Possible effects of space radiation exposure on the reproductive system and fetal development

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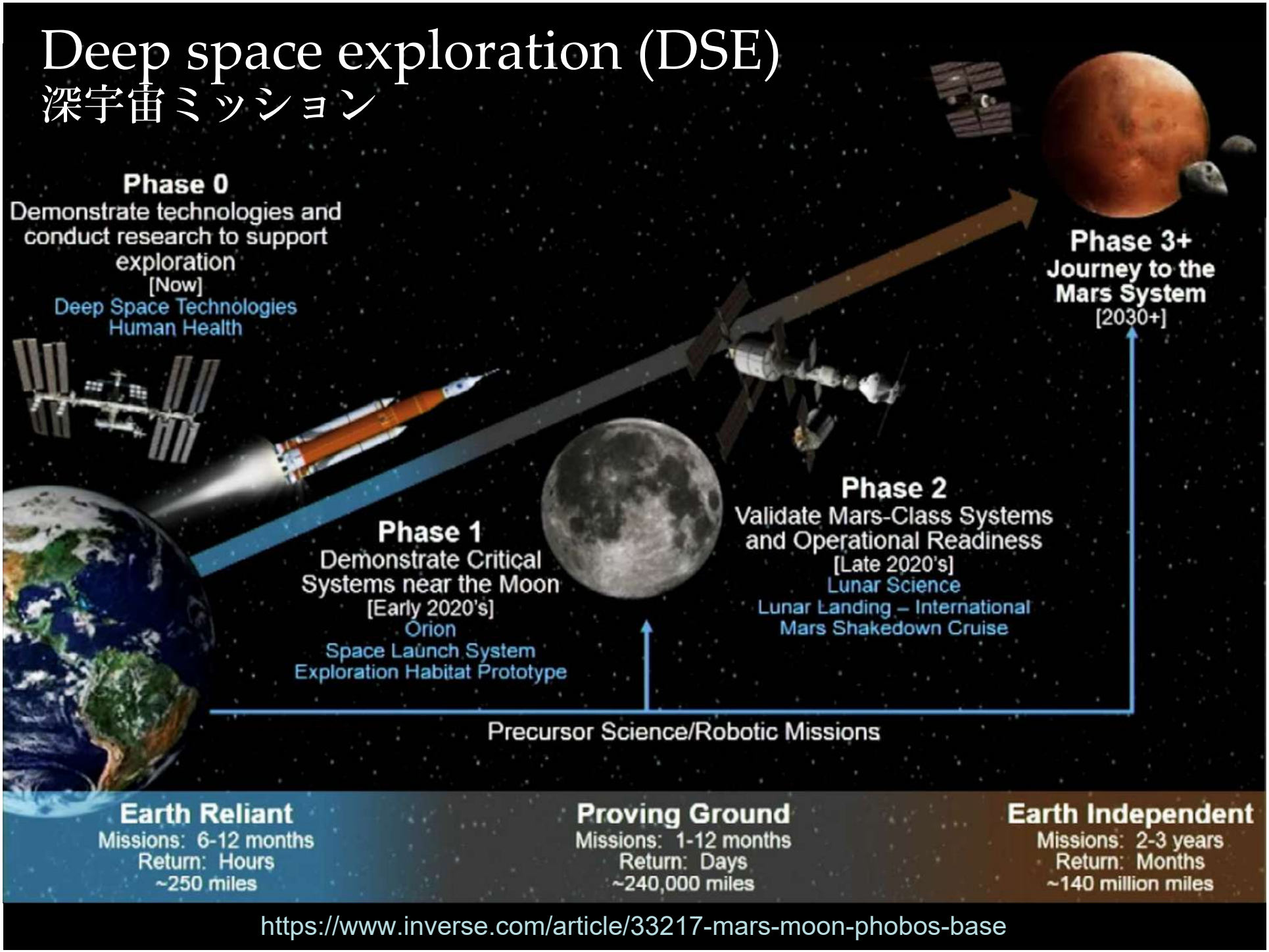
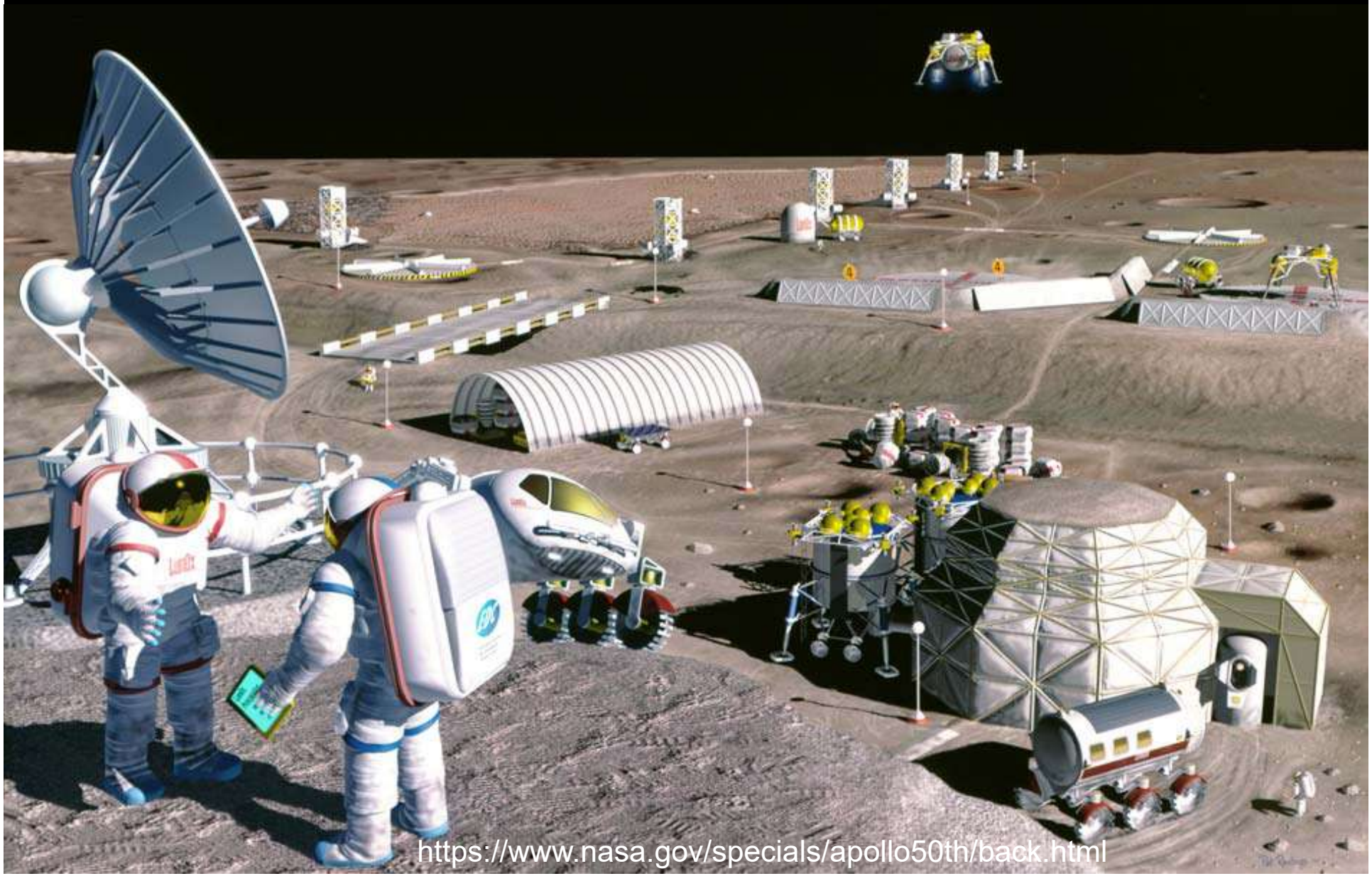
Possible space radiation exposure and its biological effects in future interplanetary missions

Deep space exploration (DSE)
深宇宙ミッション



https://www.inverse.com/article/33217-mars-moon-phobos-base

Mission to the moon
月へのミッション



Mars mission - it's long..
火星ミッション—これは長い..

