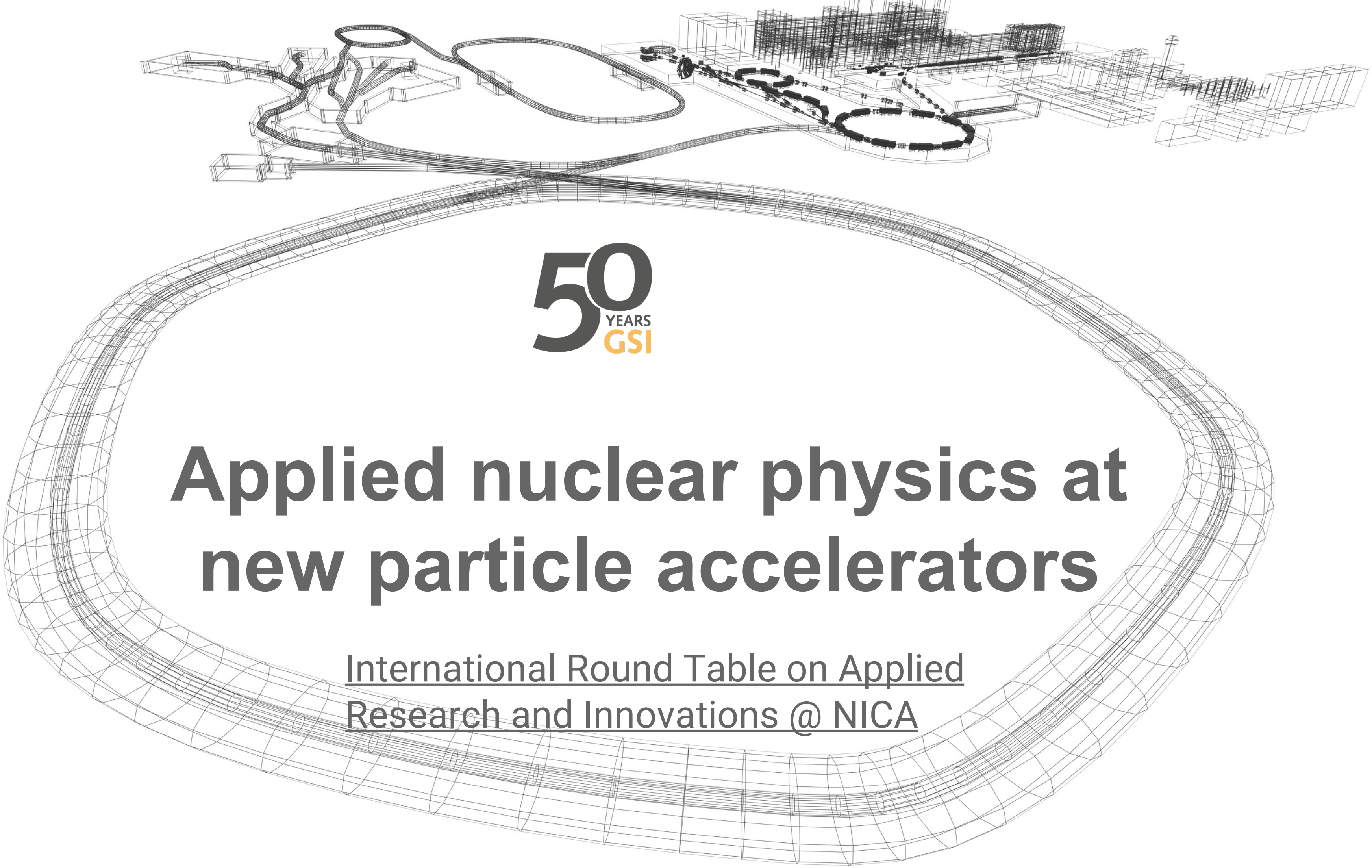
Marco Durante

Director, Biophysics Department

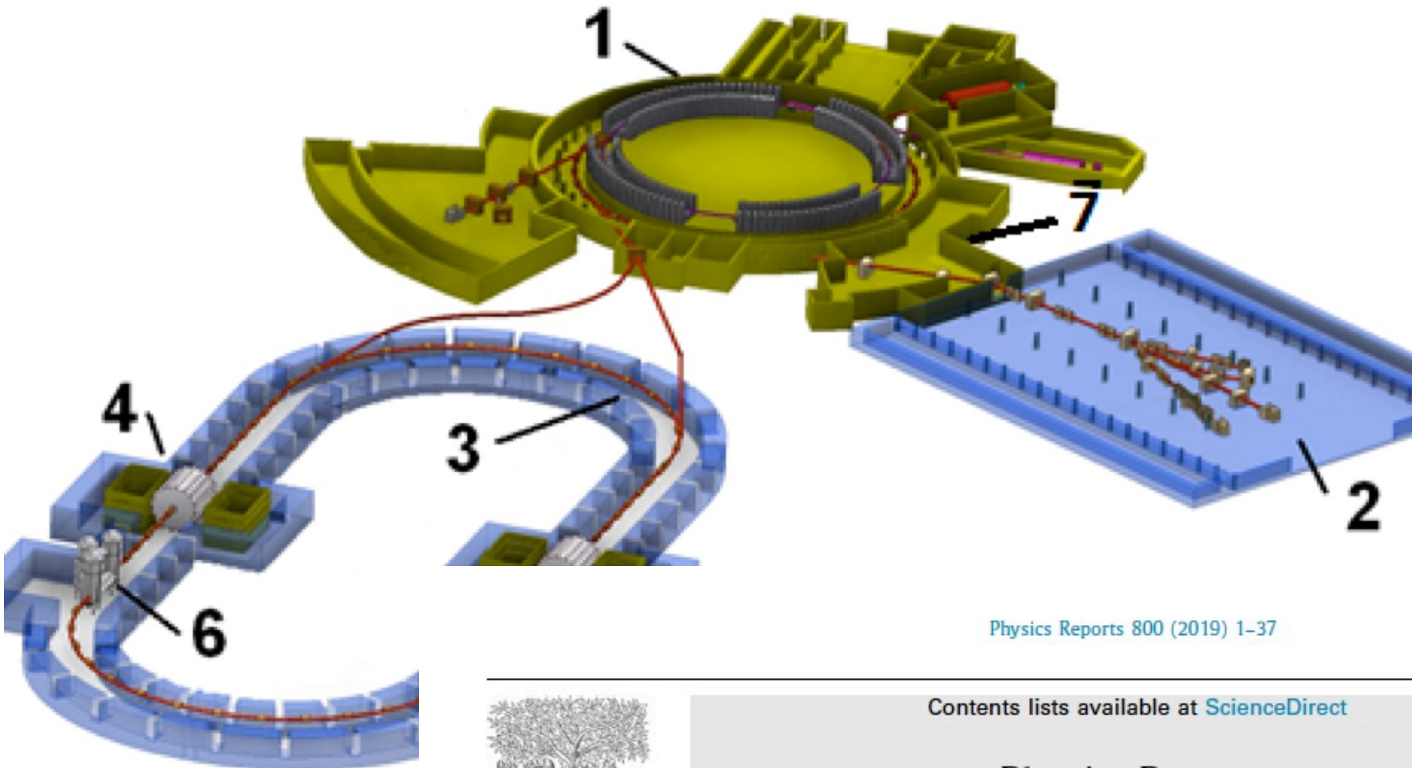


Applied nuclear physics at new particle accelerators

International Round Table on Applied Research and Innovations @ NICA

NEW NUCLEAR PHYSICS ACCELERATORS: FAIR, ELI, SPIRAL2, SPES, NICA, RAON,….

