Heavy ions in therapy and space

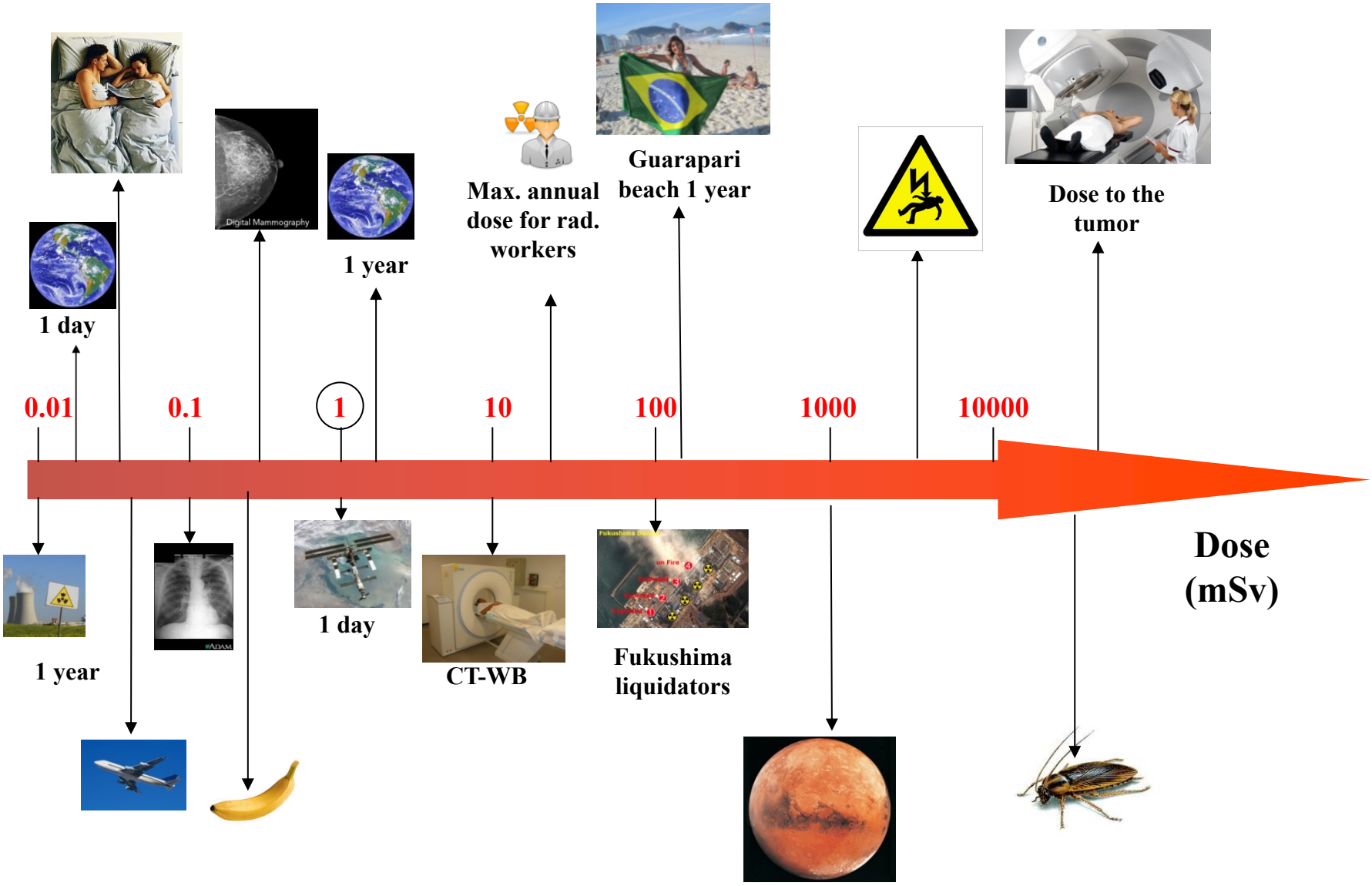
Marco Durante, TIFPA

www.tifpa.infn.it

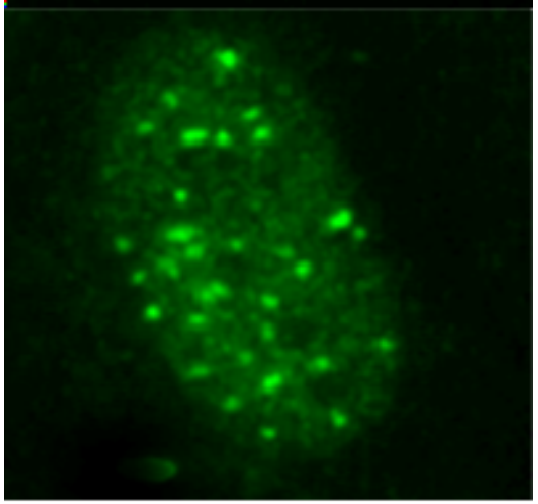
20.1.2017

Radiation effects depends on the DOSE

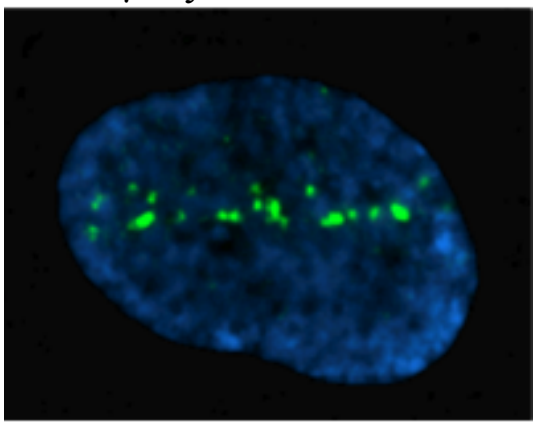
Dose is an energy per unit mass and is measured in Sievert = Joule/kg



