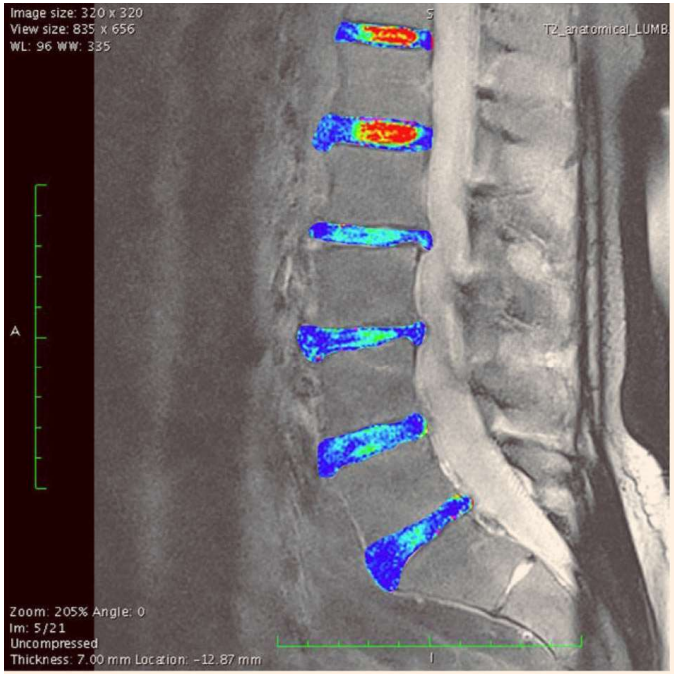
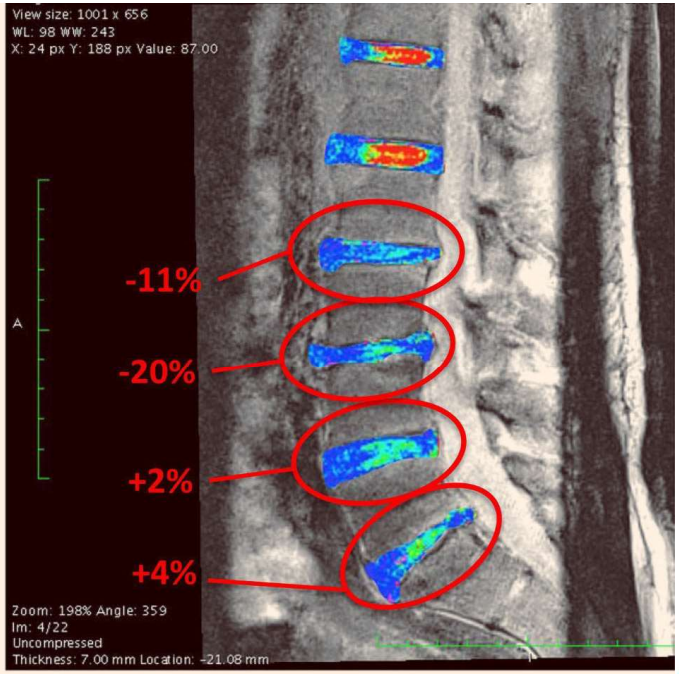








Pre-Flight **Post-Flight**

Dr. Fabio Flenda

National Aeronautics and Space Administration

SANS

Spaceflight Associated Neuro-ocular Syndrome

70 % Incidence

Space Station astronauts experience some amount of swelling in the back of the eye.

What is it?

Eye and brain changes during long-duration spaceflight

Most astronauts' eyes and brain structure change in space. The long-term health consequences are unknown, but are currently being monitored and investigated.

What is causing it?

Headward fluid shifts that occur in weightlessness

Weightlessness causes blood and cerebrospinal fluid to shift toward the head. This fluid shift is believed to be the underlying cause of the eye and brain structural changes.

Mission Impact

Long-duration astronauts may experience some or all of these changes; there is biological variation. Vision changes may impact an astronaut's inflight performance. The longer they are in space, the more they may be impacted. Many astronauts only experience effects in space, but some changes may be permanent in some astronauts. Researchers are studying ways, including fluid shift countermeasures, to prevent SANS during spaceflight and determine any long-term health effects in astronauts.