NICA



Physics Reports 800 (2019) 1–37

Contents lists available at ScienceDirect

Physics Reports

journal homepage: www.elsevier.com/locate/physrep

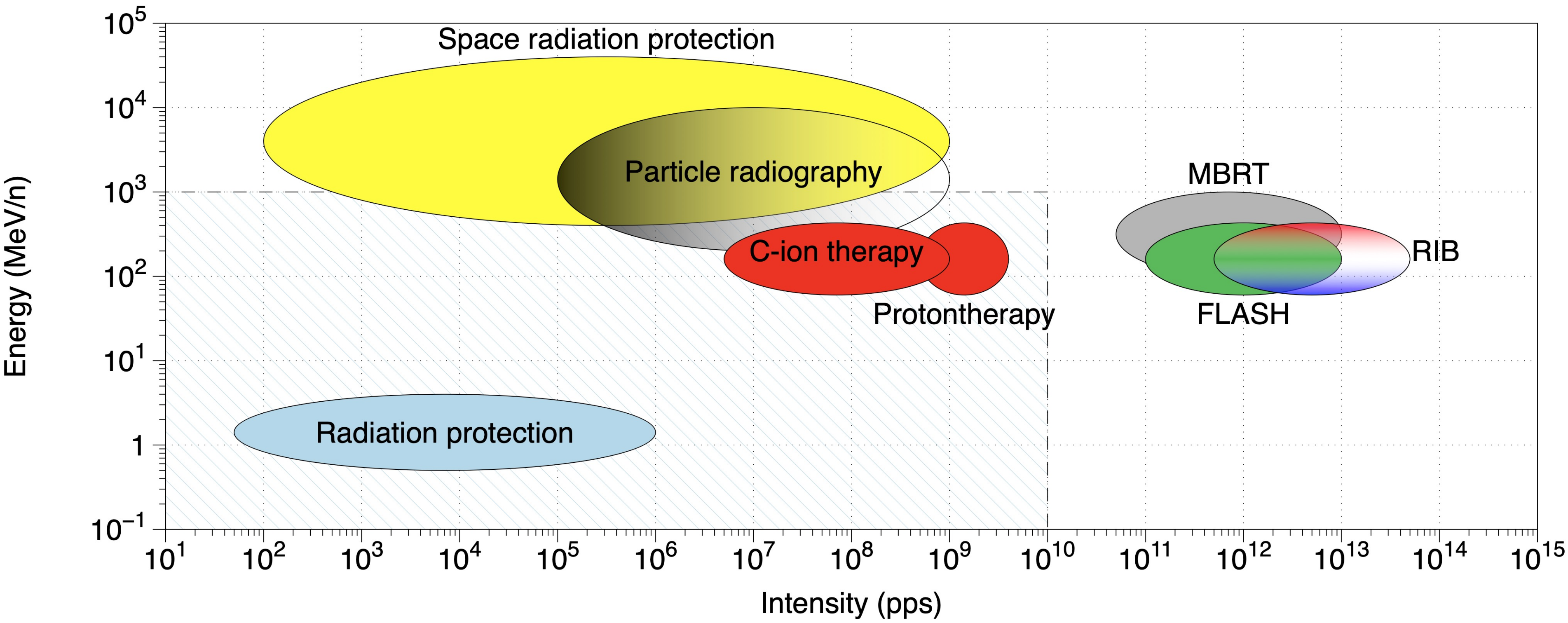
ELSEVIER

Applied nuclear physics at the new high-energy particle accelerator facilities

Marco Durante [a,b,*], Alexander Golubev [c,d], Woo-Yoon Park [e], Christina Trautmann [f,g]

Check for updates

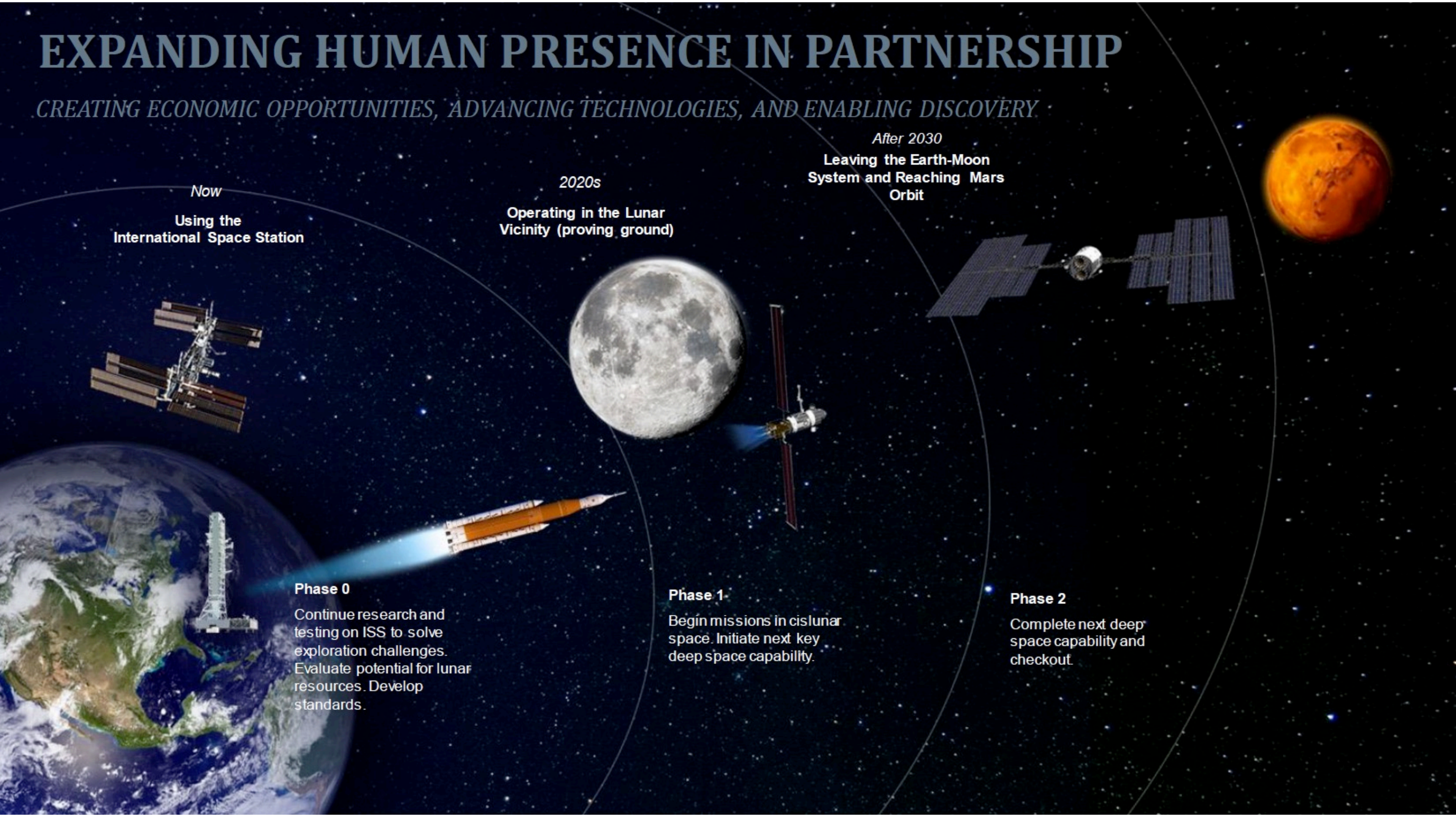
Biomedical applications: opportunities from new accelerators



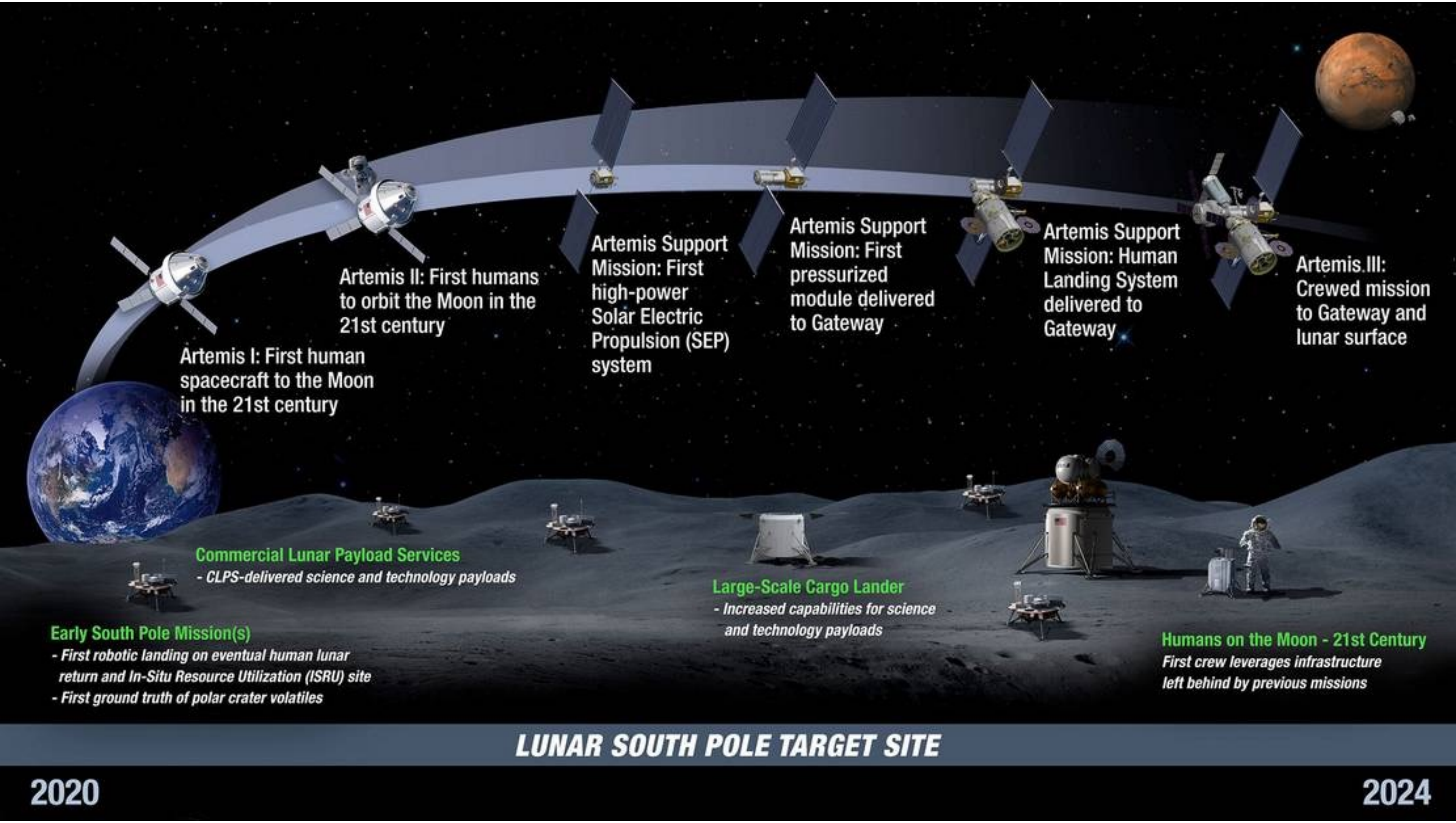
Patera *et al., Front. Phys.* 2020

- 250 participants from 27 countries in 5 continents

High-energy: space research



Lunar exploration is coming….