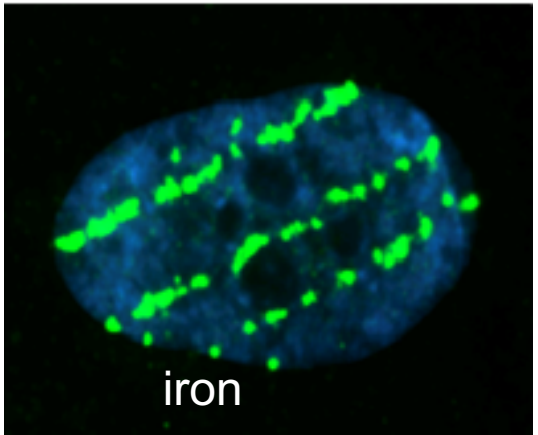
Charged particles



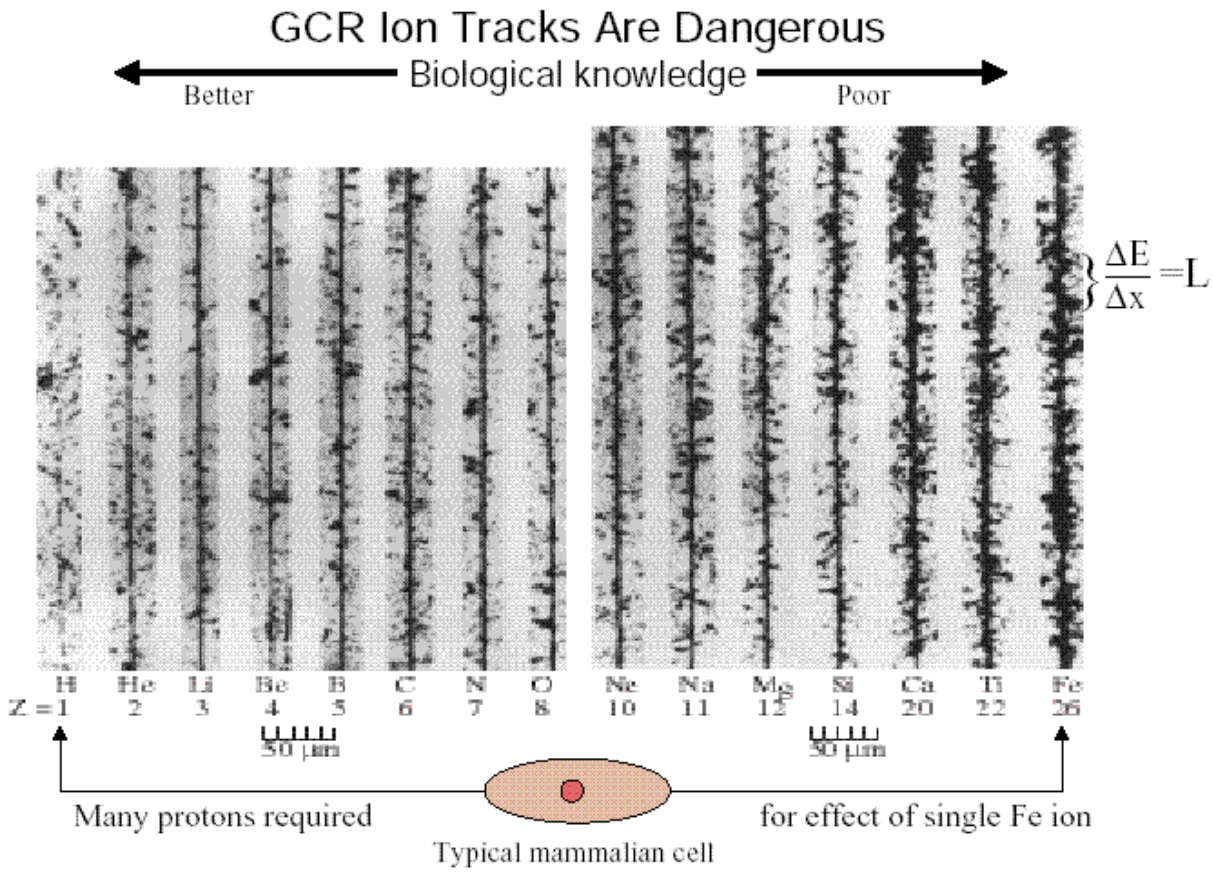
γ-rays



silicon



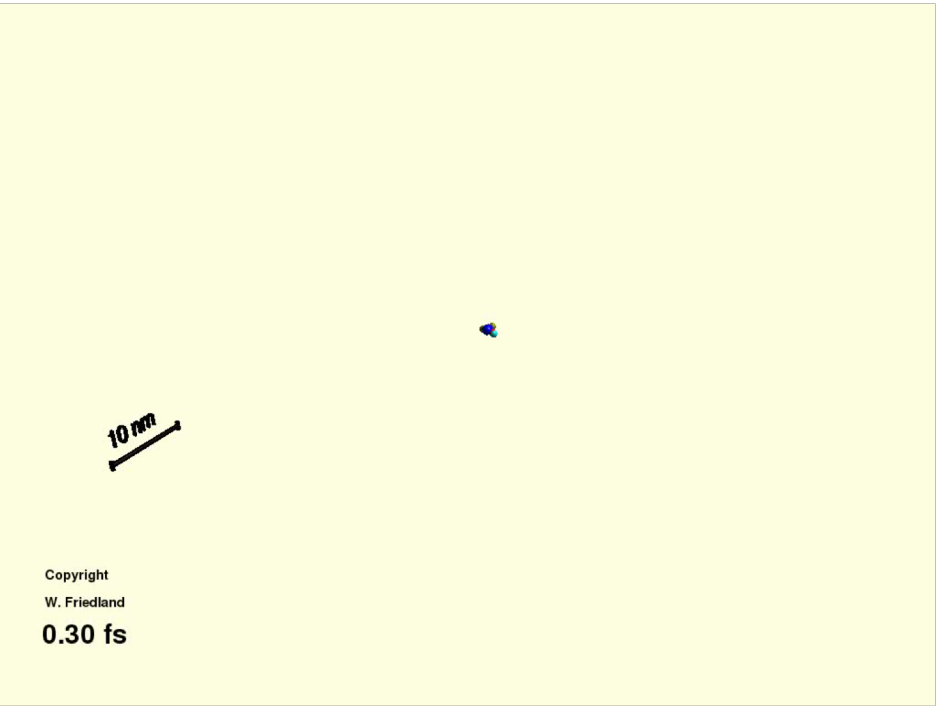
iron



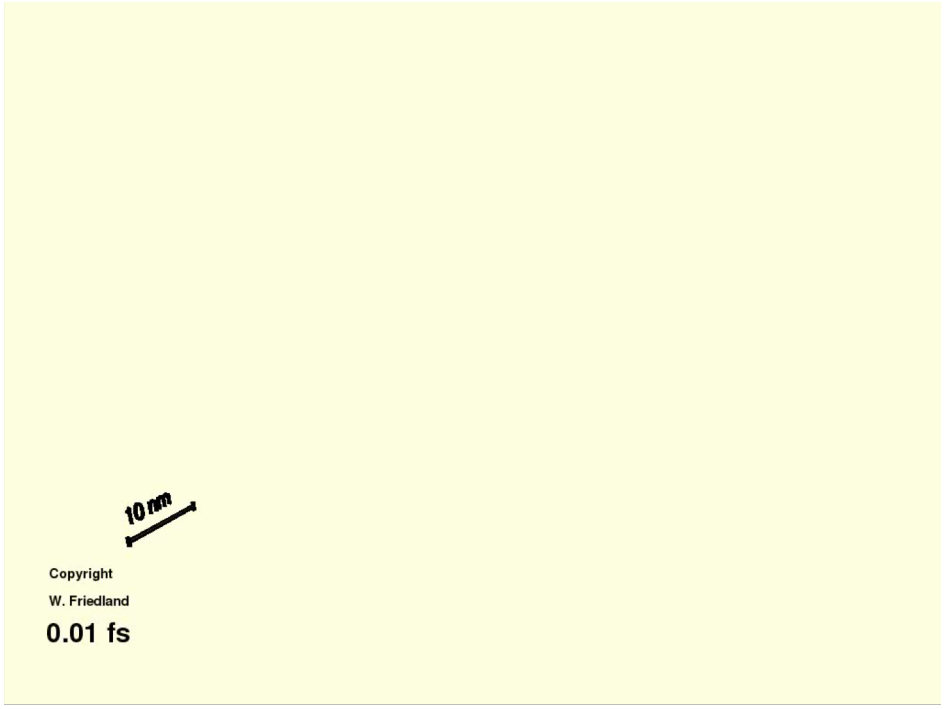
Cucinotta and Durante, *Lancet Oncol.* 2006

Light vs. heavy ions at the same linear energy transfer (LET=140 keV/μm)