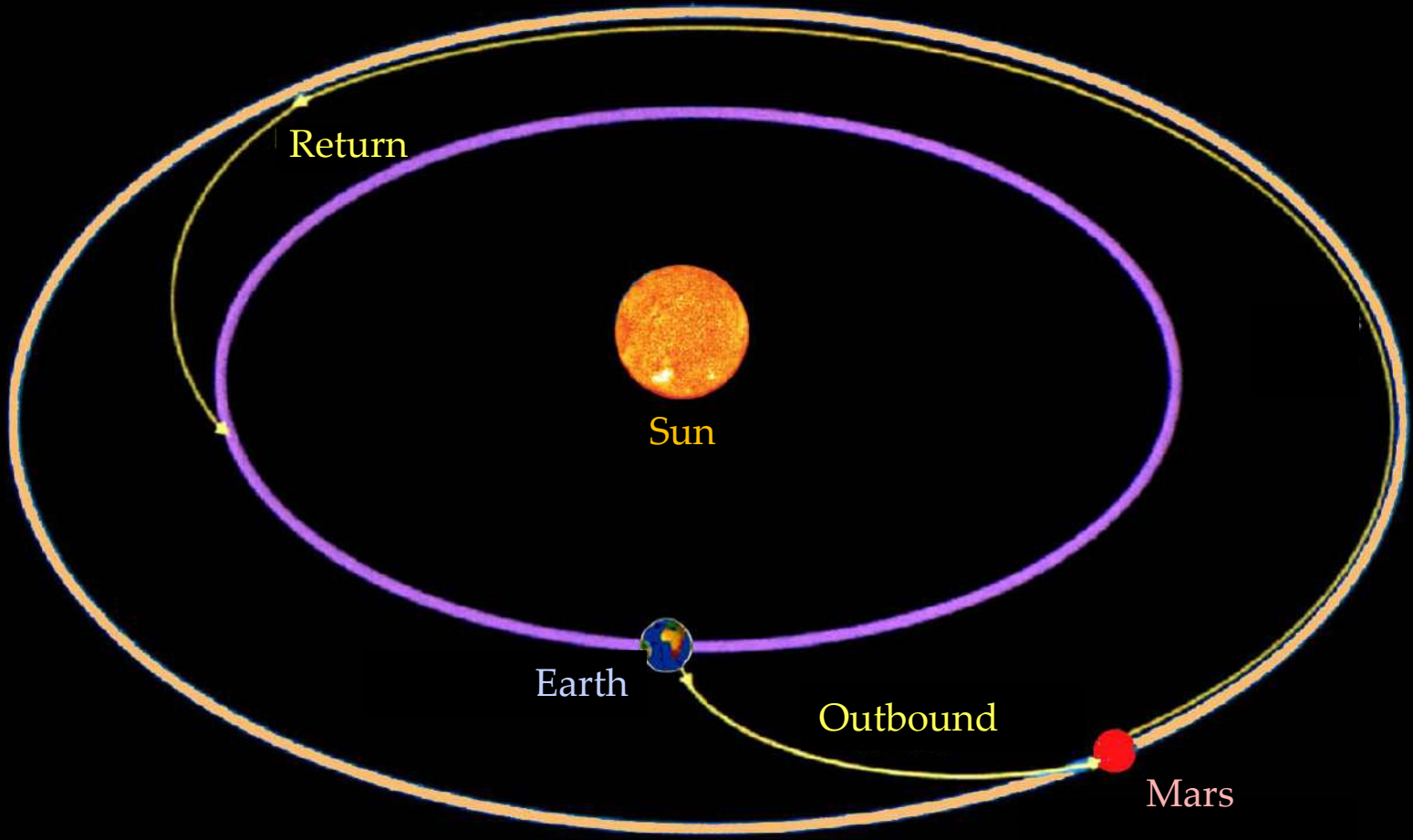
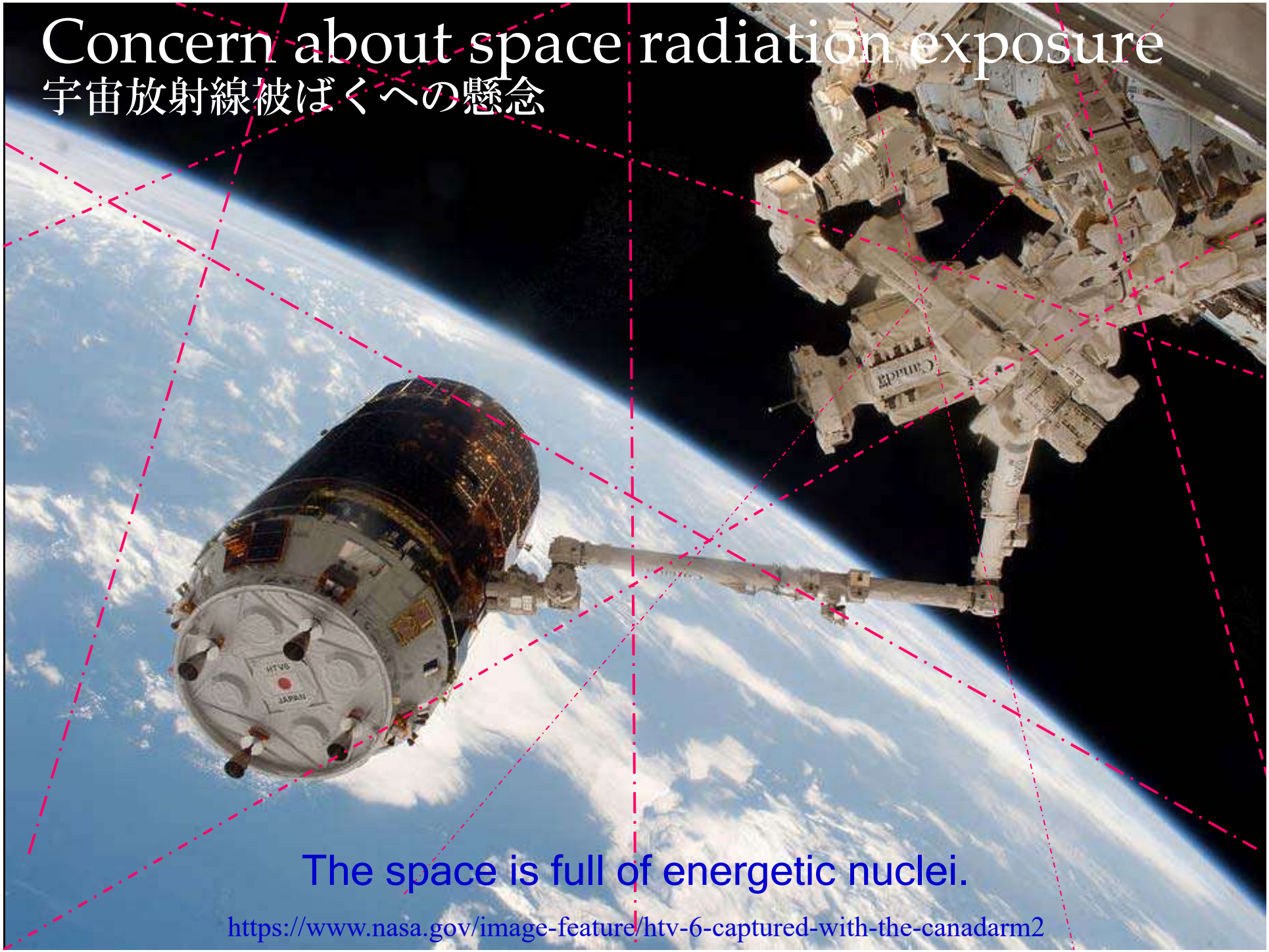


Fig. A typical route of Mars Mission planned by NASA.

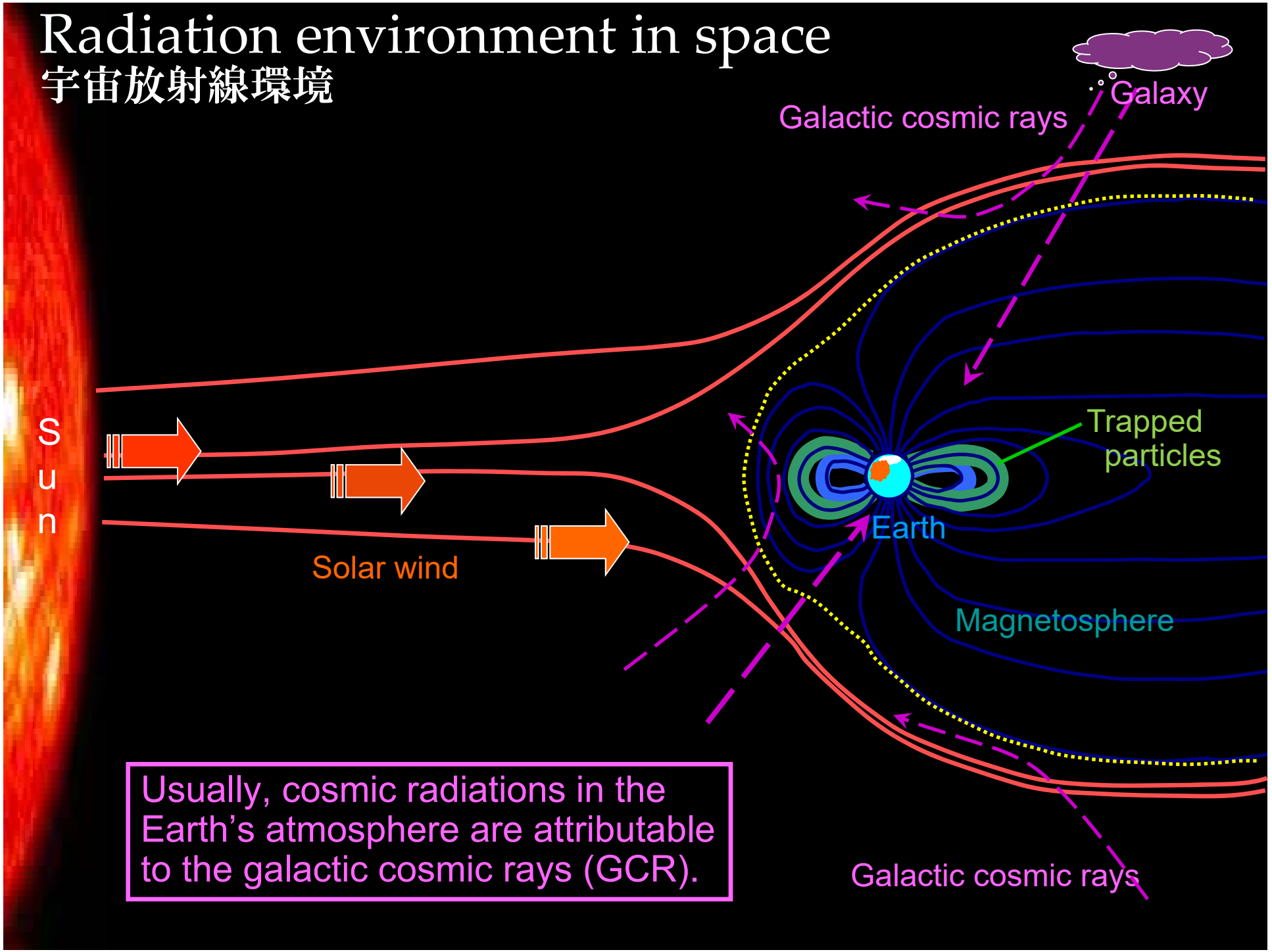
Concern about space radiation exposure
宇宙放射線被ばくへの懸念



The space is full of energetic nuclei.