Life **2014**, *4*, 491-510; doi:10.3390/life4030491

OPEN ACCESS

life

ISSN 2075-1729

www.mdpi.com/journal/life

Review

Space Radiation: The Number One Risk to Astronaut Health beyond Low Earth Orbit

Jeffery C. Chancellor [1,2], Graham B. I. Scott [1,3] and Jeffrey P. Sutton [1,4,*]

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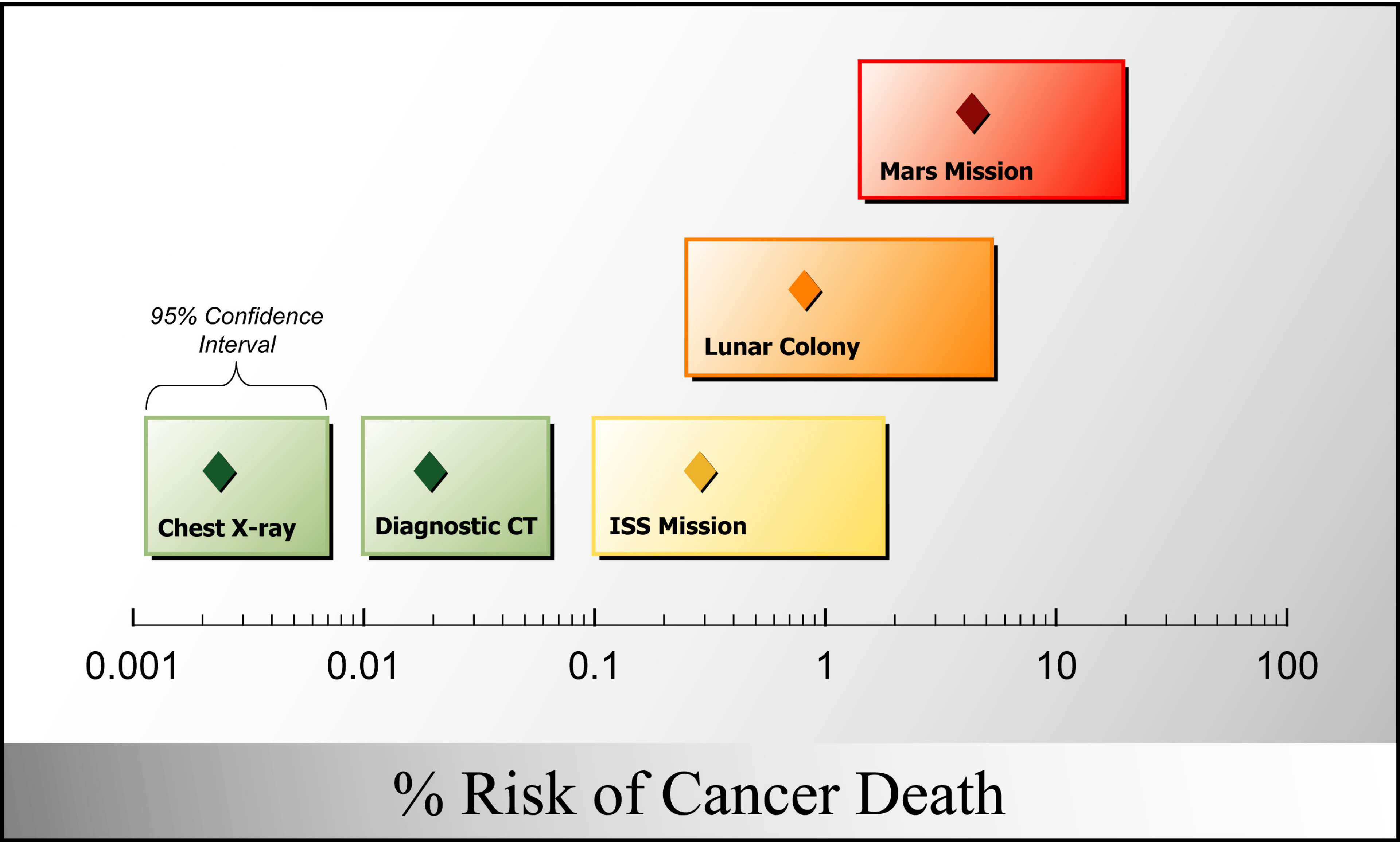
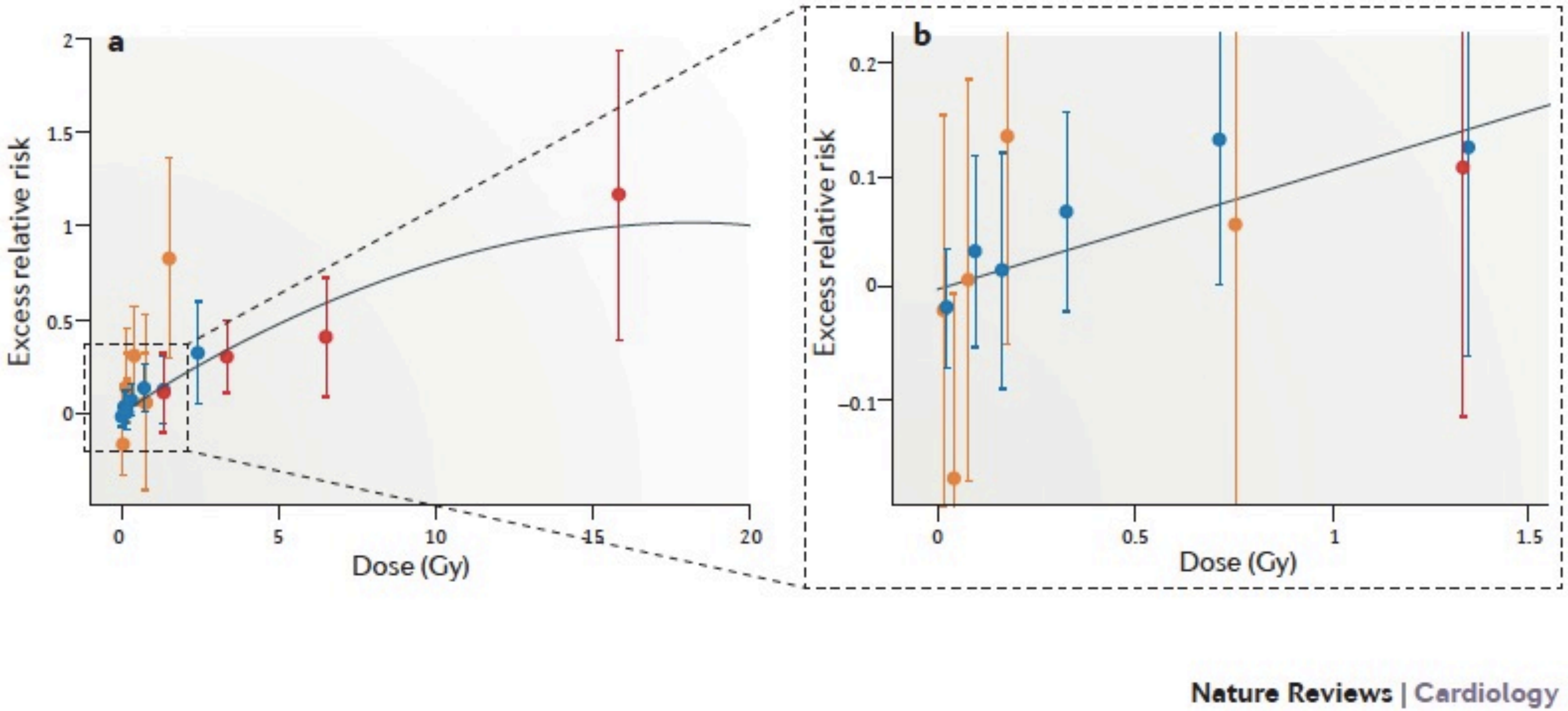
2. Department of Materials Science and Engineering, Dwight Look College of Engineering, Texas A&M University, 3003 TAMU, College Station, TX 77843-3003, USA
3. Department of Molecular and Cellular Biology, Baylor College of Medicine, 6500 Main Street, Suite 910, Houston, TX 77030-1402, USA
4. Department of Medicine, Baylor College of Medicine, 6500 Main Street, Suite 910, Houston, TX 77030-1402, USA