α-particles, 2 MeV

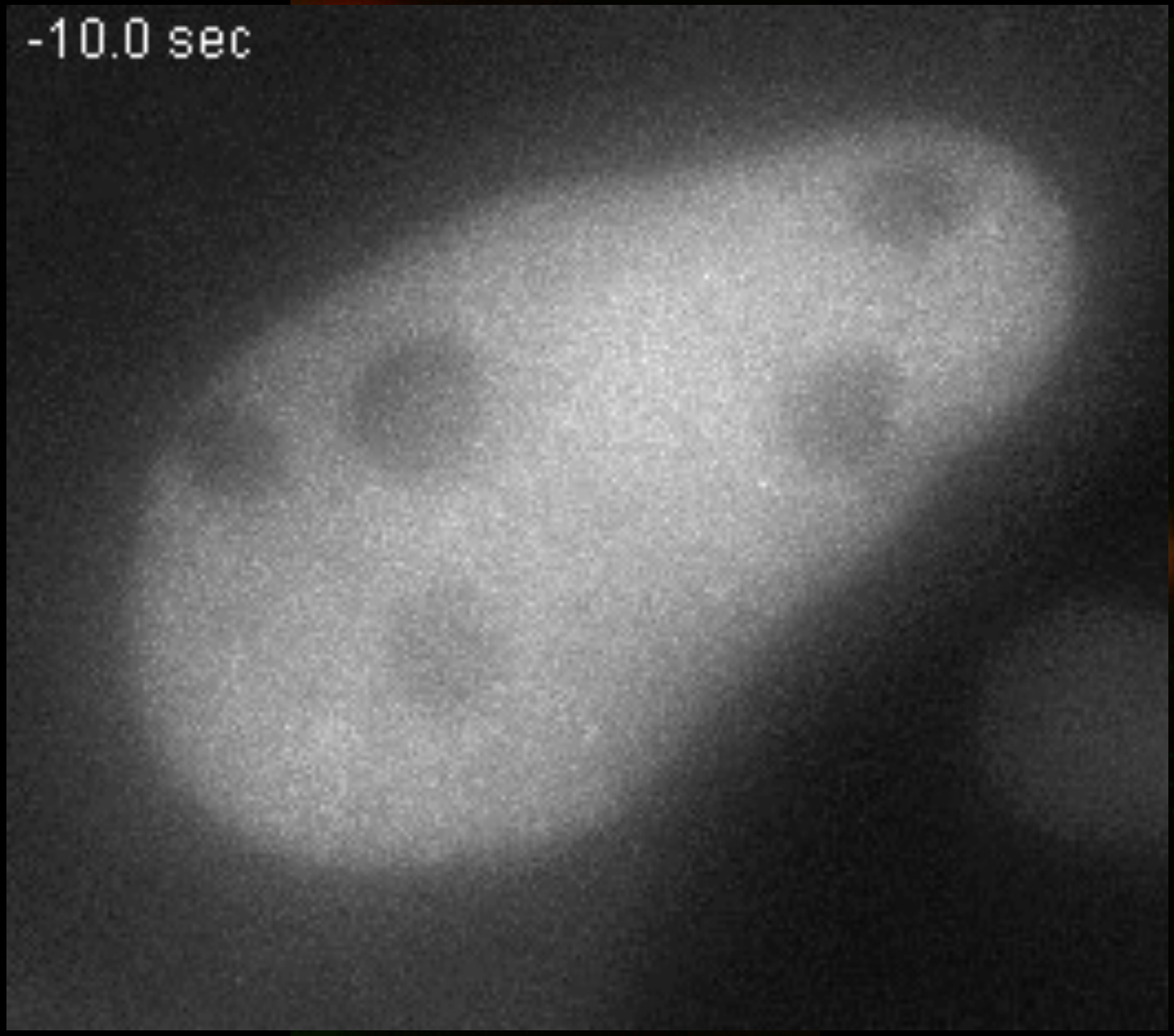


Fe-ions, 1 GeV/n

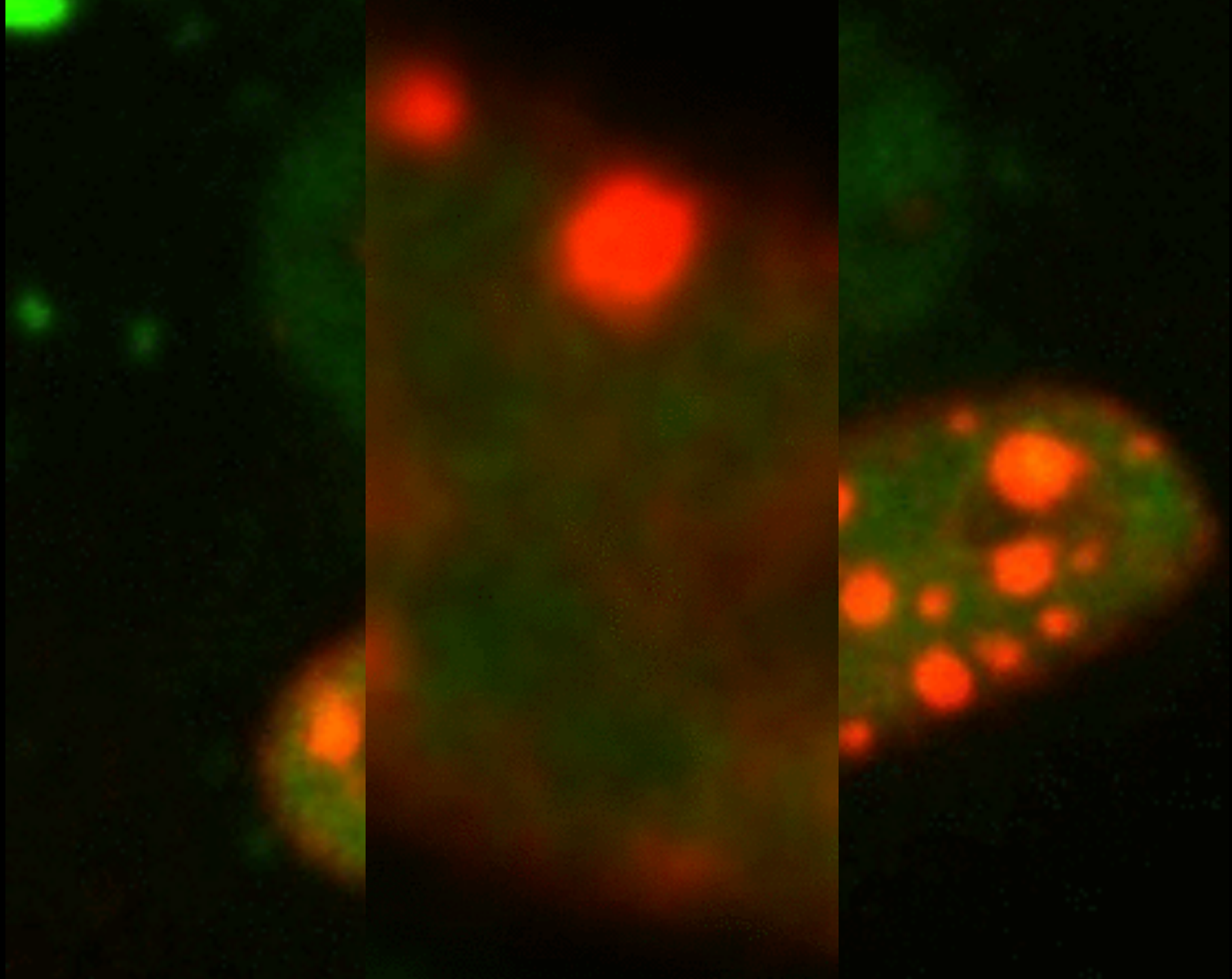


courtesy of Werner Friedland

Live cell imaging of heavy ion traversals in euchromatin and heterochromatin



Jakob *et al., Proc. Natl. Acad. Sci. USA* 2009*; Nucl. Acids Res*. 2011

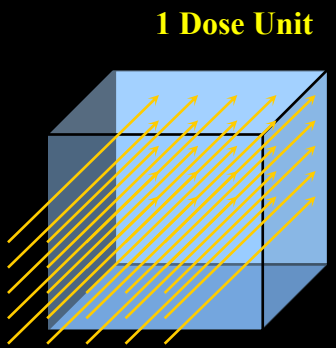


An Analogy for Structured Energy Deposition and its Consequences

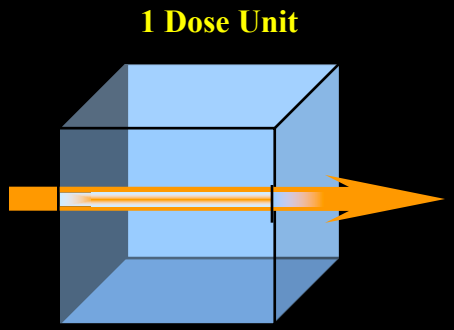
Low LET radiation produces isotropic damage to organized targets.

High LET radiation produces correlated damage to organized targets.

LET: Linear Energy Transfer



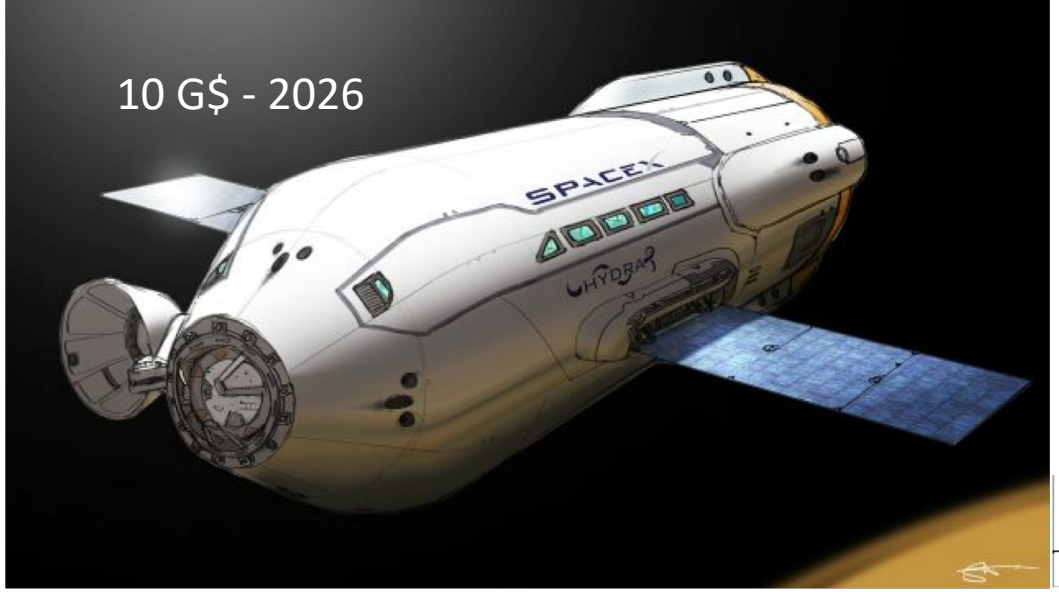
Low LET radiation deposits energy in a uniform pattern



High LET radiation deposits energy in a non-uniform pattern

Why are we interested in energetic heavy ions?