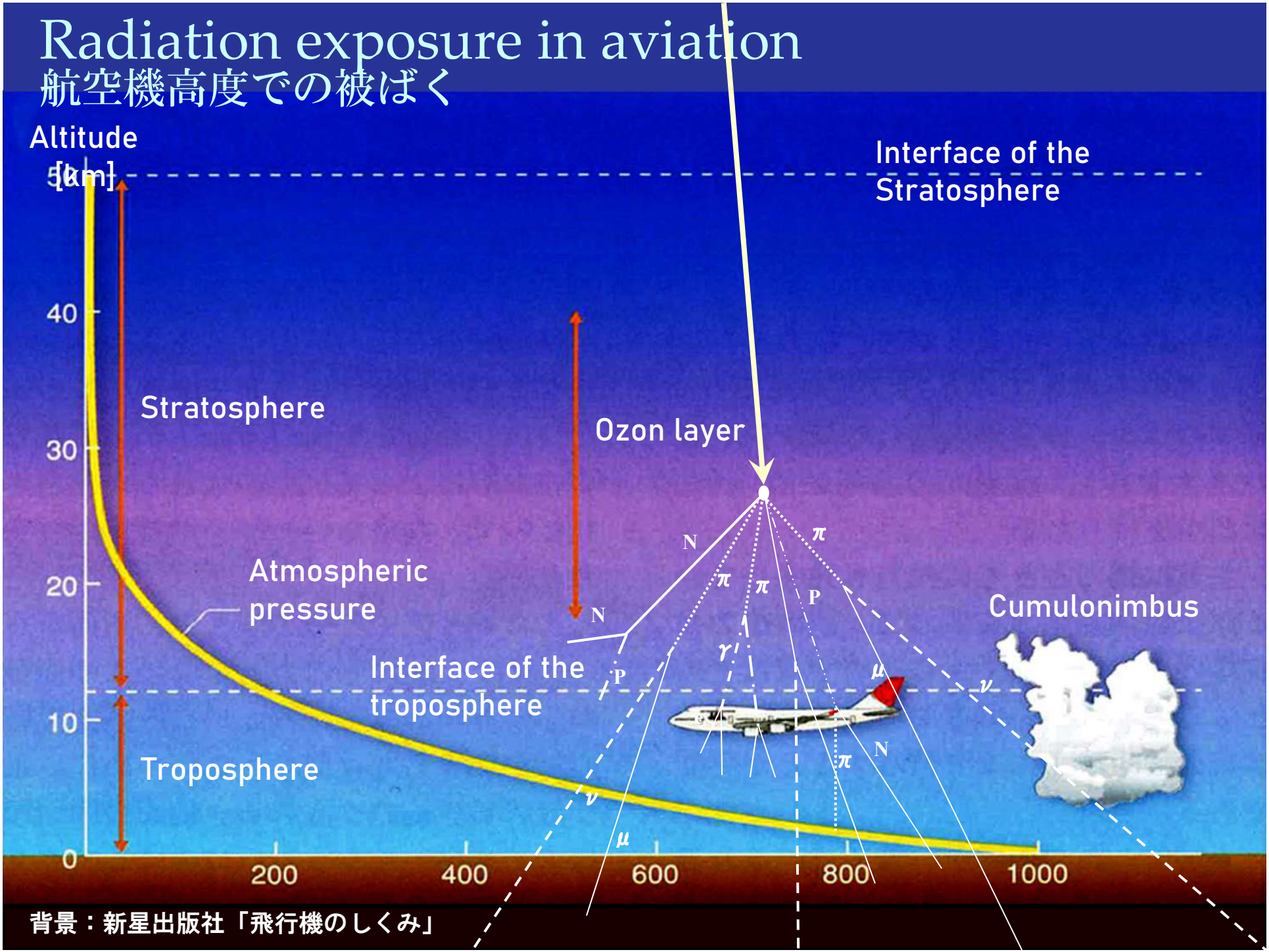
https://www.nasa.gov/image-feature/htv-6-captured-with-the-canadarm2

Radiation environment in space
宇宙放射線環境



Usually, cosmic radiations in the Earth's atmosphere are attributable to the galactic cosmic rays (GCR).

Radiation exposure in aviation
航空機高度での被ばく



背景：新星出版社「飛行機のしくみ」

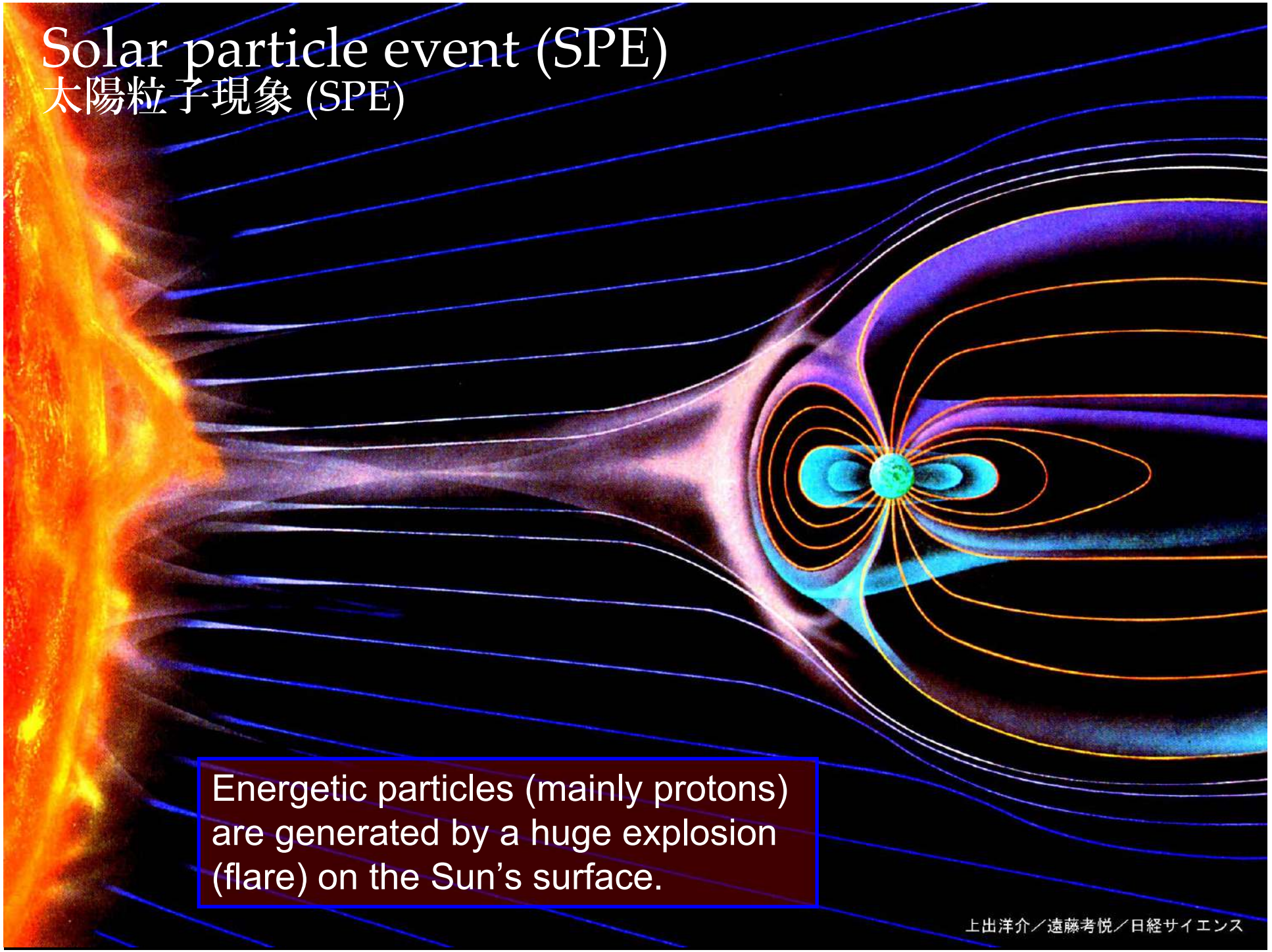
Space radiation exposure in LEO missions
低軌道宇宙飛行における宇宙放射線被ばく

Table. Assessed bone marrow dose rates (at 5 cm depth) received by the astronauts who were involved in the NASA space programs performed in the 20th century.

Program	Inclination [°]	Altitude [km]	Absorbed dose rate [mGy d^{-1}]	Dose equivalent rate [mSv d^{-1}]
Mercury	-	-	0.3	0.55
Gemini	-	-	0.49	0.87
Apollo	-	-	0.43	1.2
Skylab	50	430	0.71	1.4
Shuttle	28.5	<400	0.1	0.18
Shuttle	28.5	>400	1.2	2.1
Shuttle	>50	<400	0.2	0.45
Shuttle	>50	>400	0.44	1.1
Shuttle-Mir	51.6	~390	0.37	0.84
ISS	51.6	330~440	0.19	0.48

Courtesy of Dr. Francis Cucinotta (NASA-JSC)

Solar particle event (SPE)
太陽粒子現象 (SPE)



Energetic particles (mainly protons) are generated by a huge explosion (flare) on the Sun's surface.