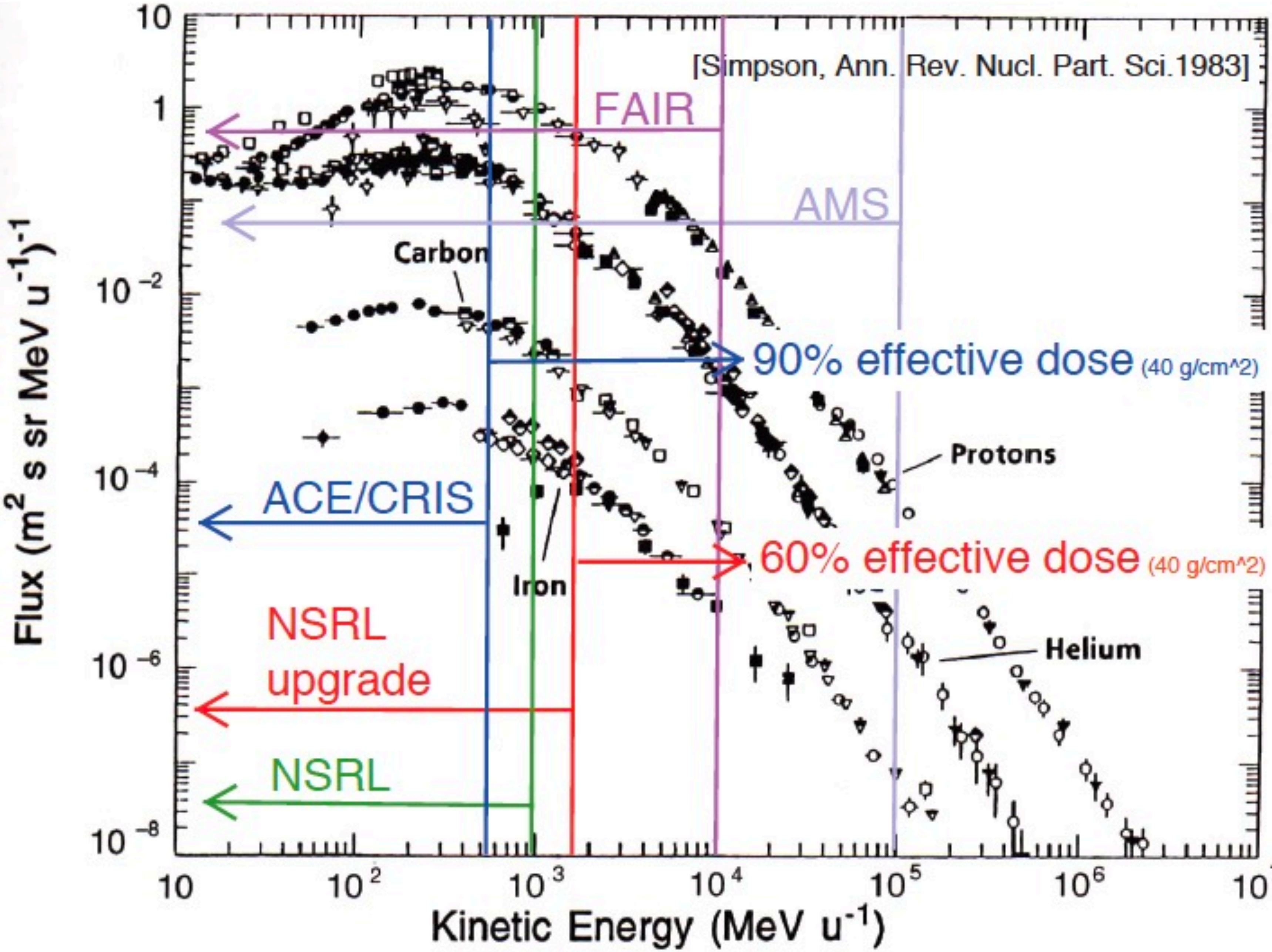
Durante & Cucinotta, *Nat. Rev. Cancer* 2008

Risk of radiation-induced late cardiovascular disease



Hughson, Helm & Durante, *Nat. Rev. Cardiol*. 2018

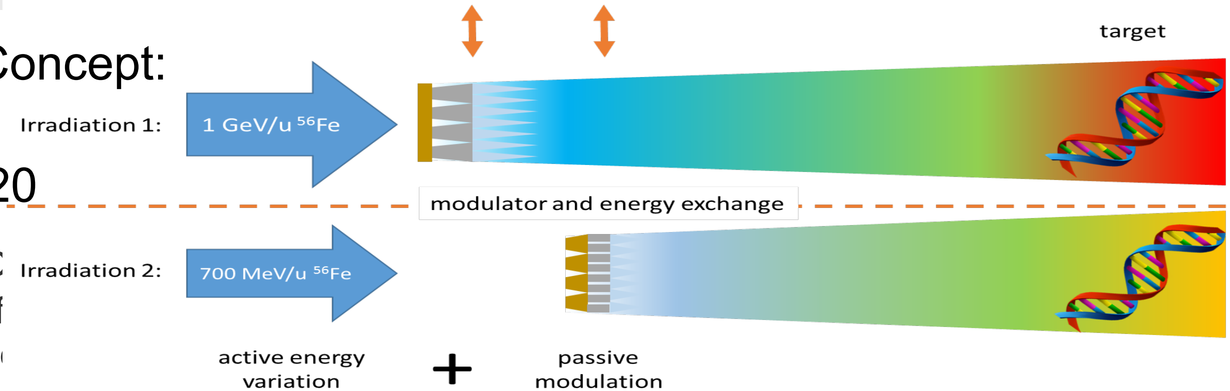
Accelerator tests


[Simpson, Ann. Rev. Nucl. Part. Sci.1983]
FAIR
AMS
Carbon
90% effective dose (40 g/cm^2)
Protons
ACE/CRIS
Iron
60% effective dose (40 g/cm^2)
NSRL upgrade
Helium
NSRL
Flux (m^2 s sr MeV u^-1)^-1
Kinetic Energy (MeV u^-1)
10
1
10^-2
10^-4
10^-6
10^-8
10^2
10^3
10^4
10^5
10^6
10^7

Ground-based GCR simulators

Schuy *et al.*, *Front. Phys.* 2020

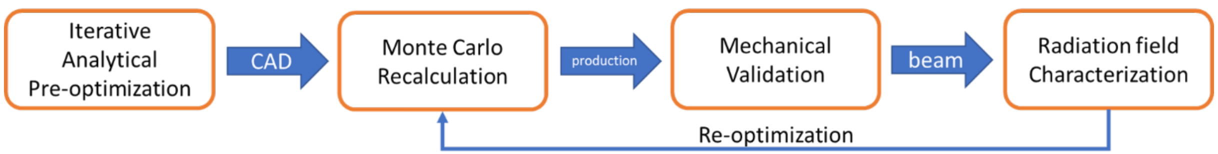
Concept:



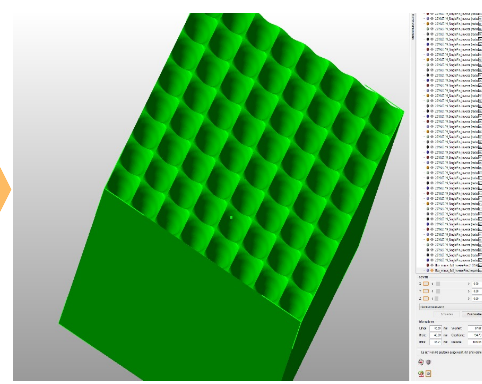
- NASA Space Radiation Lab
  - Fast sequential irradiation of
  - Accelerator setup time & irra

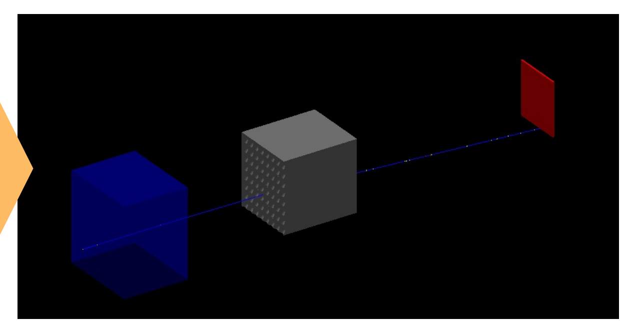
- Hybrid active-passive system @GSI
  - Active energy variation of ^{56}Fe
  - Complex passive modulators
  - Control over kinetic energy, nuclear fragmentation and scattering -> composition of radiation field

Superposition of radiation fields at target position => realistic space radiation field



Input spectra (LET, yield, kinetic energies)