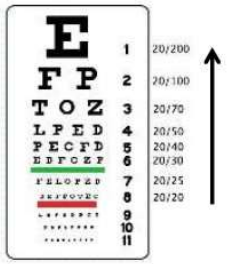
www.nasa.gov

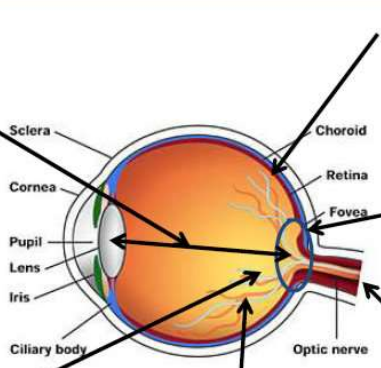
NP-2020-05-011-JSC

Visual Impairment/Intracranial Pressure symptoms

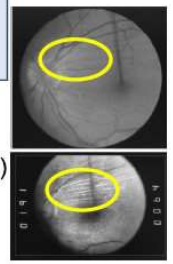
- 10 cases identified (7 of 34 US long duration astronauts) with in-light visual changes and pre-to-postflight refractive changes.
- Elevated Intracranial Pressure measured post flight (n=3)
- All males , average age 50.2 ± 4.2 years.

•Hyperopic Shifts
-Up to +1.75 diopters (5)



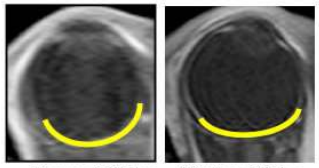


•Choroidal Folds - parallel grooves in the posterior pole (5)



•Optic Disc Edema (swelling) (5)

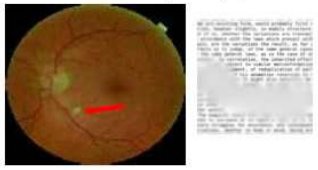
•Globe Flattening (same 5 as above)



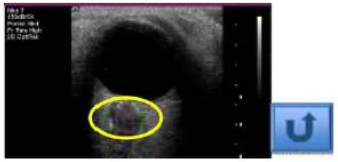
Normal Globe Flatten Globe

MRI Orbital Image showing globe flattening

•Altered Blood flow
•"cotton wool" spots (3)



•Increased Optic Nerve Sheath Diameter by OCT (6)



(OCT: tomografia ottica a radiazione coerente)