上出洋介／遠藤考悦／日経サイエンス

Predicted dose from SPE
SPEによる予測線量

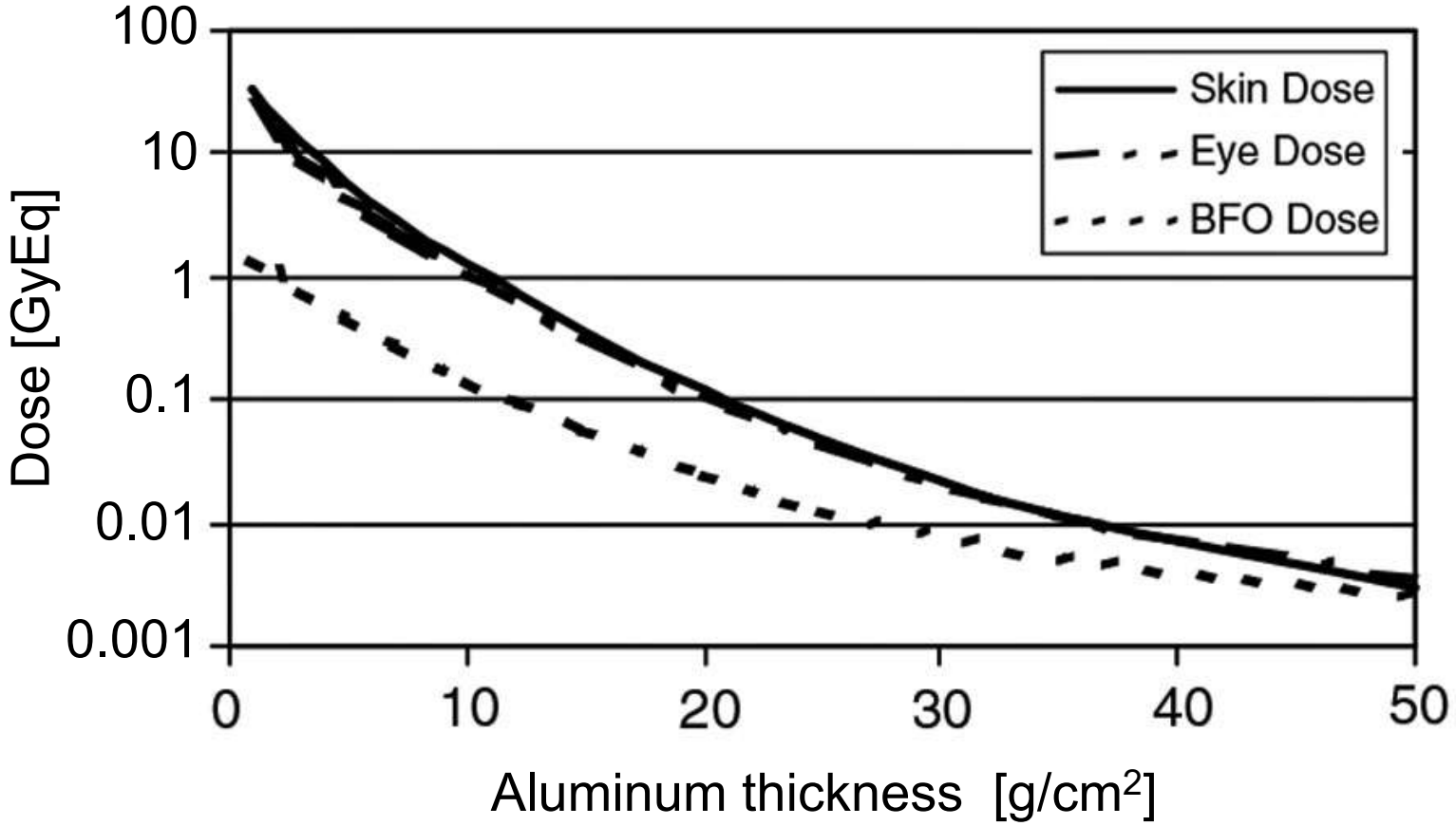


Fig. Predicted doses of selected organs as functions of the thickness of aluminum shielding for the hypothetical largest SPE (comparable to the Carrington event) with RBE=1.5 [Townsend et al., 2006].

Organ dose limits for LEO astronauts (NASA)
低軌道宇宙飛行士のための組織線量限度 (NASA)

Table. Recommended RBE-weighted dose limits regarding the deterministic effects for LEO astronauts [NCRP, 2000].

Period	RBE-weighted dose limit [GyEq]		
	Bone marrow	Lens of the eye	Skin
Career	-	4.0	6.0
1 year	0.50	2.0	3.0
30 days	0.25	1.0	1.5

* These limits are applied to all ages. The career effective-dose limits for stochastic effects are given separately.

Effects of space radiation exposures on the reproductive potentials of astronauts have not yet been considered...

Can they keep their reproductive potentials?
宇宙飛行士は生殖能を維持できるか？

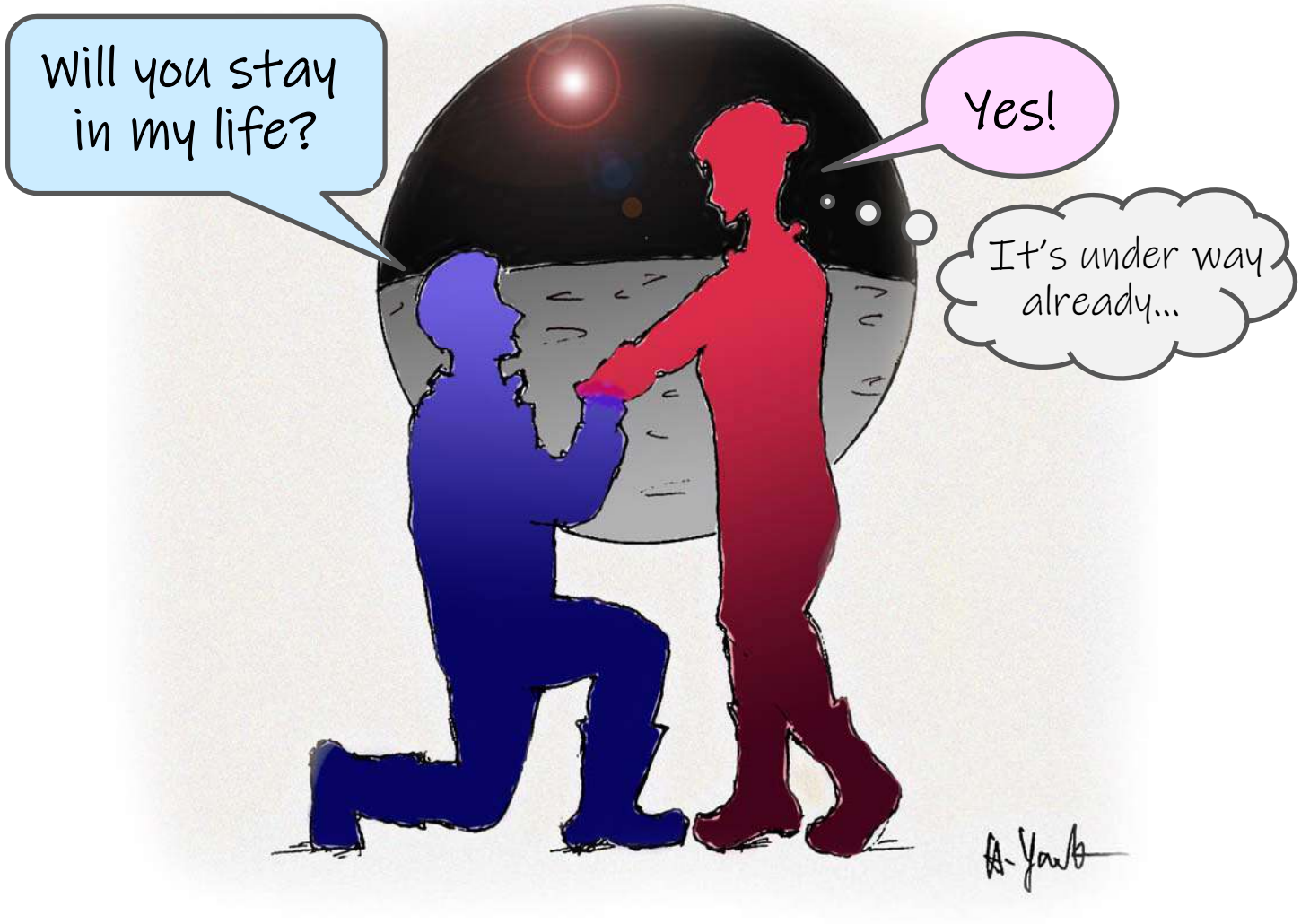


Figure. Possible situation in a future interplanetary mission.

Threshold doses on reproductive organs
生殖器に関するしきい線量

Table. Threshold dose estimates of the acute absorbed doses for 1% incidences of morbidity for testes and ovaries after whole-body **γ-ray** exposures [ICRP, 2007].

Organ/Tissue	Effect	Threshold dose	Time to develop
Testes	Temporary sterility	～0.1 Gy	3～9 weeks
	Permanent sterility	～6 Gy	～3 weeks
Ovaries	Permanent sterility	～3 Gy	～1 week

Threshold doses on human embryo & fetus
胚及び胎児に関するしきい線量

Table. Threshold dose estimates of the acute absorbed doses of **low-LET particles** for the deterministic effects other than cancer in the human embryo and fetus [NCRP, 2013].

Post-conception period	Effect	Threshold dose
1 to 2 weeks	Embryo lethality	0.15～0.2 Gy
3 to 5 weeks	Embryo lethality	0.25～0.5 Gy
6 to 13 weeks	Fetus lethality	>1 Gy
	Permanent growth retardation in the adult	0.25～6 Gy
8 to 25 weeks	Mental retardation and decrease in IQ scores	>0.5 Gy
>14 week	Fetus lethality	>1.5 Gy
	Gross anatomic malformation	>0.5 Gy