Heavy ion radiation is not present naturally on Earth



The New York Times

Space & Cosmos

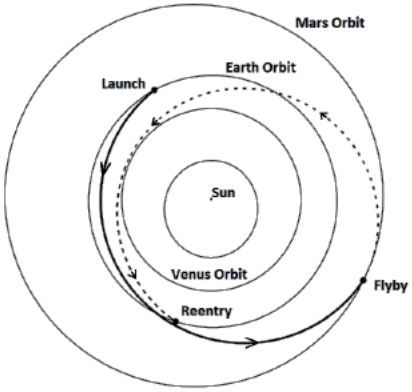
WORLD | U.S. | N.Y. / REGION | BUSINESS | TECHNOLOGY | SCIENCE | HEALTH | SPORTS | OPINION

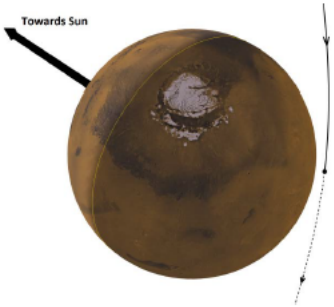
ENVIRONMENT | SPACE & COSMOS

May, 30, 2013

Data Point to Radiation Risk for Travelers to Mars

- A 501-day "free-return" Mars flyby passing within a hundred miles of the surface
  - Only small correction maneuvers are needed during transit
- Simple mission architecture lowers risk
  - No entry into Mars atmosphere
- An exceptionally quick free return occurs twice every 15 years
  - 1.4 years duration vs. 2 to 3.5 years typical
  - Launch Jan 5, 2018, (or 2031)
  - Mars on 20 Aug 2018 (227 days)
  - Earth on 20 May 2019 (274 days)
  - At Mars, Earth is 38,000,000 miles away
- Video
  - http://www.youtube.com/watch?v=IBGIYNd2tmA





Dose=1.8 mSv/dayx501x2=1.8 Sv

NASA might build an ice house on Mars

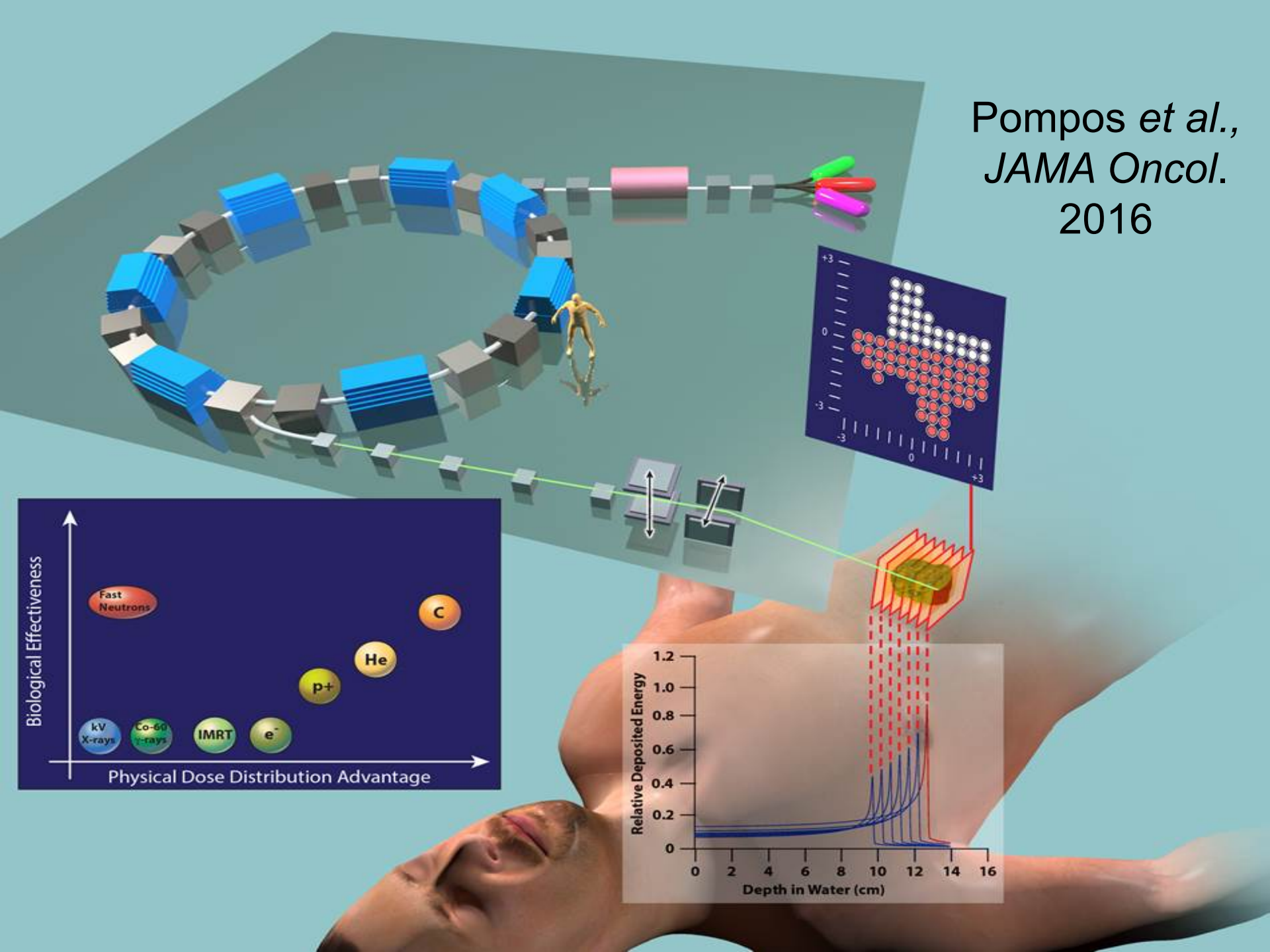
December 30, 2016 by Nancy Atkinson, Universe Today