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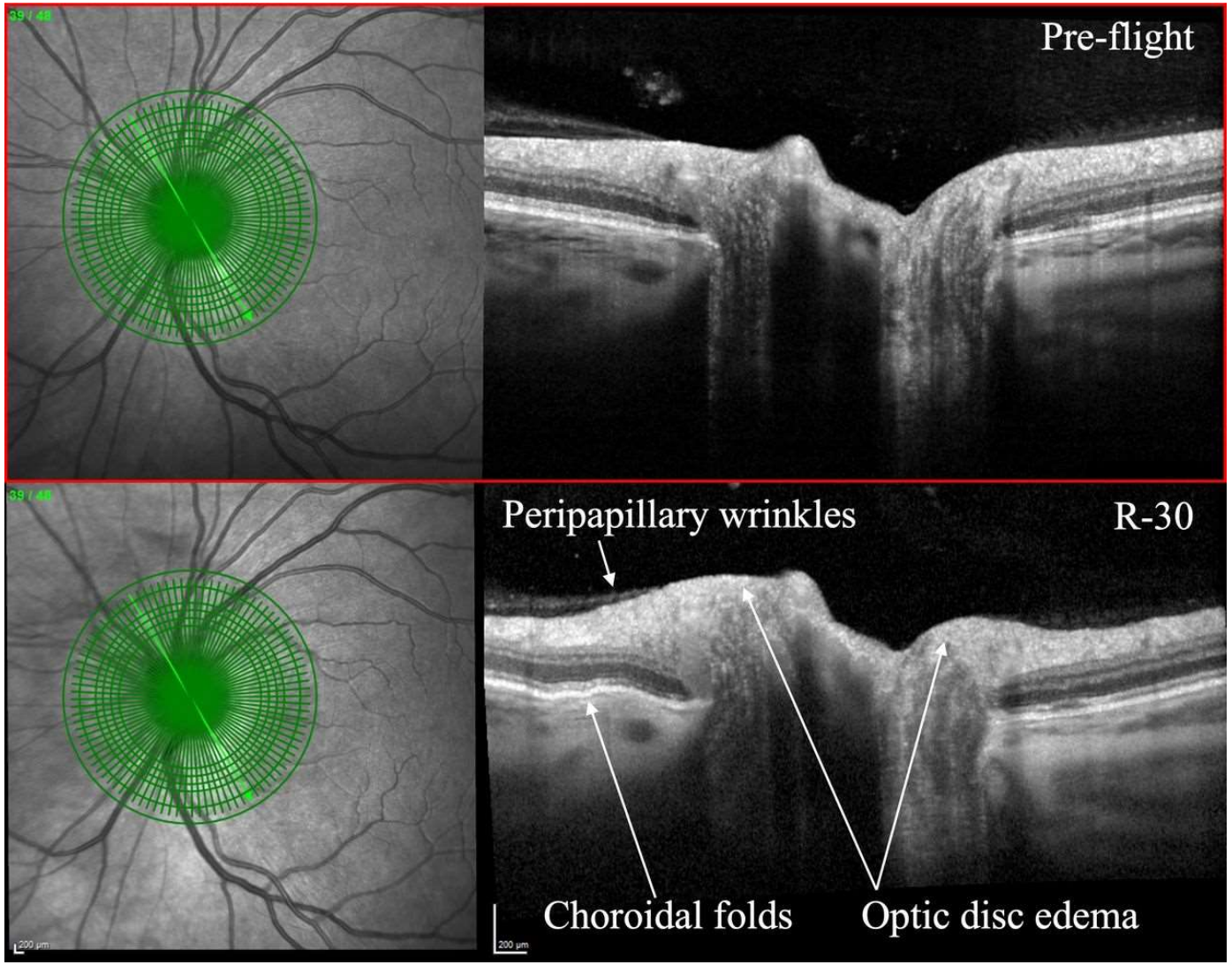
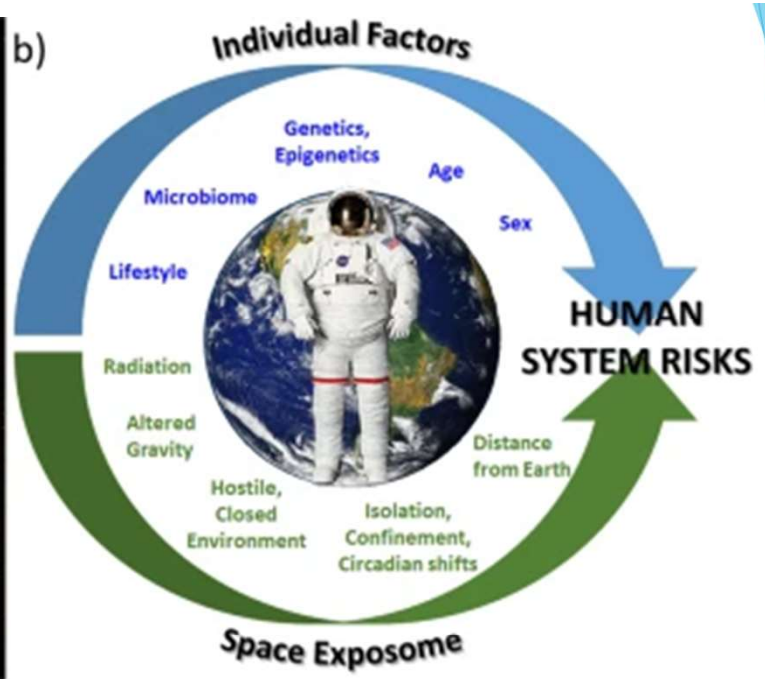
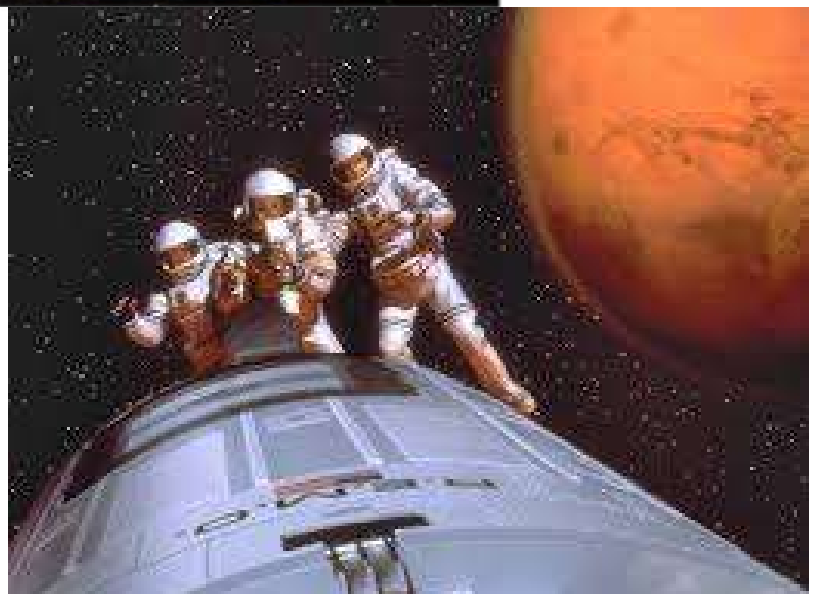