Life Sciences in Space Research 30 (2021) 66–71

Contents lists available at ScienceDirect

Life Sciences in Space Research

journal homepage: www.elsevier.com/locate/lssr

ELSEVIER

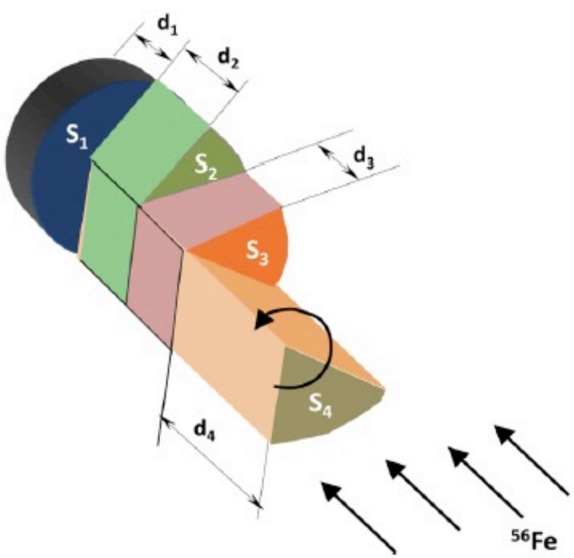
Check for updates

A new type of ground-based simulator of radiation field inside a spacecraft in deep space

I.S. Gordeev [a,b], G.N. Timoshenko [a,b,*]

[a] Joint Institute for Nuclear Research, 141980, Dubna, Moscow region, Russia
[b] Dubna State University, 141980, Dubna, Moscow region, Russia

$D_1 = d_1$;
$D_2 = d_1 + d_2$;
$D_3 = d_1 + d_2 + d_3$;
$D_4 = d_1 + d_2 + d_3 + d_4$

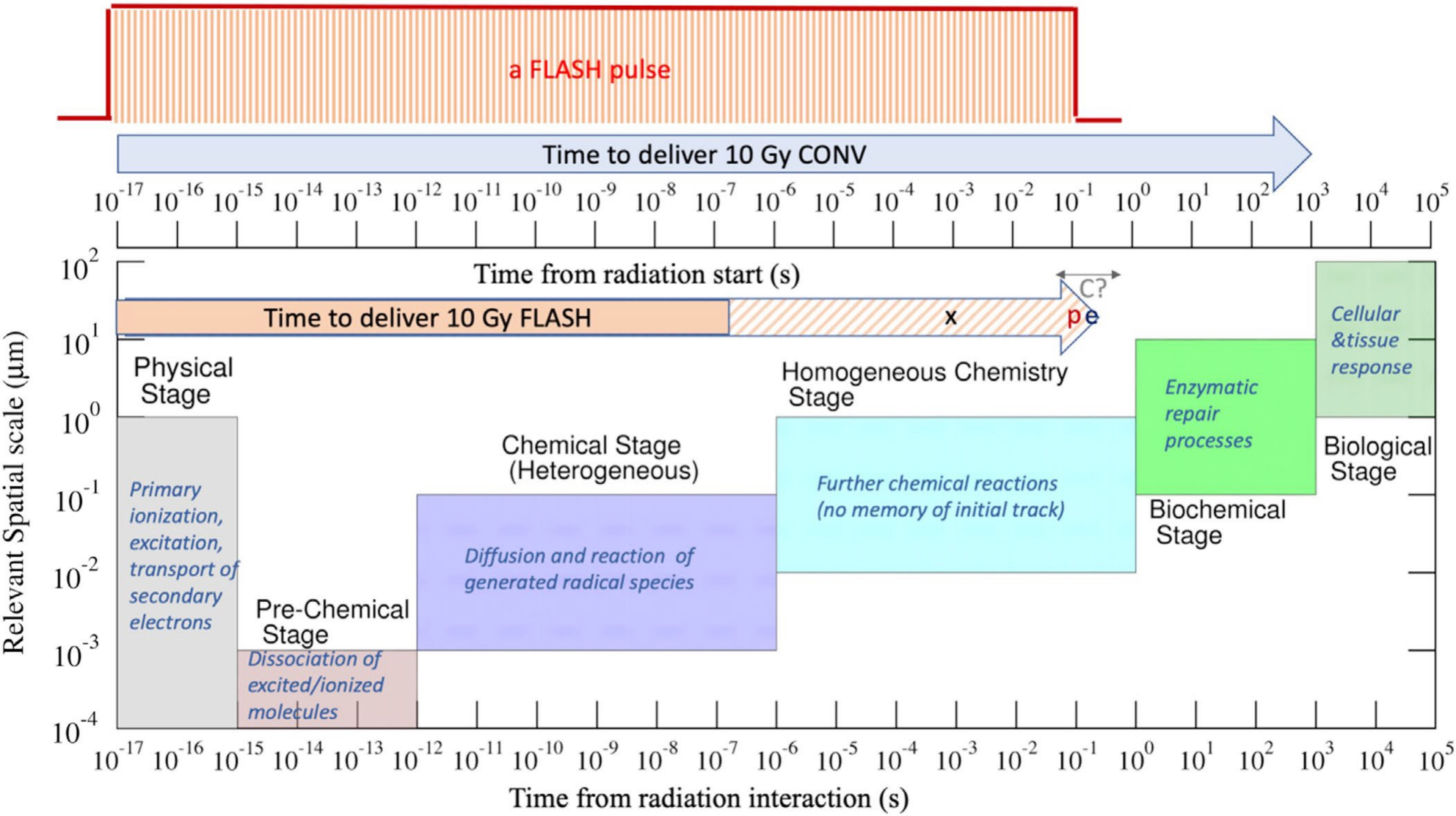


JINR

HELMHOLTZ

High intensity

FLASH radiotherapy



Weber, Scifoni & Durante, *Med. Phys.* 2021

FLASH clinical trials ongoing with electrons and protons

Radiotherapy and Oncology xxx (xxxx) xxx

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original Article

Treatment of a first patient with FLASH-radiotherapy

Jean Bourhis [a,b,*], Wendy Jeanneret Sozzi [a], Patrik Gonçalves Jorge [a,b,c], Olivier Gaide [d], Claude Bailat [c], Fréderic Duclos [a], David Patin [a], Mahmut Ozsahin [a], François Bochud [c], Jean-François Germond [c], Raphaël Moeckli [c,1], Marie-Catherine Vozenin [a,b,1]

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ARTICLE INFO

Article history:
Received 1 April 2019
Received in revised form 12 June 2019
Accepted 14 June 2019
Available online xxxx

Keywords:
FLASH-RT
Normal tissue protection
Differential effect
Clinical translation

ABSTRACT

Background: When compared to conventional radiotherapy (RT) in pre-clinical studies, FLASH-RT was shown to reproducibly spare normal tissues, while preserving the anti-tumor activity. This marked increase of the differential effect between normal tissues and tumors prompted its clinical translation. In this context, we present here the treatment of a first patient with FLASH-RT.
Material & methods: A 75-year-old patient presented with a multiresistant CD30+ T-cell cutaneous lymphoma disseminated throughout the whole skin surface. Localized skin RT has been previously used over 110 times for various ulcerative and/or painful cutaneous lesions progressing despite systemic treatments. However, the tolerance of these RT was generally poor, and it was hypothesized that FLASH-RT could offer an equivalent tumor control probability, while being less toxic for the skin. This treatment was given to a 3.5-cm diameter skin tumor with a 5.6-MeV linac specifically designed for FLASH-RT. The prescribed dose to the PTV was 15 Gy, in 90 ms. Redundant dosimetric measurements were performed with GafChromic films and alanine, to check the consistency between the prescribed and the delivered doses.
Results: At 3 weeks, i.e. at the peak of the reactions, a grade 1 epithelitis (CTCAE v 5.0) along with a transient grade 1 oedema (CTCAE v5.0) in soft tissues surrounding the tumor were observed. Clinical examination was consistent with the optical coherence tomography showing no decrease of the thickness of the epidermis and no disruption at the basal membrane with limited increase of the vascularization. In parallel, the tumor response was rapid, complete, and durable with a short follow-up of 5 months. These observations, both on normal skin and on the tumor, were promising and prompt to further clinical evaluation of FLASH-RT.
Conclusion: This first FLASH-RT treatment was feasible and safe with a favorable outcome both on normal skin and the tumor.