Predicted dose from SPE – is this correct?
SPEによる予測線量 – これは正しい？

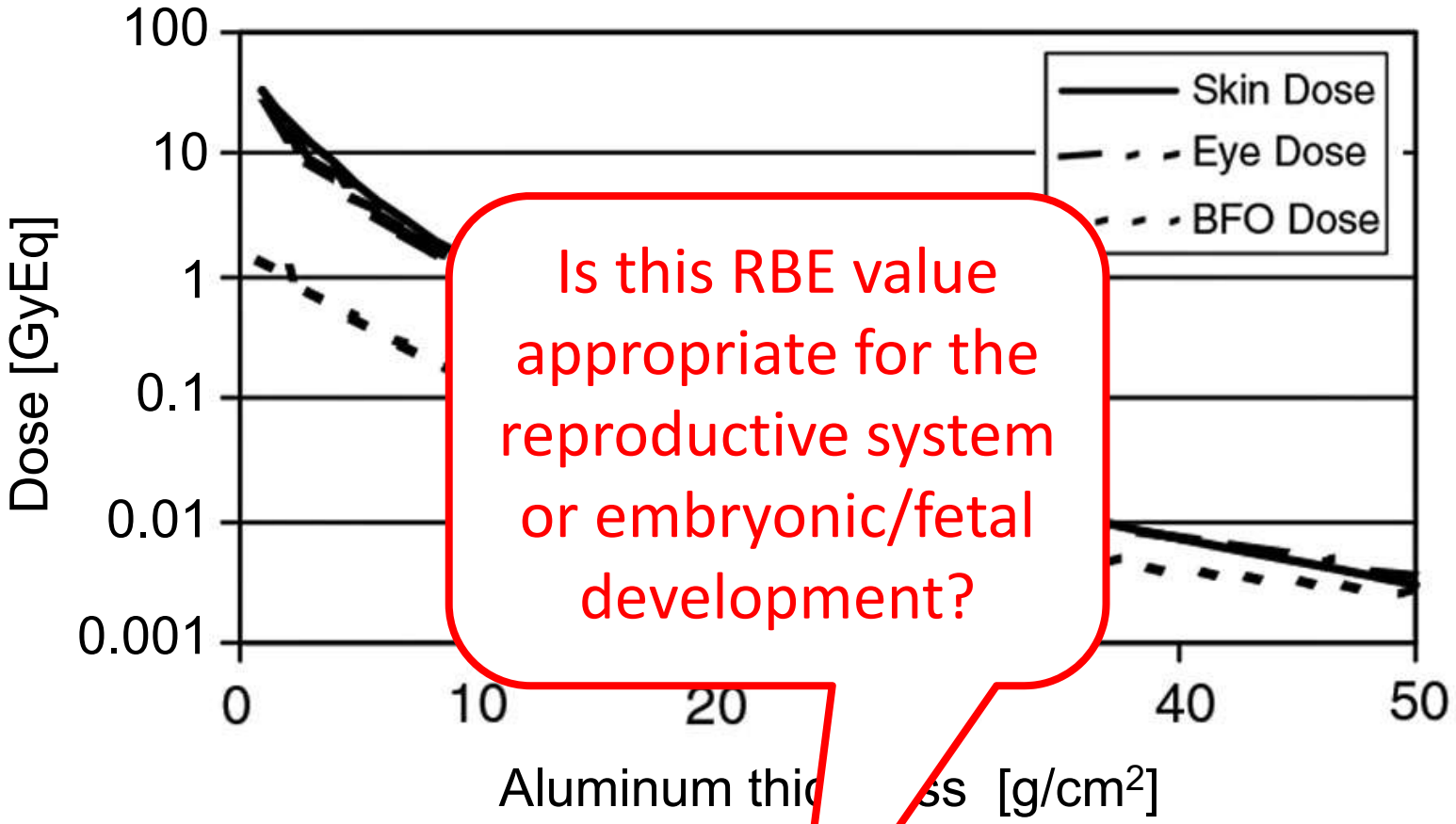
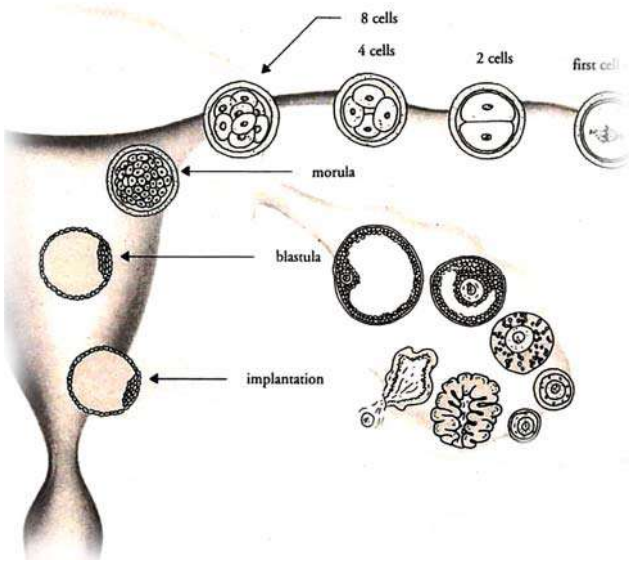


Fig. Predicted doses of selected organs functions of the thickness of aluminum shielding for the largest-scale SPE (a hypothetical Carrington event) with **RBE=1.5** [Townsend et al., 2006].

Relative biological effectiveness (RBE) of high-LET particles with regard to reproductive potential



Difference of energy deposition patterns
エネルギー付与のパターンに観られる違い

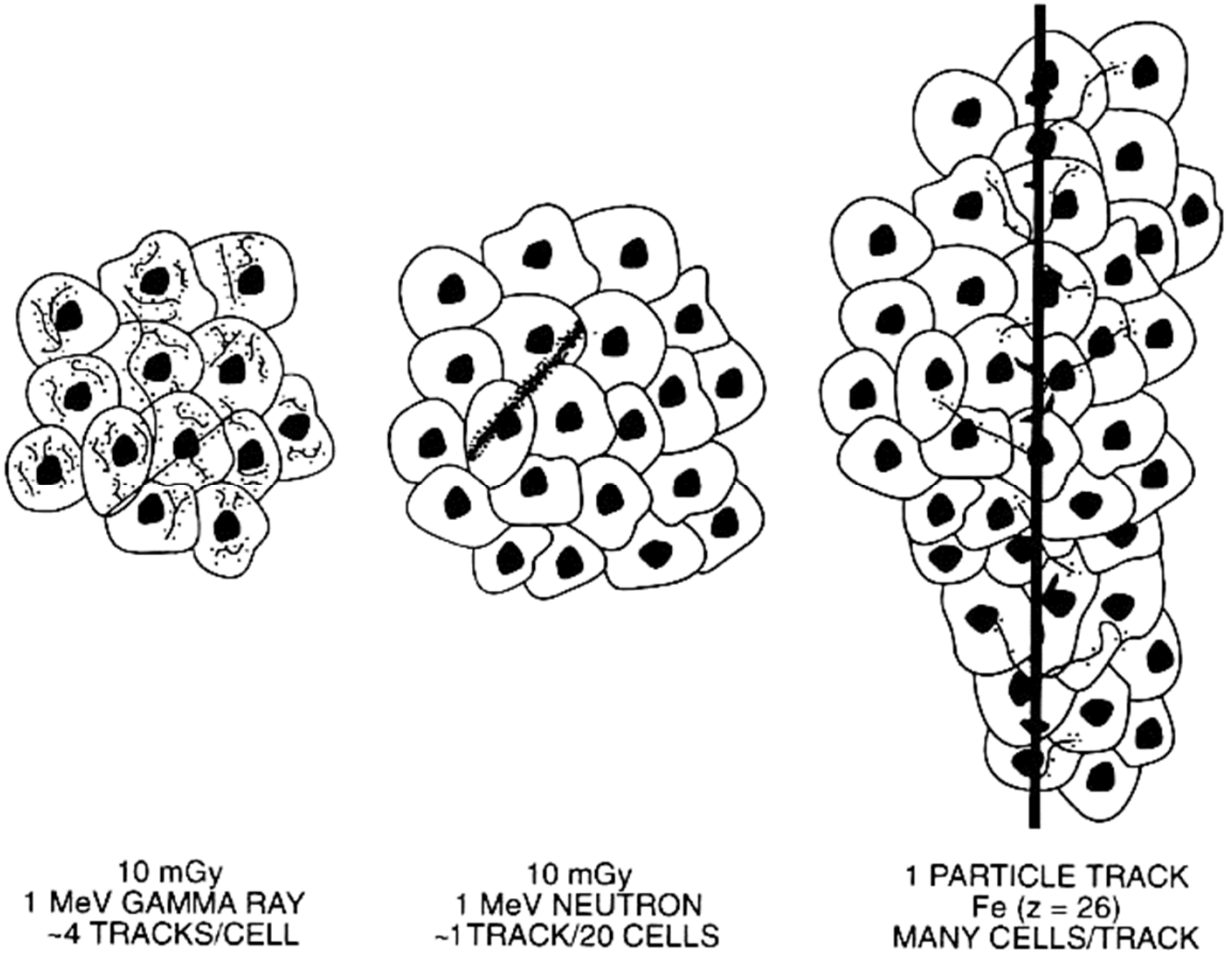


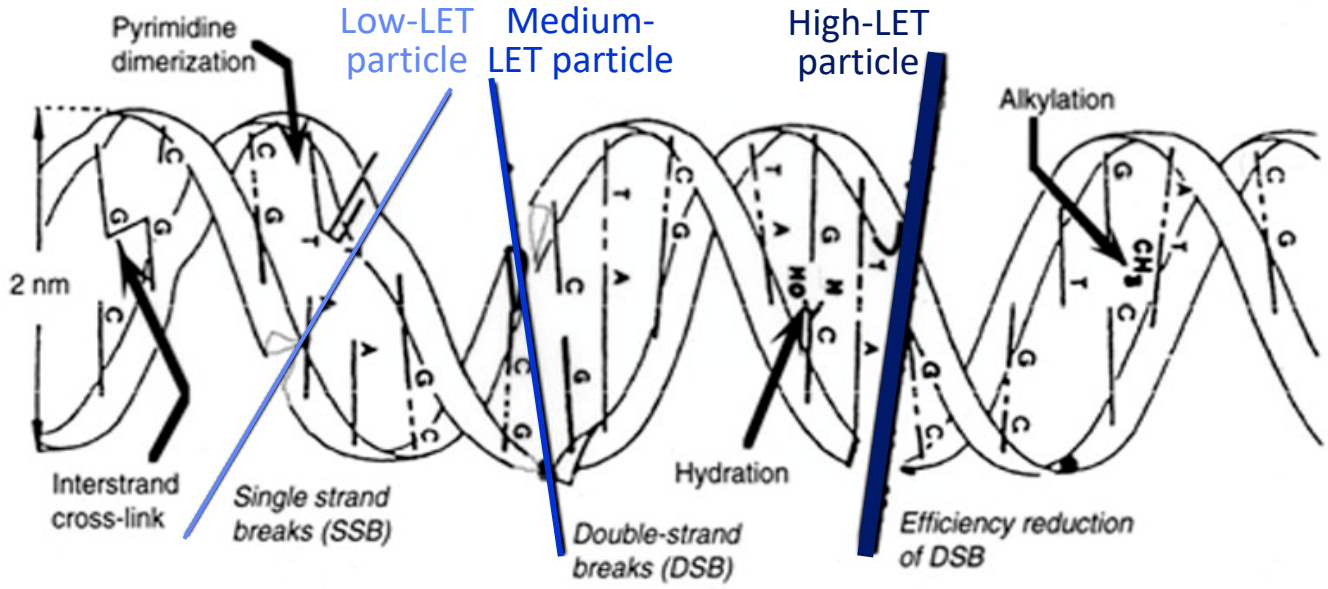
Fig. Illustration showing the difference of energy depositions to tissue cells from photon (left), neutron (center) and heave ion (right).