Protection by ISRU materials

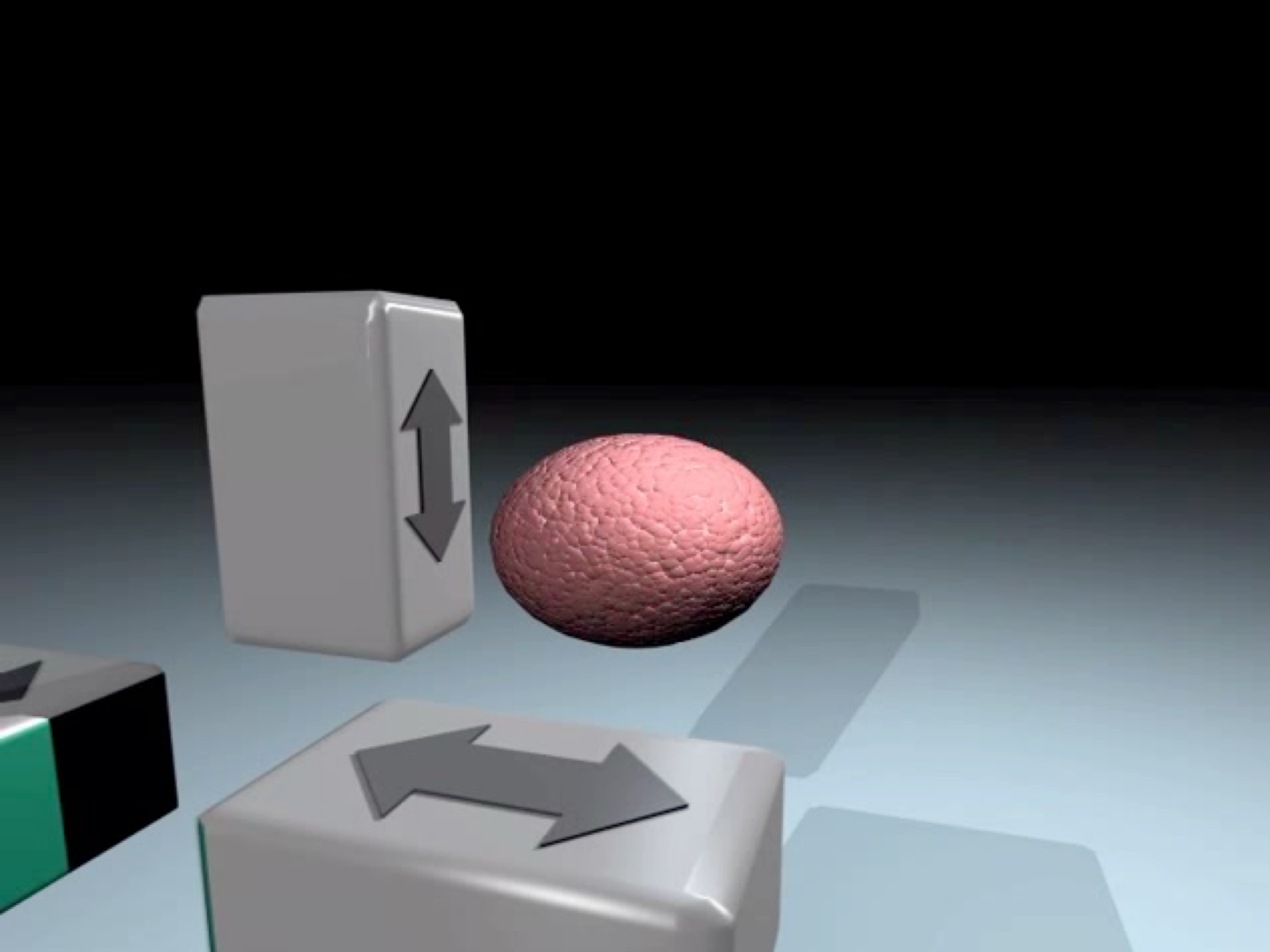
Health in Deep Space

1. Protection from space radiation (particularly very high energy heavy ions)
2. Psychosocial and behavioural problems
3. Physiological changes caused by microgravity