July 11, 2019

FLASH with carbon ions

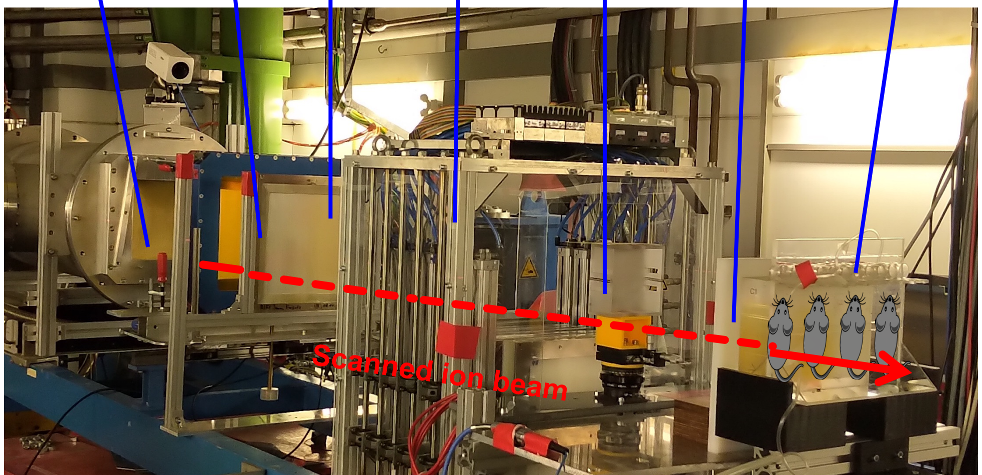
<u>Beam</u>: 240 MeV/u ; ^{12}C ; Ø ≈ 8 mm (FWHM)

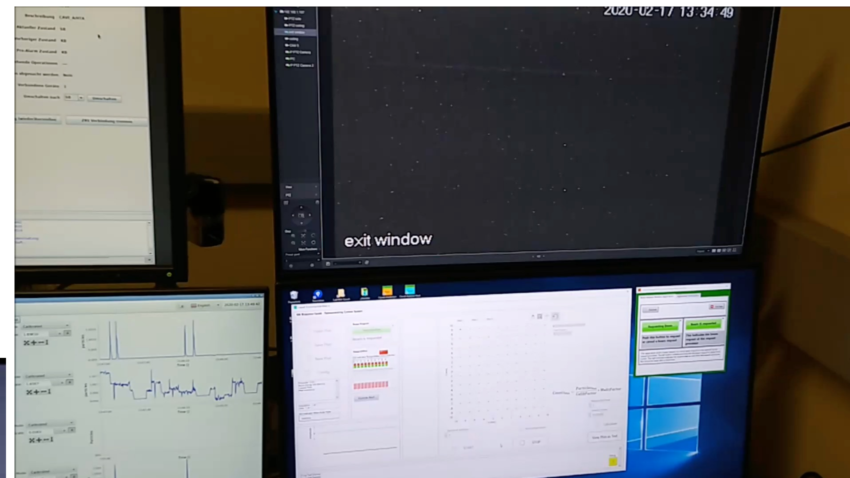
<u>Beam intensity</u> : 5×10⁹ ± 20% ions per spill
> 3×10⁹ ions per spill (for all spills)

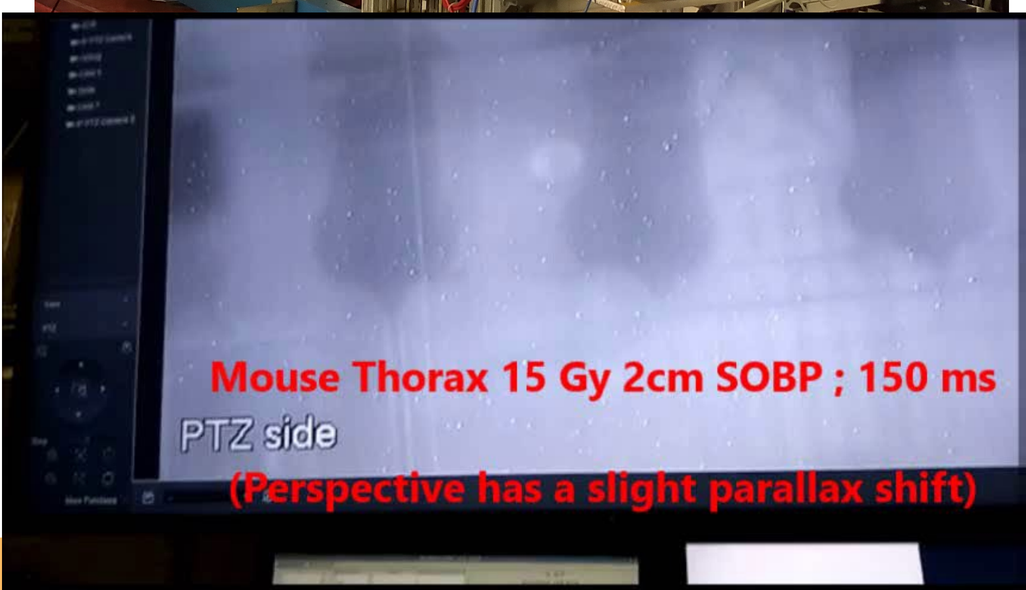
<u>Extraction time</u>: < 200 ms

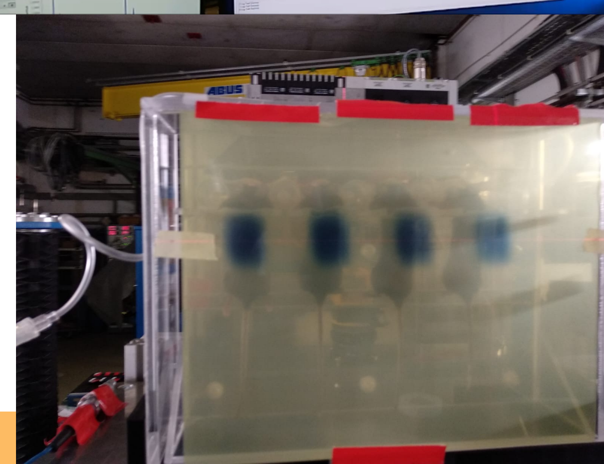
<u>Doses</u>: 12-18 Gy. <u>Dose-rate</u>: typ. **100 Gy/s**

<u>Field size</u>: ~ 20 x 16 mm² <u>SOBP</u>: 2 cm (> 60 keV/µm)