Courtesy of NCRP

Linear energy transfer (LET)
線エネルギー付与 (LET) とは

The energy transferred from a radiation to the material per unit length of the track.

粒子飛跡の単位長さ（通常はμm）当たりに物質に付与されるエネルギー.



Courtesy of NCRP

Definition of RBE
RBEの定義

The relative biological effectiveness (RBE) is defined as the ratio of the dose of a radiation in respect to that of a reference radiation (usually γ/X-rays) required by those radiations to cause the same level of biological effect.

生物学的効果比 (RBE) **は、対象とする放射線が、基準となる放射線 (通常γ/Ｘ線)に比べ、同じ生物効果を生じるのに要する線量の比として定義される.**

$$RBE = \frac{D_{X/\gamma-rays}}{D_{Particle}} \quad (1)$$

$$D_{Total} = D_{X/\gamma-rays} + RBE \times D_{Particle} \ \text{[GyEq]} \quad (2)$$

Relationship between LET and RBE
LETとRBEの関係

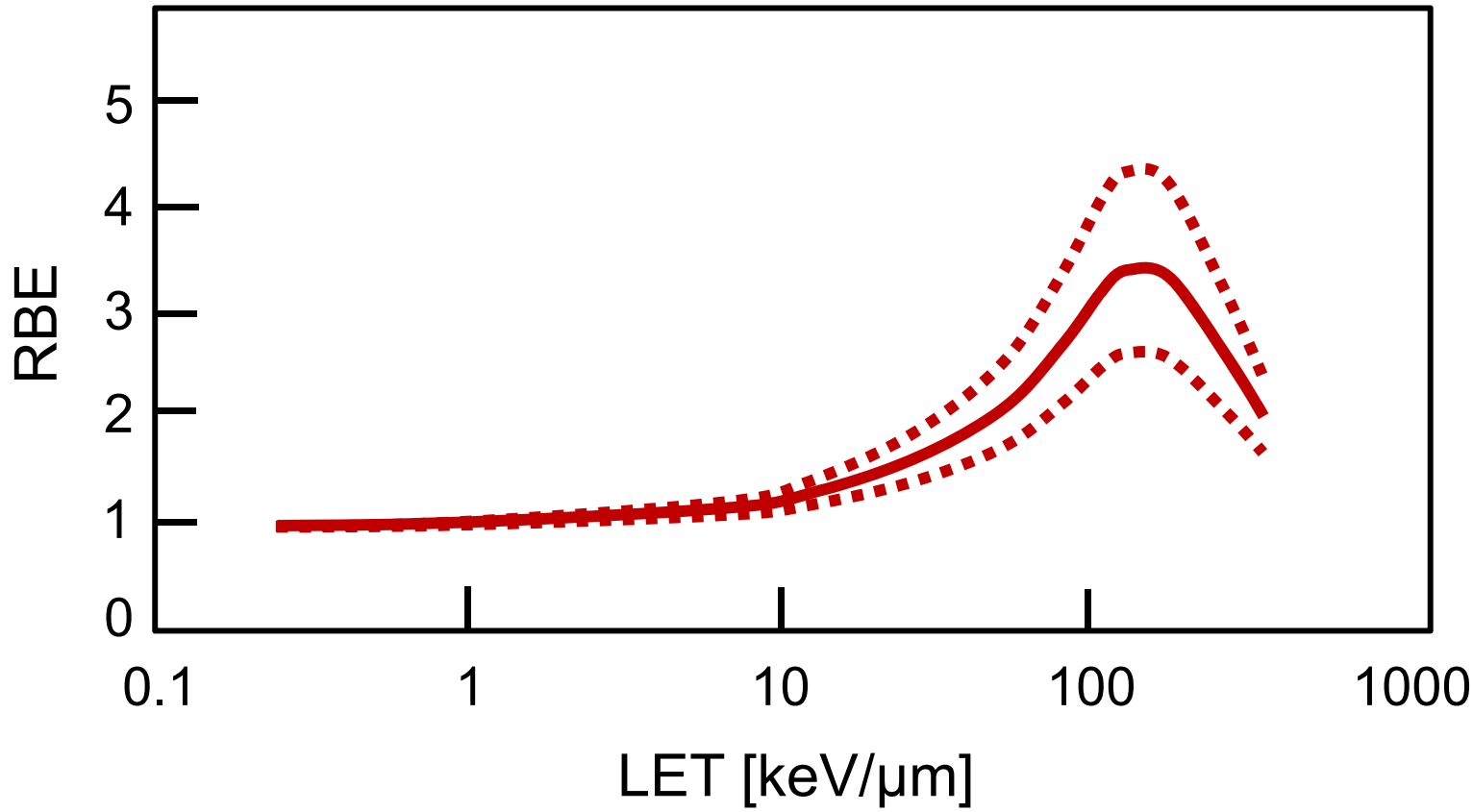


Fig. A typical LET dependency of RBE.

RBE .vs. Severity

RBE .vs. 重篤度

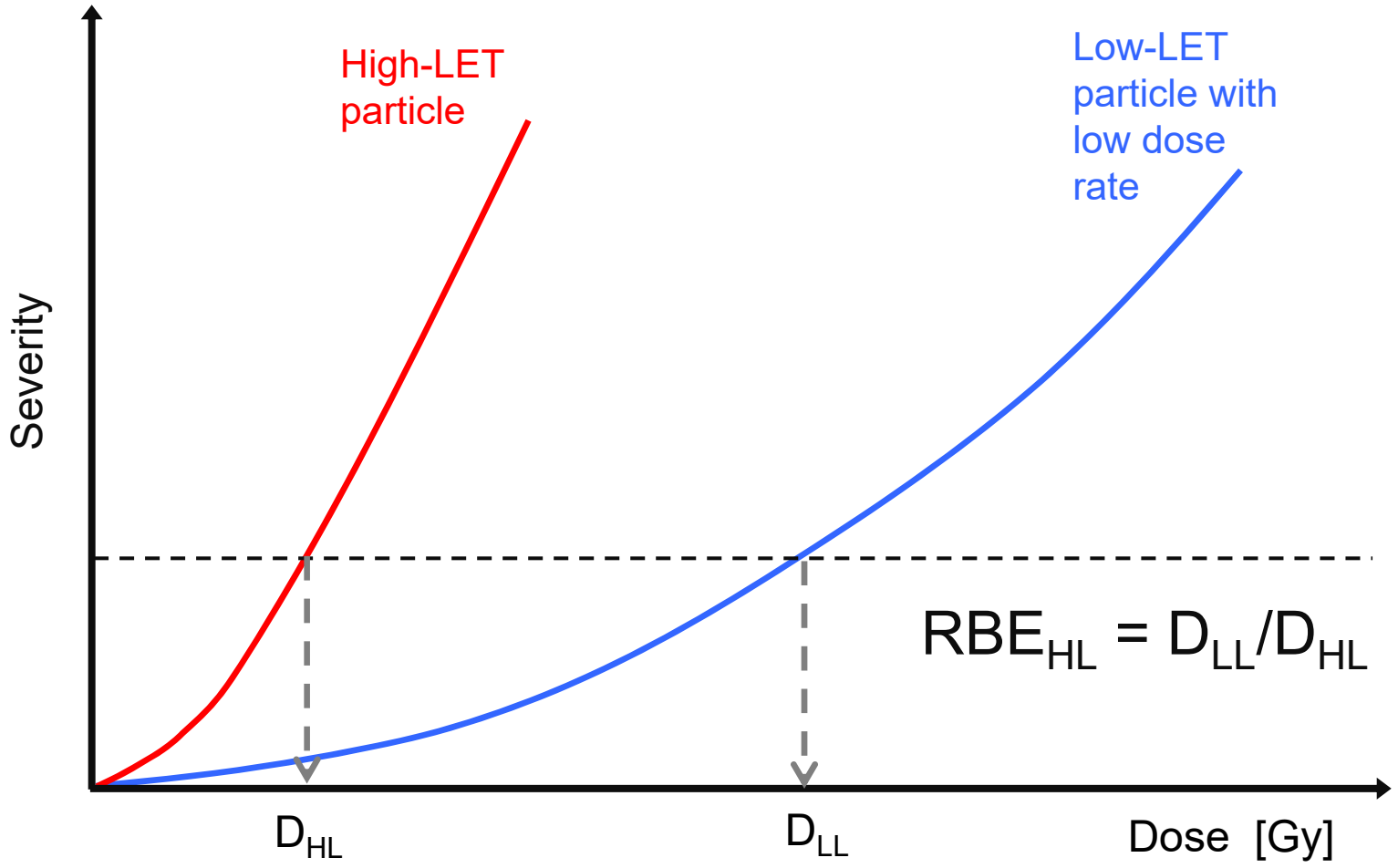


Fig. Relationship between dose and severity of a deterministic effect.
RBE is calculated as the ratio of the high-LET particle dose (D_{HL}) to the low-LET particle dose (D_{LL}) at the same level of severity.