Modified by Mike Lockwood



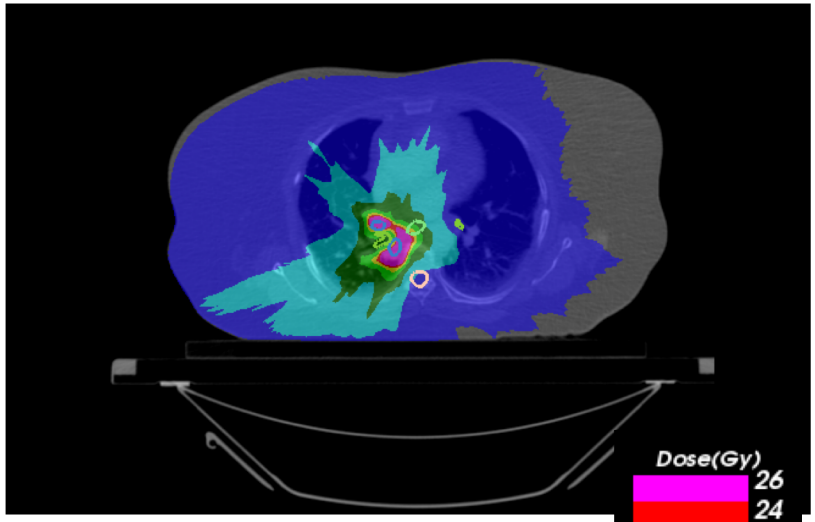
Pompos *et al.*, *JAMA Oncol*. 2016



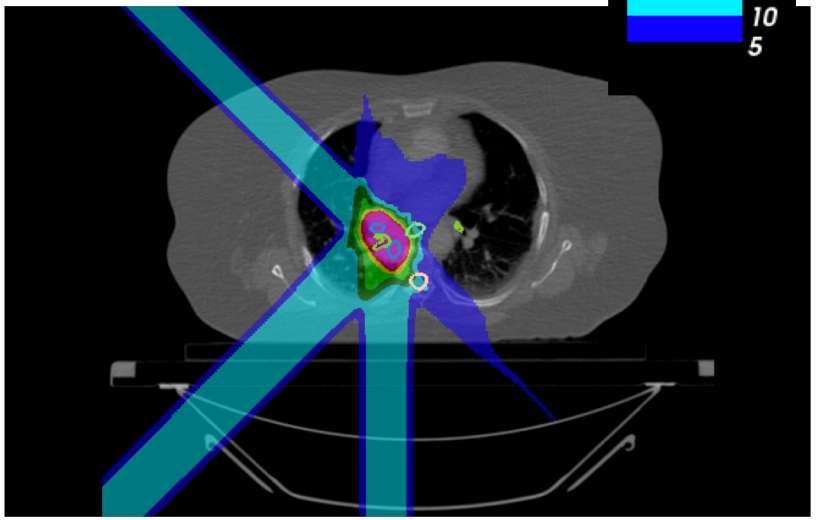
Lung tumors: SBRT vs. C-ions

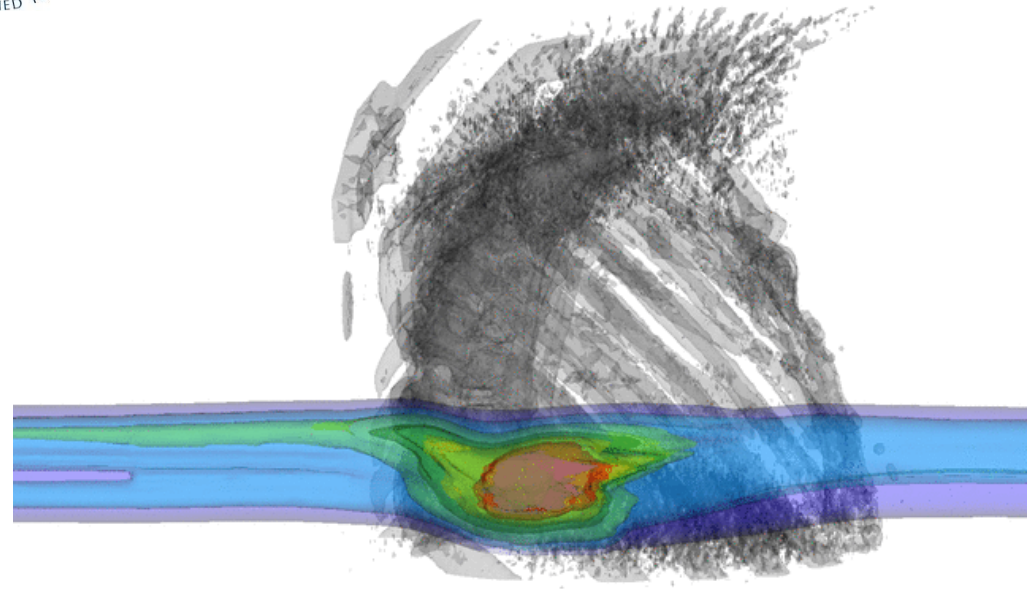
Single fraction, 25 Gy

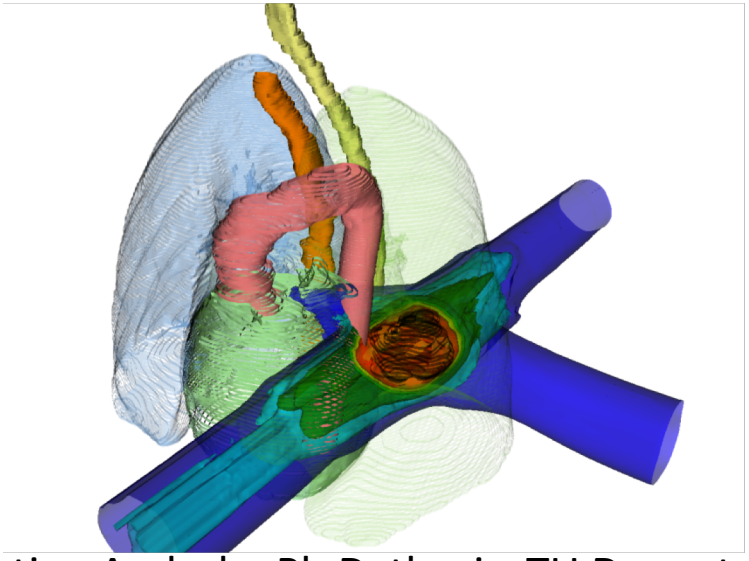
X-rays



C-ions



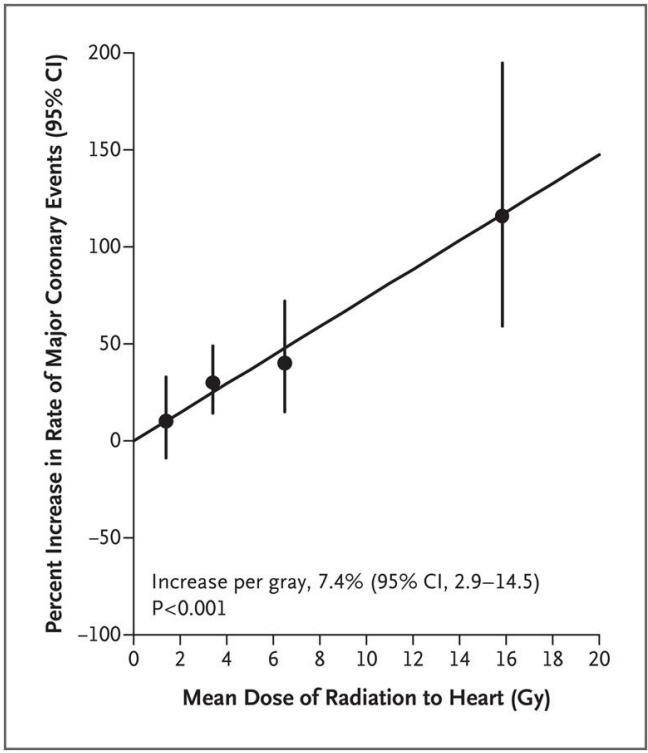


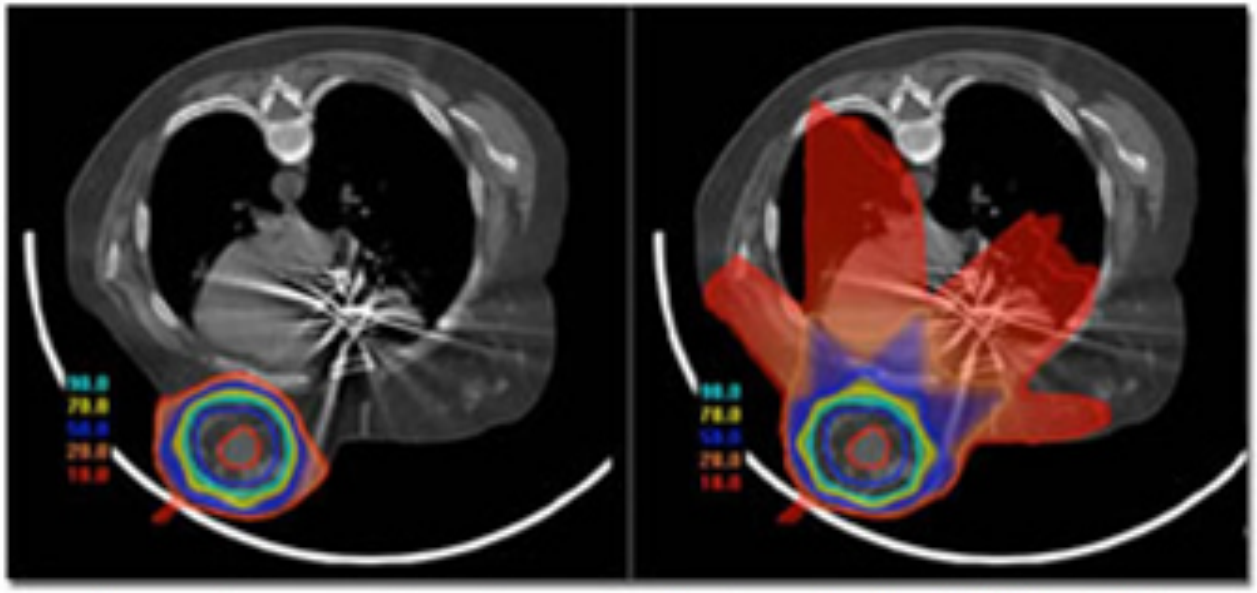


Kristjan Anderle, Ph.D. thesis, TU Darmstadt, 2014

Breast cancer

- 1st cancer in women (1 in 8)
- survival rate 80%
- high risk of late cardiac morbidity