Pre-flight
Peripapillary wrinkles
R-30
Choroidal folds
Optic disc edema



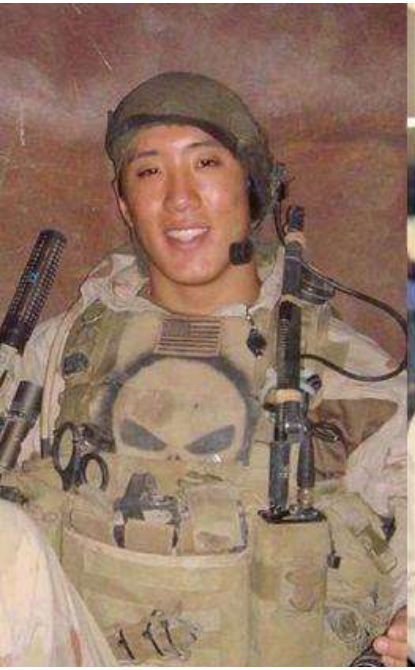


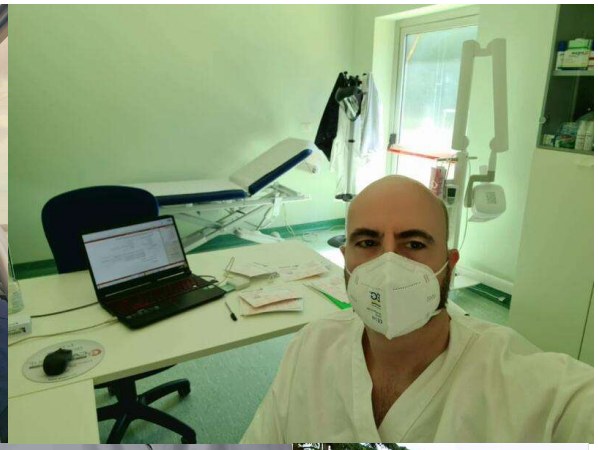
Dr. Fabio Flenda

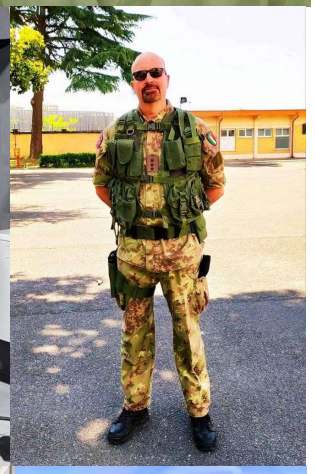
Chi inviare su Marte per missioni di anni forse senza ritorno?

Crew di soli medici?

- Astronauti-piloti-dottori esperti di medicina di emergenza?
- Droni e robot? Gli ingegneri già sanno la riposta
- Sistemi di gravità artificiale?
- Quale protezione dalle radiazioni?







Grazie dell’attenzione!