RBE .vs. Severity

RBE .vs. 重篤度

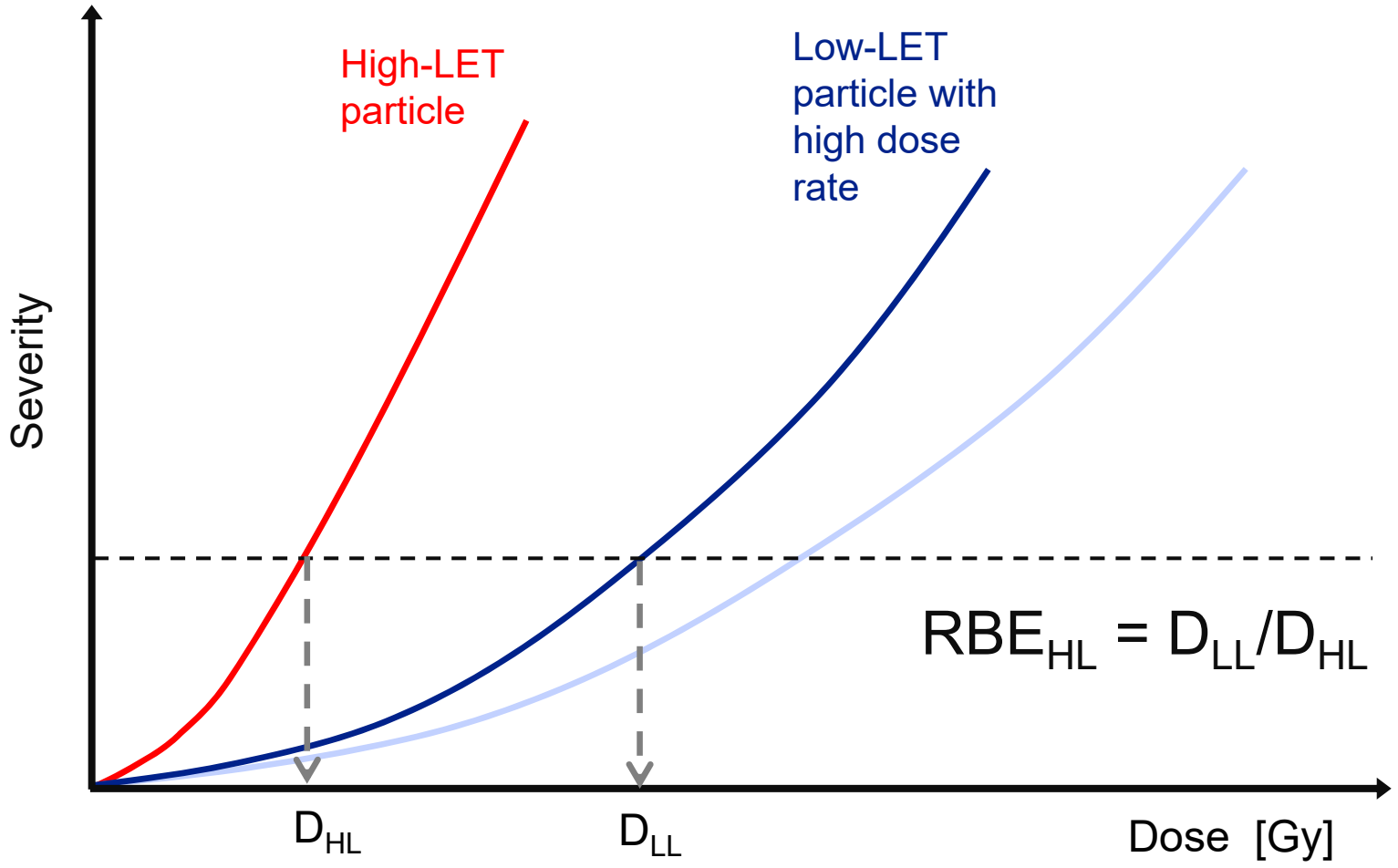


Fig. Relationship between dose and severity of a deterministic effect. RBE is calculated as the ratio of the high-LET particle dose (D_{HL}) to the low-LET particle dose (D_{LL}) at the same level of severity.

RBE .vs. Severity

RBE .vs. 重篤度

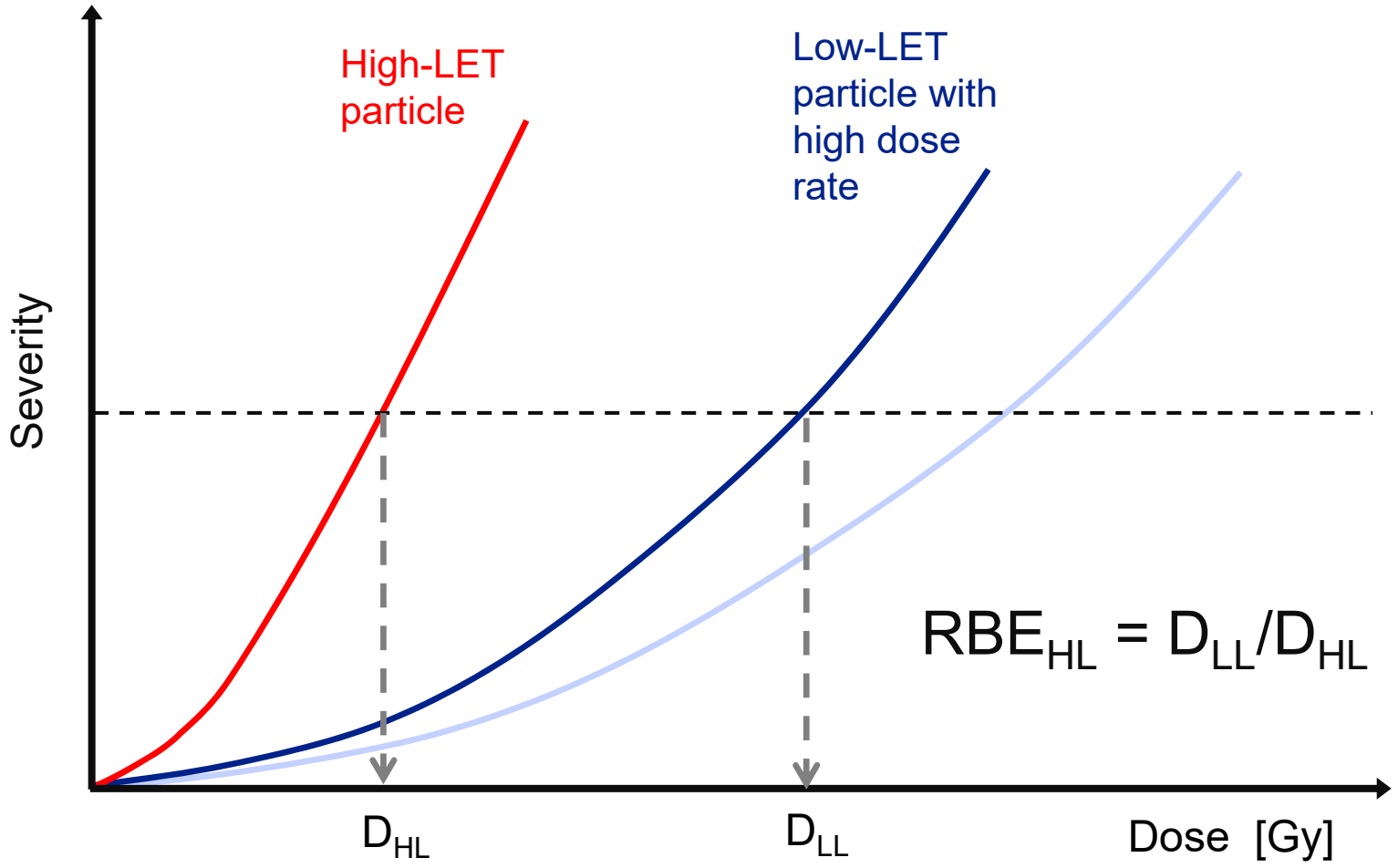


Fig. Relationship between dose and severity of a deterministic effect. RBE is calculated as the ratio of the high-LET particle dose (D_{HL}) to the low-LET particle dose (D_{LL}) at the same level of severity.

Variability of the RBE value
RBE値の変動性

Even for the same combination of two radiations, the RBE value could considerably change due to the following conditions:

- Tissue/Organ
- Biological endpoint
- Ionization density
- Dose rate

同じ線質の組み合わせでも、以下の条件が違うとRBE値は大きく変わり得る：

- **対象組織／臓器**
- **着目する症状**
- **電離密度**
- **線量率、等**

Male reproductive organ – Testis –
男性の生殖器 —精巣—

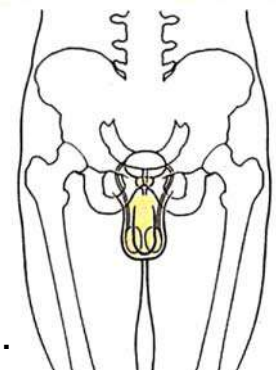


Table. The RBE values of neutrons and selected heavy ions for spermatogorium killing in mice [Wang and Yasuda, 2020].

Particle	Energy or source	RBE value	Reference
Helium	from ^{210}Po	6.7	Rao et al. (1991)
Carbon	400-670 MeV/u	< 3	Alpen et al. (1981)
Oxygen	400-670 MeV/u	< 3	Alpen et al. (1981)
Neon	400-670 MeV/u	< 3	Alpen et al. (1981)
Argon	400-670 MeV/u	< 3	Alpen et al. (1981)
Neutron	1 MeV	5.7	Gasinska et al. (1985)
Neutron	5.5 MeV	4.6	Gasinska (1985)

Courtesy of Dr. Bing Wang (QST)

Female reproductive organ – Ovary –
女性の生殖器 —卵巣—

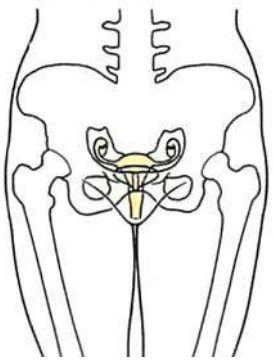


Table. The RBE values of neutrons and selected heavy ions for oocyte killing in mice [Wang and Yasuda, 2020].

Particle	Energy or source	RBE value	Reference
Carbon	80 MeV/u	1.3－1.5	Zhang et al. (2006)
Neon	450 MeV/u	0.4－0.6	ICRP (1989)
Silicon	670 MeV/u	0.4－3.0	ICRP (1989)
Argon	570 MeV/u	0.4－2.2	ICRP (1989)
Neutron	0.43 MeV	1.7	Straume et al. (1987)
Neutron	from ^{252}Cf	1.6 – 3.5	Satow et al. (1989)

Courtesy of Dr. Bing Wang (QST)

Embryonic/fetal development (HCPs)
胚又は胎児への影響 (HCPs)

Table. The RBE values of protons and selected heavy ions for embryonic/fetal development [Wang and Yasuda, 2020].