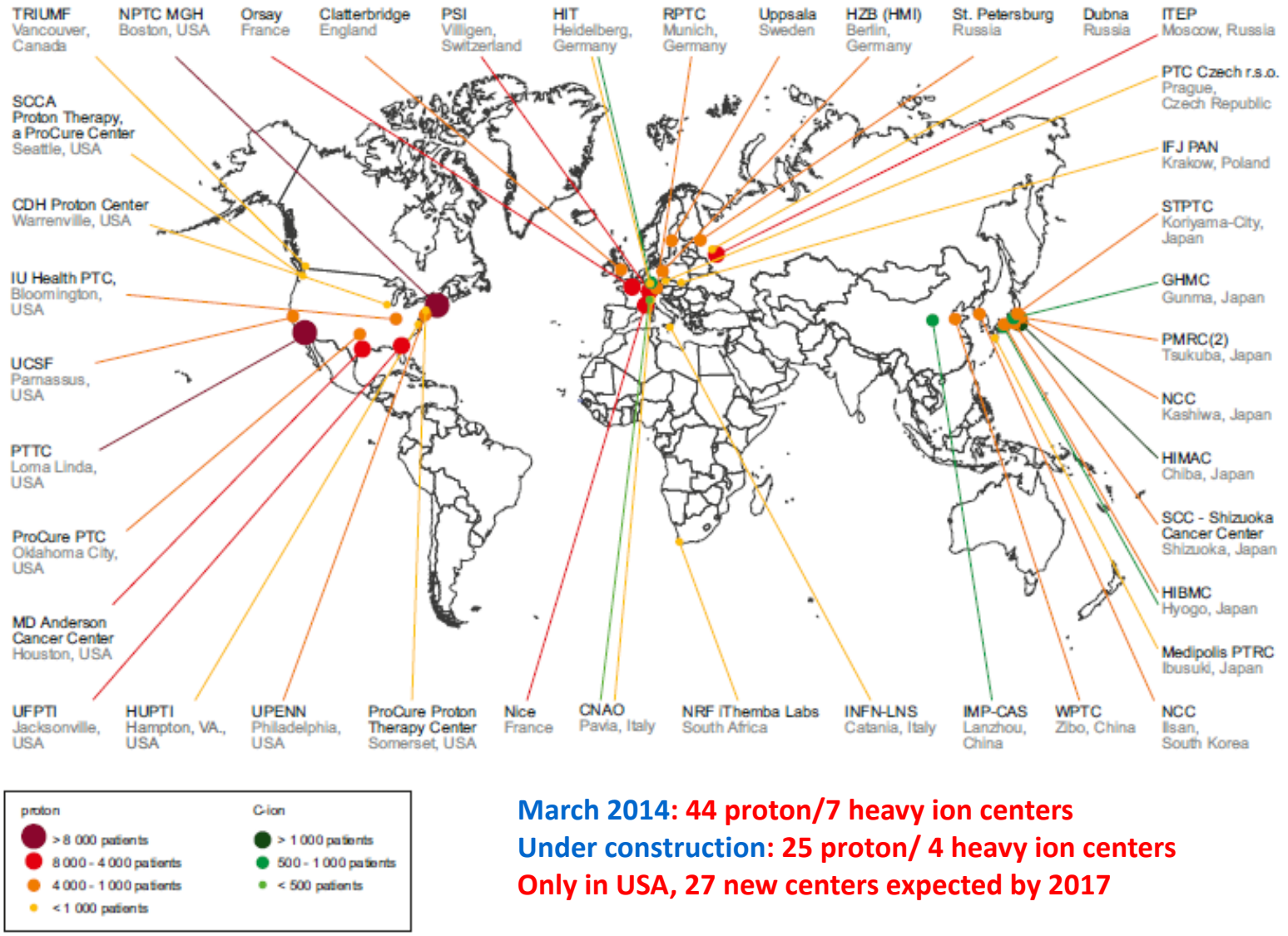




Breast cancer treatment: Proton left, IMRT right

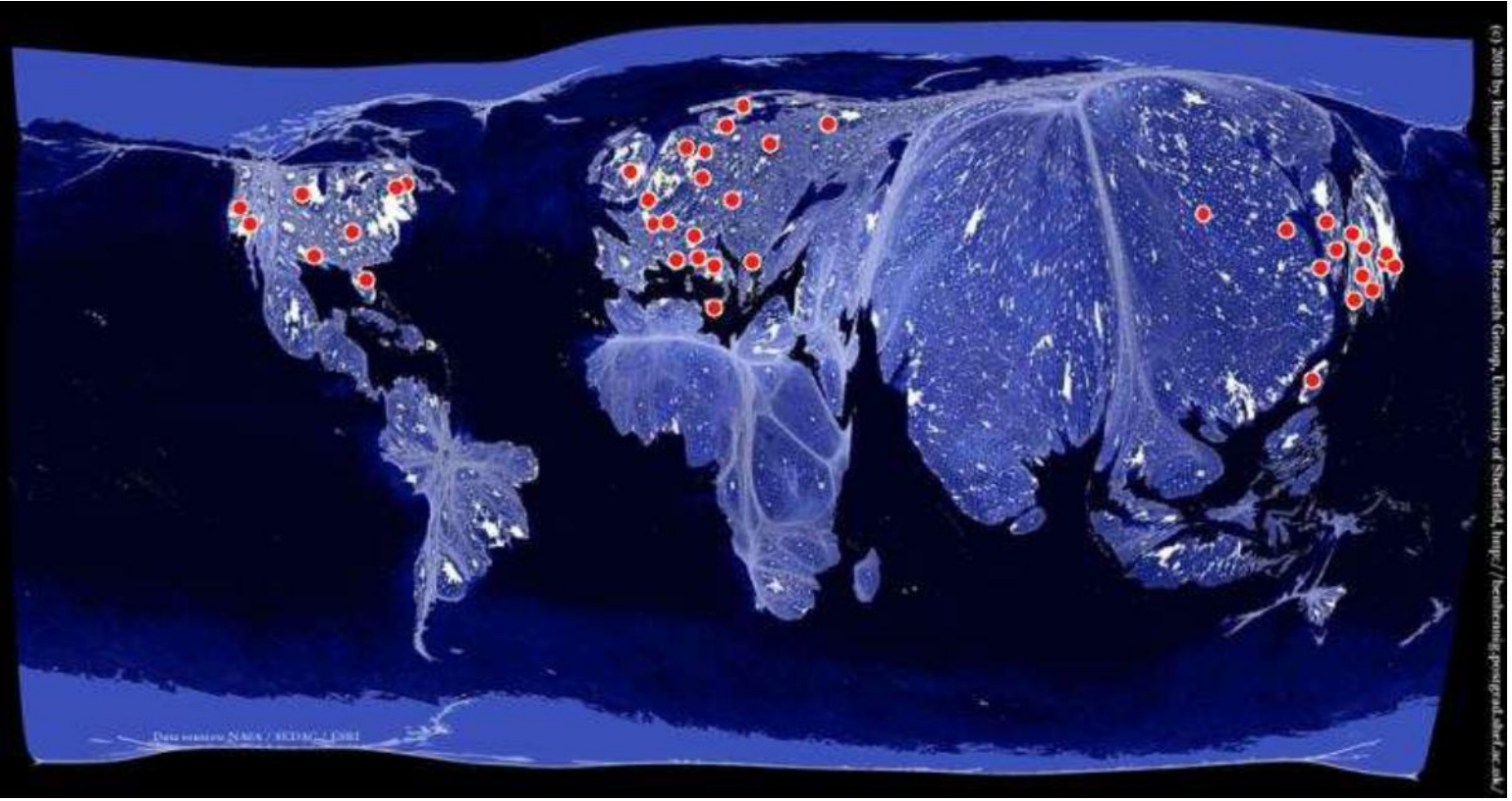
NEJM

14.3.2013

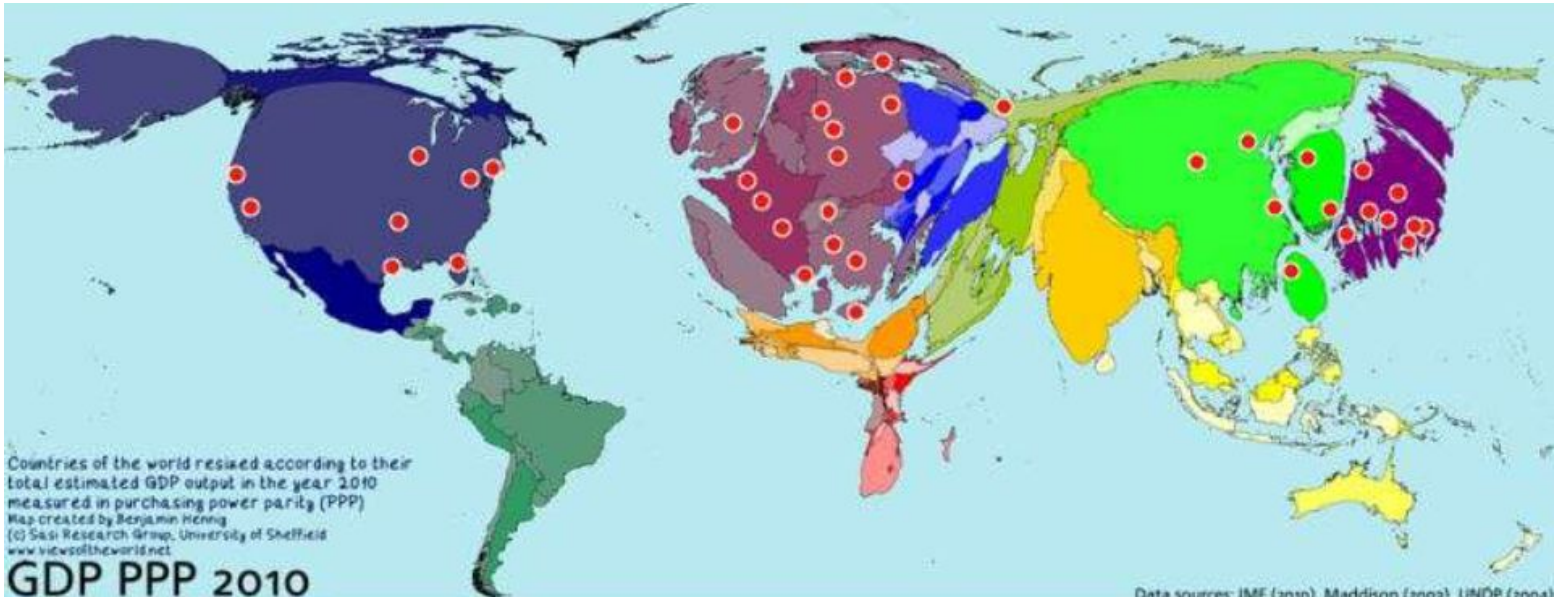


March 2014: 44 proton/7 heavy ion centers
Under construction: 25 proton/ 4 heavy ion centers
Only in USA, 27 new centers expected by 2017

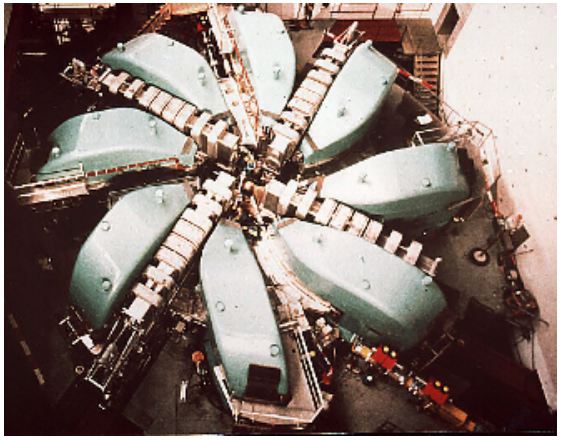
uPECC report „Nuclear Physics in Medicine“, 2014
vailable online www.nupecc.org



Population – scaled



GPD-scaled



The cost of particle therapy

Protons

$$$

Carbon

$$$$($)