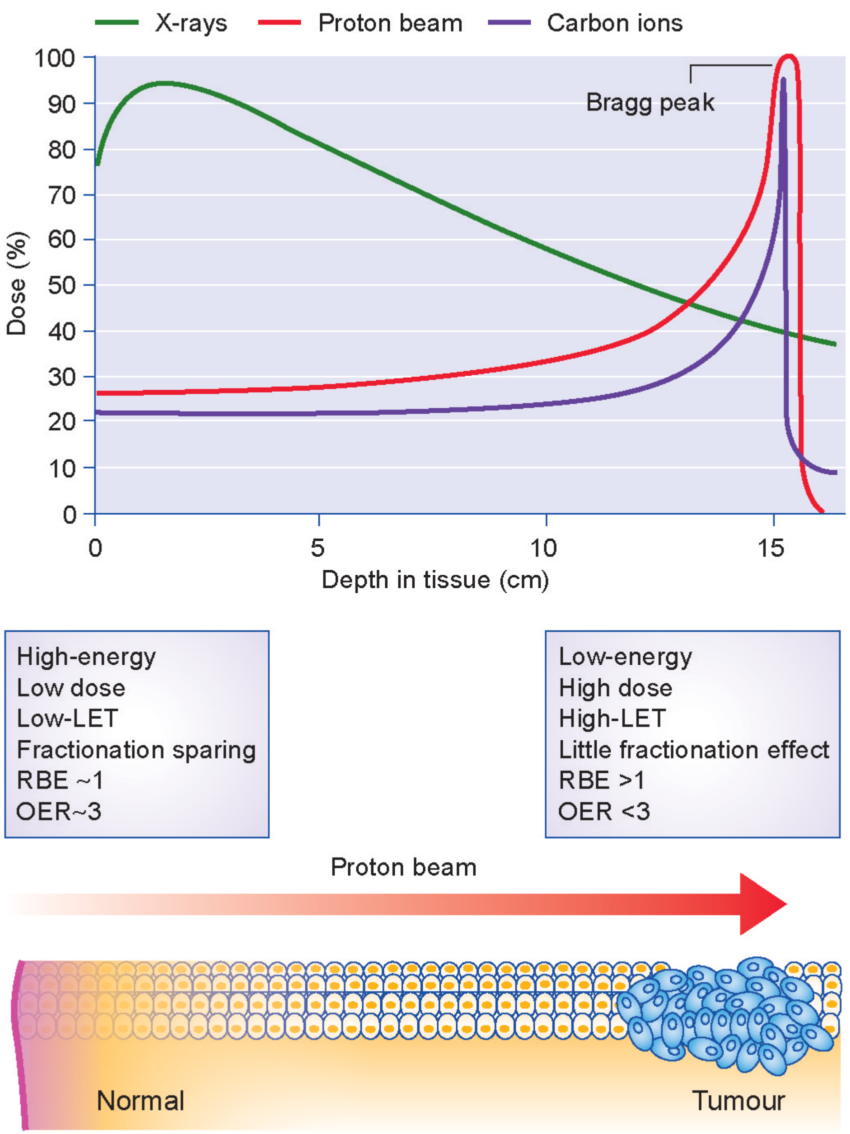




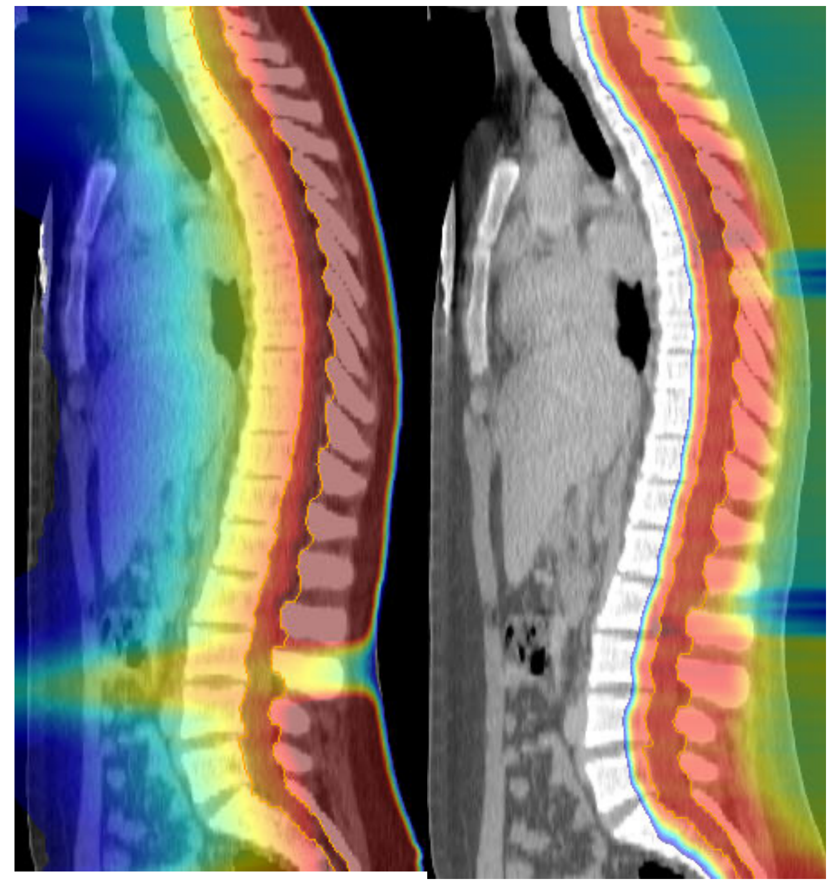




Bragg peak in particle therapy



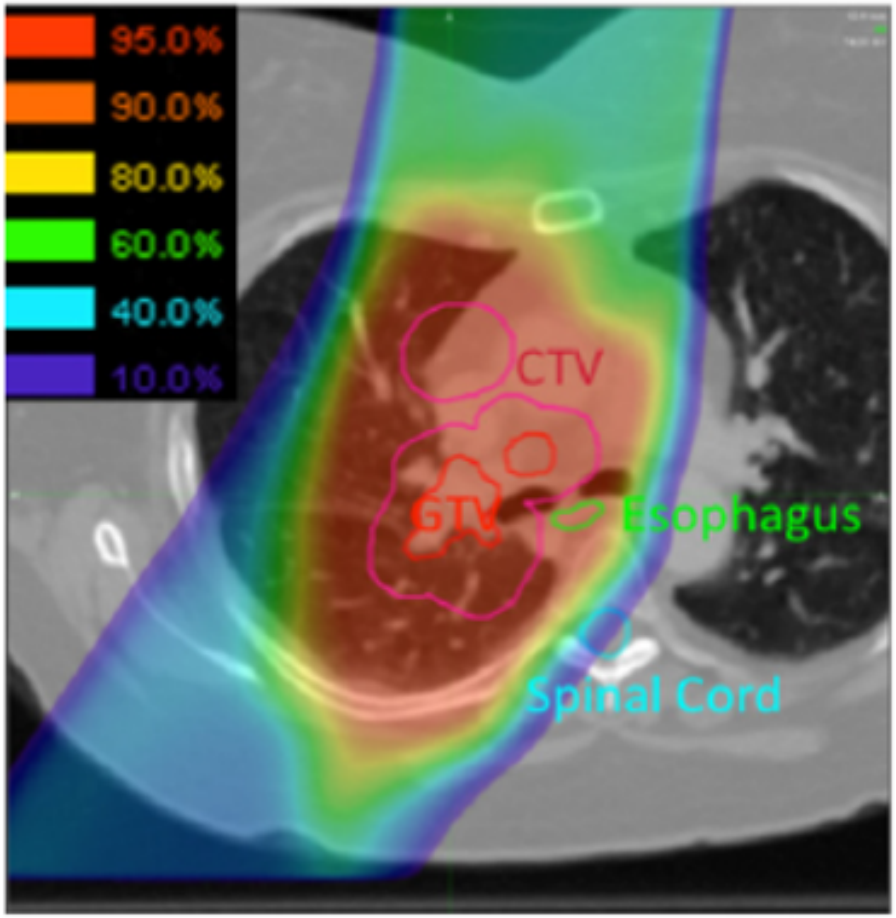
Durante, Br. J. Cancer 2019

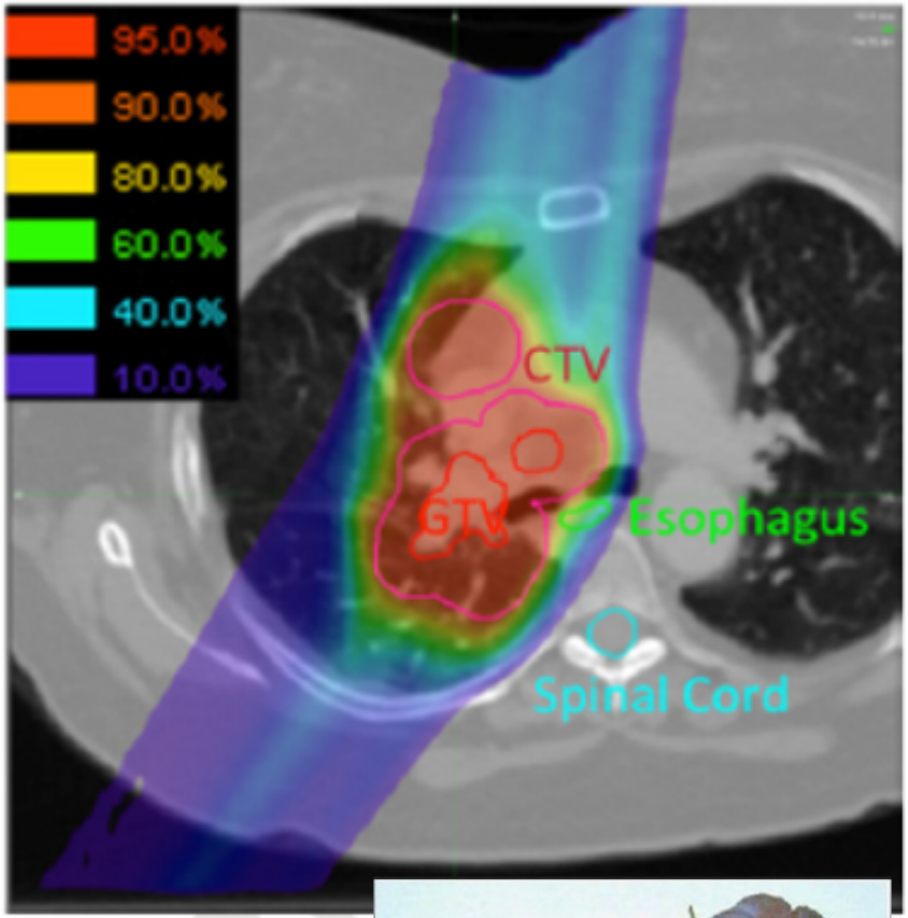


X-rays Protons

Durante *et al., Nat. Rev. Phys*. 2021

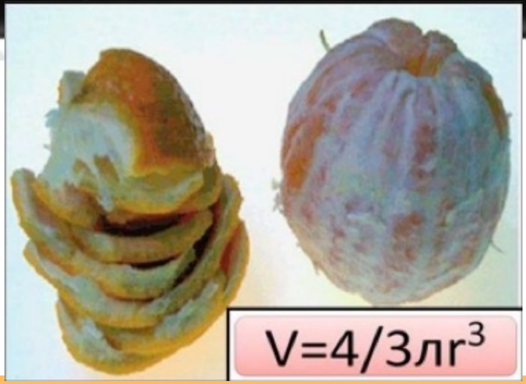
Range uncertainty jeopardizes the Bragg peak precision