Particle	Energy	Biological endpoint	RBE value	Reference
Proton	150 MeV	Embryo killing[a]	1.1-1.2	Szabó et al. (2018)
Helium	530 MeV	Fetal lethality[b]	1.0-1.4	Ward et al. (1976)
Carbon	290 MeV/u	Impairment[c]	1.0-2.0	Wang et al. (2005; 2007; 2008)
Neon	400 MeV/u	Impairment[c]	1.0-2.1	Wang et al. (2005; 2007; 2008)
Iron	500 MeV/u	Apoptosis[d]	3.7-4.2	Yasuda et al. (2011)

a) Embryo killing in zebrafish; b) Fetal lethality in mice; c) Impairment of prenatal neurophysiological accomplishment in rats; d) Induction of apoptosis in the developing optic tectum in medaka fish.

Courtesy of Dr. Bing Wang (QST)

Embryonic/fetal development (neutrons)
胚又は胎児への影響 (neutrons)

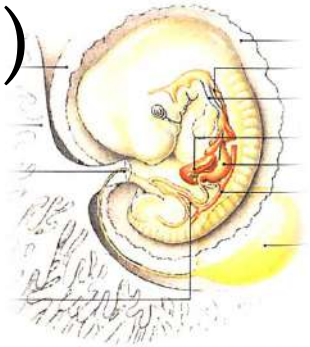


Table. The RBE values of neutrons for embryonic/fetal development [Wang and Yasuda, 2020].

Particle	Energy or source	Biological endpoint	RBE value	Reference
Neutron	from ^{252}Cf	Malformation[a]	2.3-3.1	Satow e tal. (1989)
Neutron	6.0 MeV	Chromosomal anomalies[b]	4.7-7.4	Weissenborn & Streffer (1988)
Neutron	7.0 MeV	Micronucleus[c]	2.5-3.5	Pampfer et al. (1992)
Neutron	10 MeV	Apoptosis[d]	9.8	Ishida et al. (2006)
Neutron	~800 MeV/u	Embryo killing[e]	48	Kuhne et al. (2009)

a) Malformation in mice; b) Chromosomal anomalies at 1st to 3rd mitosis in one-cell embryo in mice; c) Micronucleus induction in pre-implantation embryos in mice; d) Induction of apoptosis in fetal cerebral cortex in mice; and e) Embryo killing in medaka fish.

Courtesy of Dr. Bing Wang (QST)

Lifestyle on the moon or Mars
月や火星での生活様式

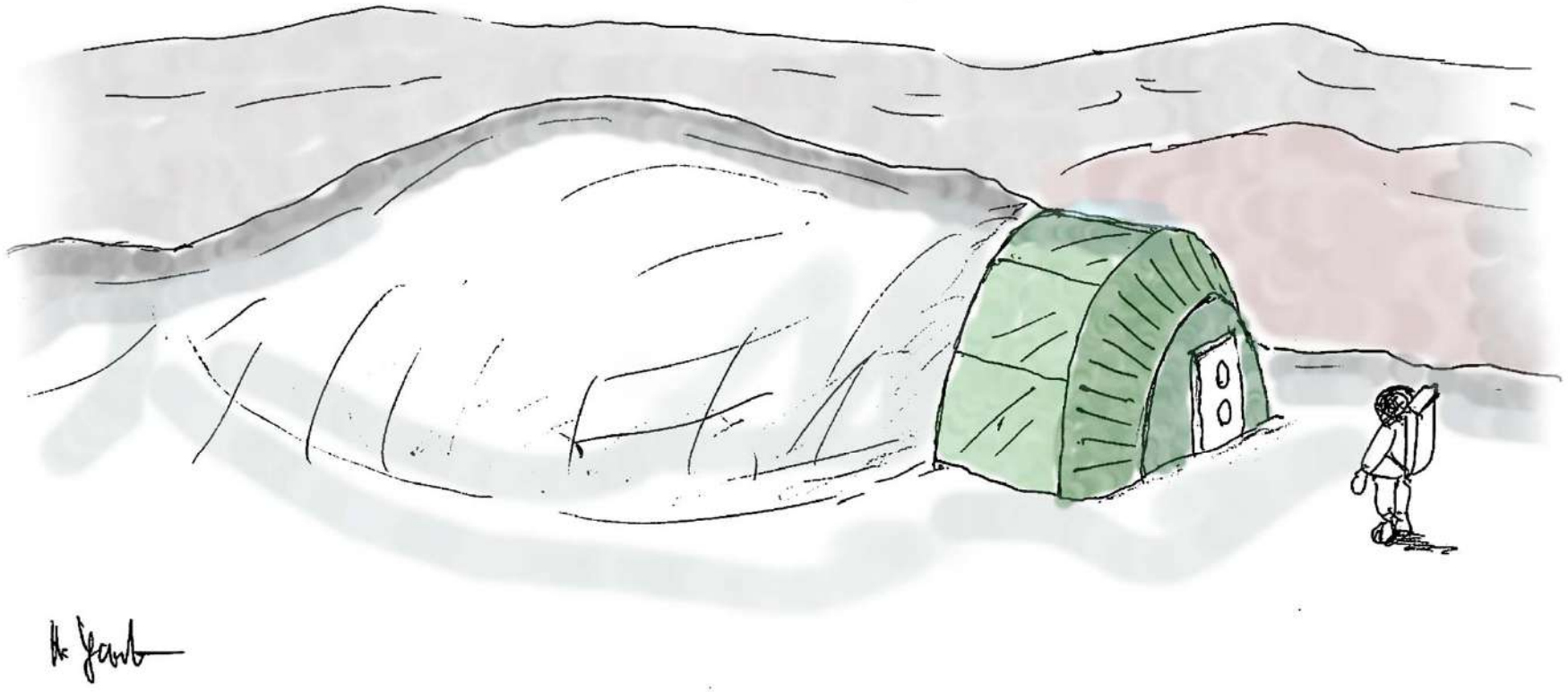


Fig. Illustration of a possible lunar base in near future.

Lifestyle on the moon or Mars
月や火星での生活様式

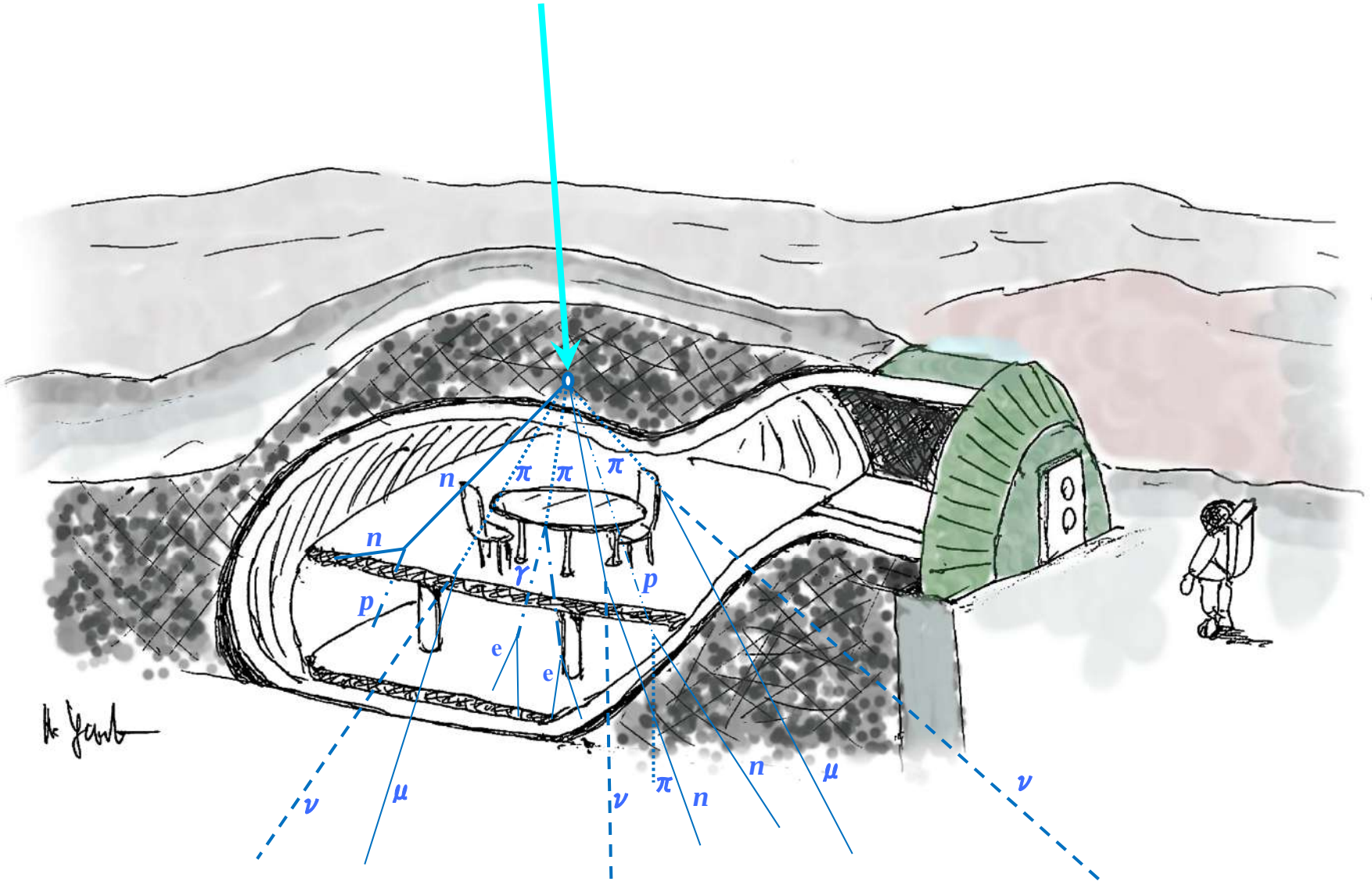


Fig. Illustration of a possible lunar base in near future.

Summary
まとめ

- The deterministic effects of space radiation exposure on the reproductive potentials of astronauts need to be carefully considered in planning of future interplanetary missions.
- It should be recognized that the RBE values of high-LET particles in space could largely change depending on particle energies and dose rates as well as biological endpoints.
- More studies are desirable for selecting the most appropriate RBE values in correspondence to possible exposure situations during the mission.

Thank you for your attention.

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