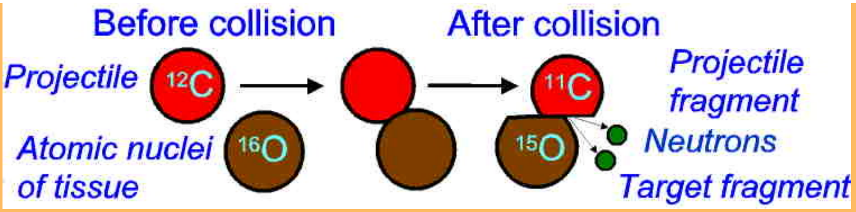
Durante & Flanz, *Semin. Oncol*. 2019

Total margins ~ 1 cm compared
to a proton penumbra ~ 2 mm



Verellen et al., *Nat. Rev. Cancer*. 2007

In-situ range verification with PET



fondazione CNAO

Radioactive Ion Beams (RIB) for simultaneous treatment and range verification

European Research Council

B · A · R · B
BIOMEDICAL APPLICATIONS OF RADIOACTIVE ION BEAMS

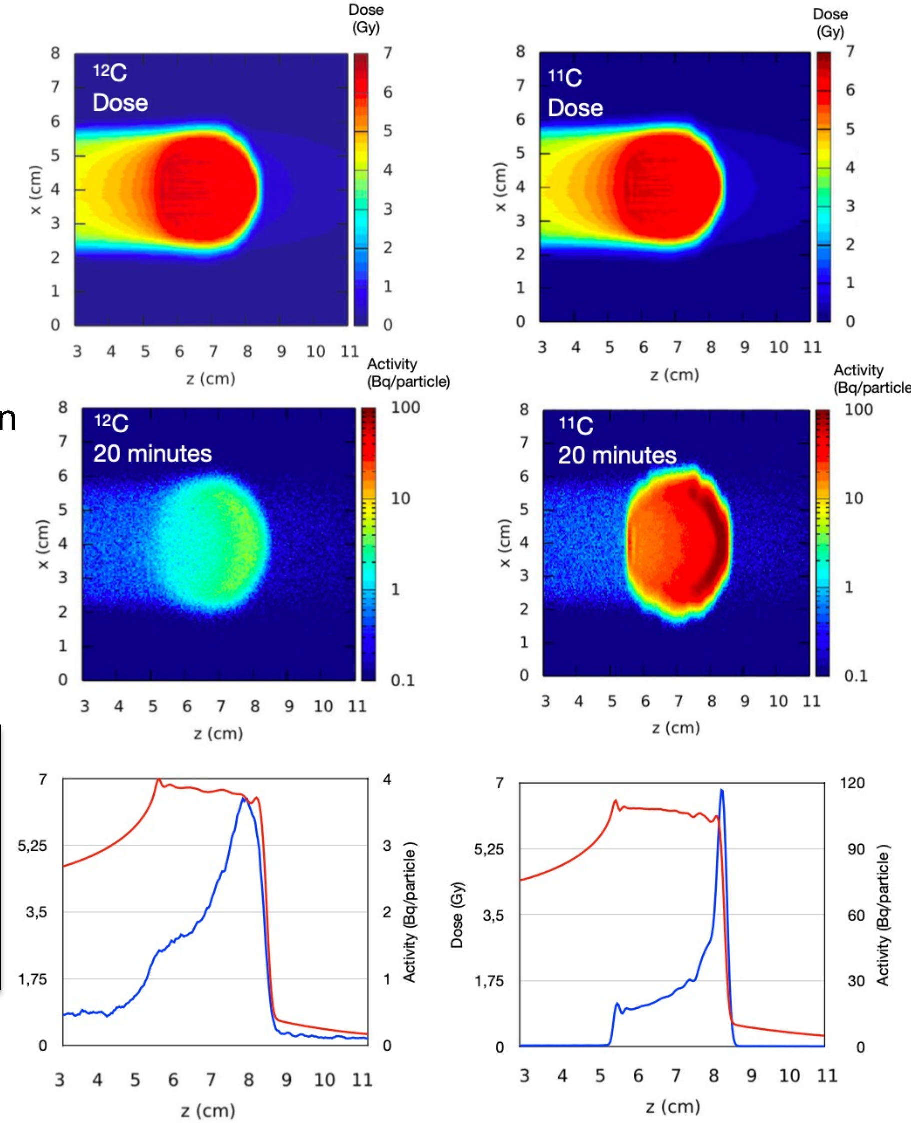
www.gsi.de/BARB

- Improved count rate (one order of magnitude larger than for stable ions)
- Improved correlation between activity and dose
- Reduced washout blur thanks to short lived isotopes

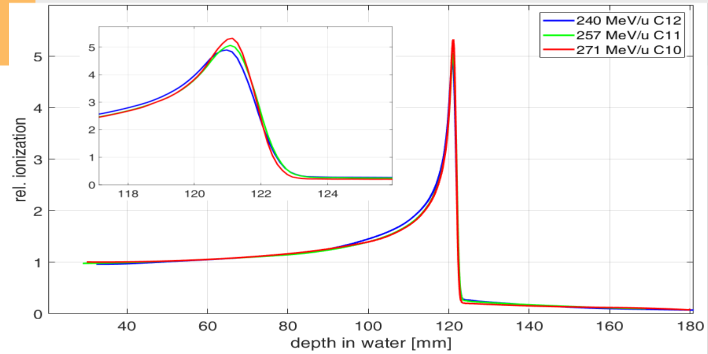
Hampered by the low intensities achievable

RIB therapy is now revived thanks to the construction of therapy compatible high-intensity accelerators.

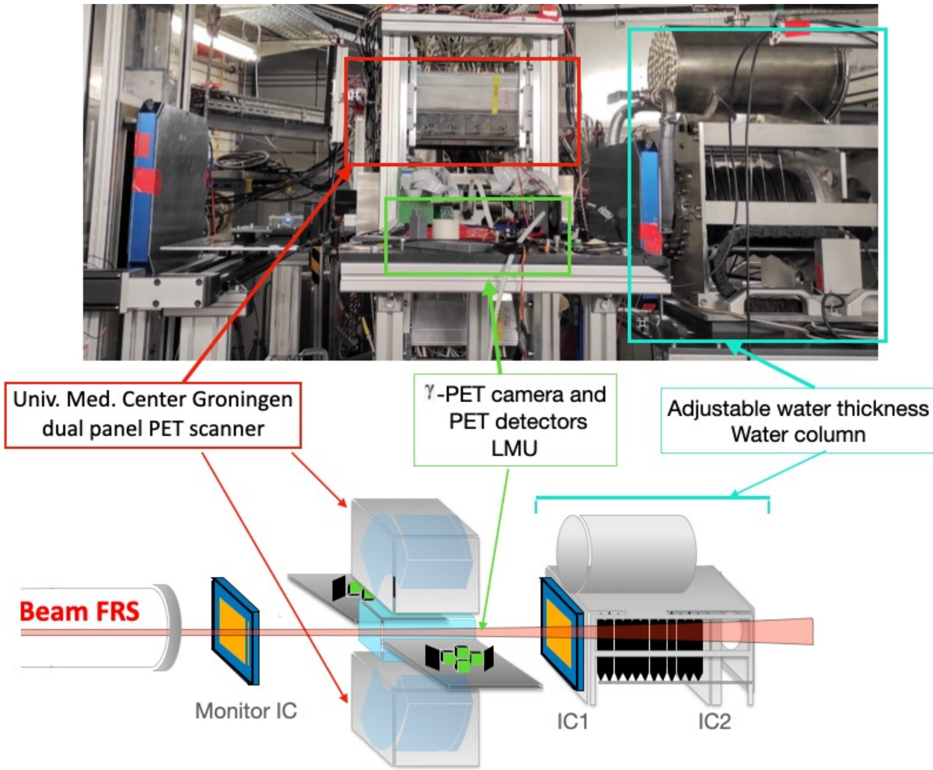
e.g. FAIR Phase 0 at GSI (Darmstadt, Germany)



Boscolo *et al., Front. Oncol*. 2021



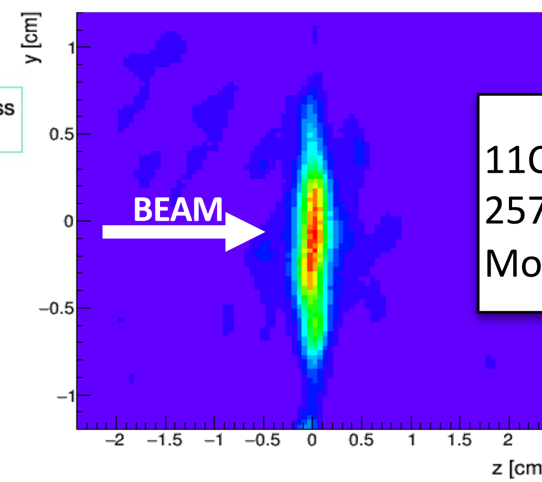
BARB: first experimental tests in June 2021



Isotopes:	^{10}C	^{11}C	^{12}C
Half-life (min):	0.322	20.36	stable
Intensities:	~10^6 pp/s	~10^7 pp/s	~10^8 pp/s

Energy: ~270 MeV/u and ~135 MeV/u
Imaging phantoms: PE and PMMA
FRS ion optical modes Monochromatic and achromatic

PET image



11C beam,
257 MeV/u
Monochromatic mode

Conclusions

- FAIR and other new accelerators (e.g. NICA, RAON, SPIRAL2, ELI…) offer new opportunities for biomedical research
- Both high energy and high intensity can have important applications in different fields such as space radiation protection and particle therapy
- Space radiation research is urgently needed to allow a safe exploration of the solar system
- High intensity (FLASH, RIB, minibeams,…) can provide breakthrough in particle therapy
- The Biophysics Collaboration at FAIR is open to contributions, ideas, proposals from the whole scientific community, and NICA should be a privileged partner

Thanks you very much!

www.gsi.de/biophysik

Thank you!

JINR

Funding agencies

HELMHOLTZ GEMEINSCHAFT

Bundesministerium für Bildung und Forschung

NIH National Institutes of Health

erc

esa

Horizon 2020
European Union Funding
for Research & Innovation