Dose Distribution

Photons

$

Neutrons

$$

Exponential

Low

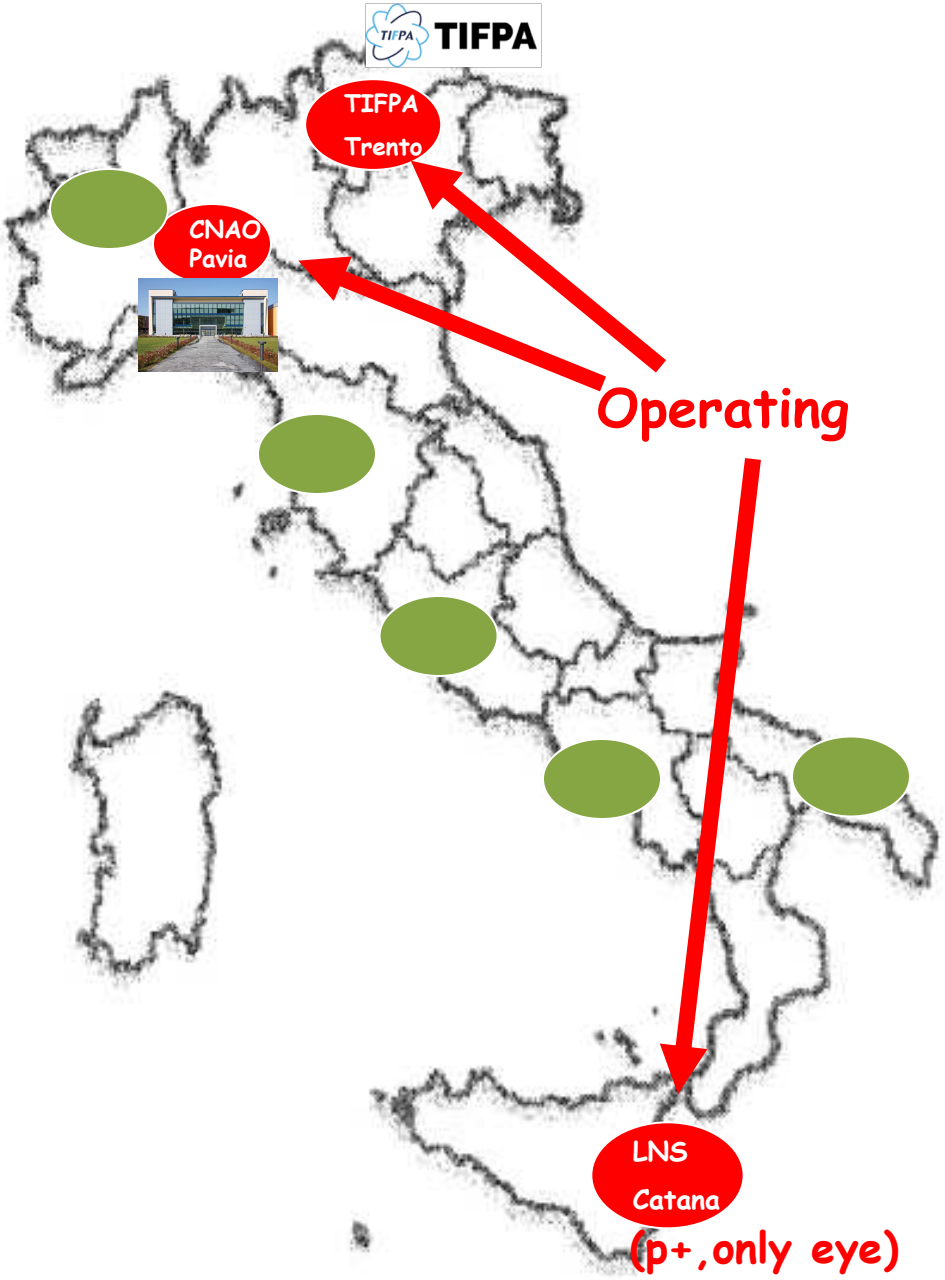
LET

High

ITALIAN NETWORK FOR HADRONTHERAPY

EXISTING CENTRES

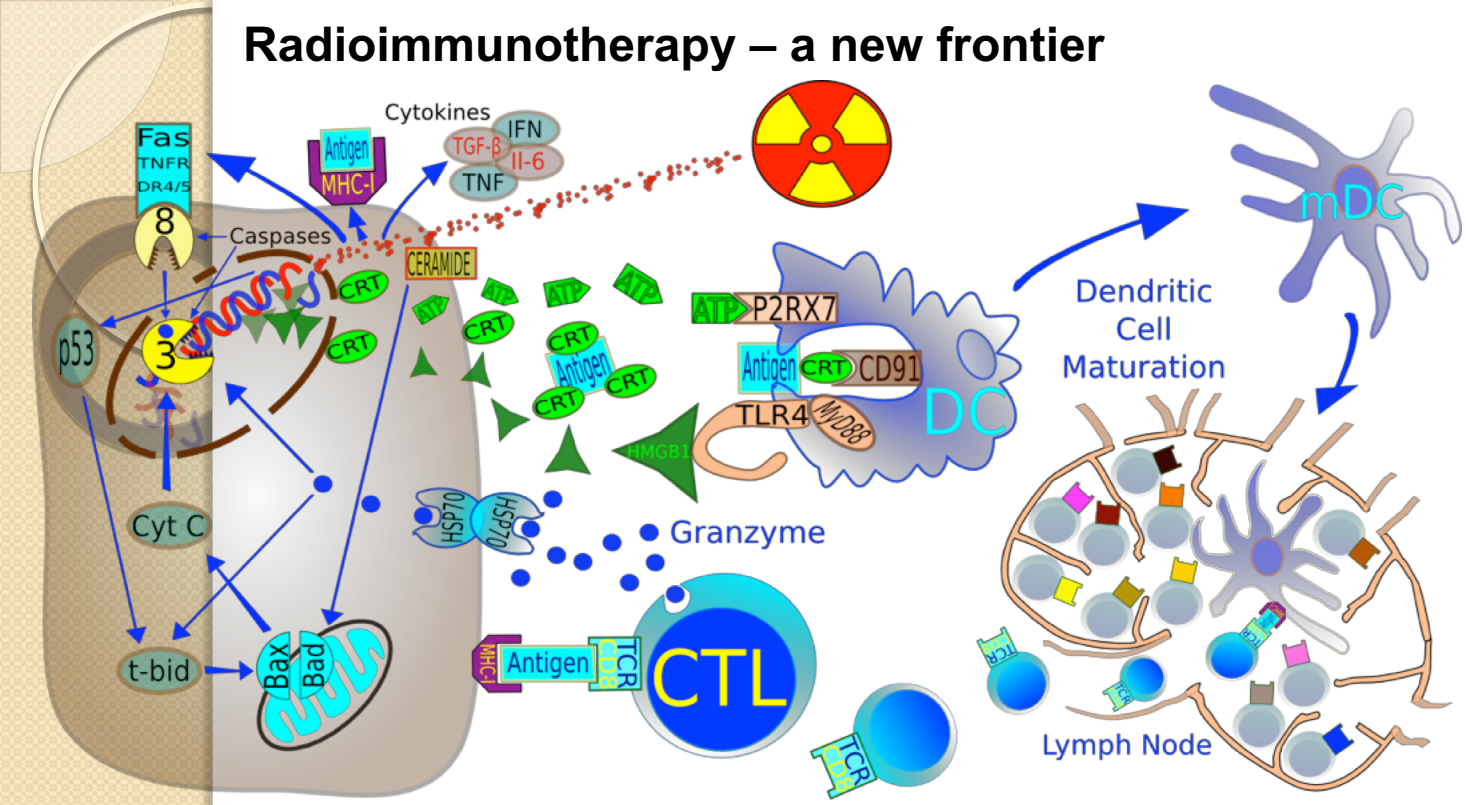
INTEREST FOR PROTONS



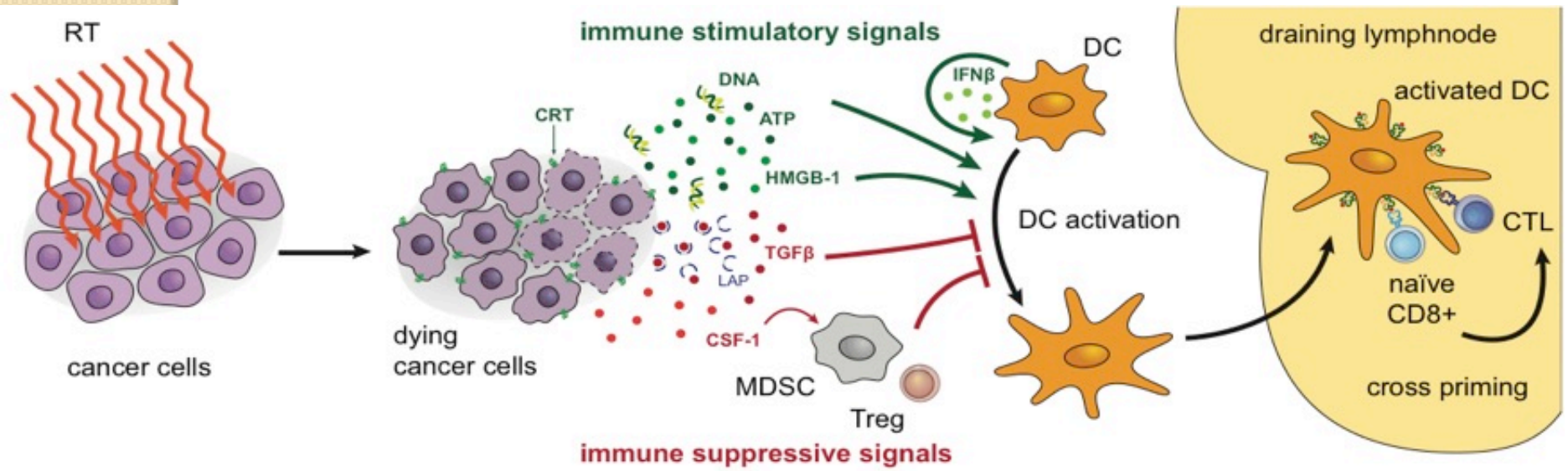
LEA adroterapia – Settembre 2016

- Cordomi e condrosarcomi della base del cranio e del rachide;
- Tumori del tronco encefalico (esclusi i tumori intrinseci diffusi del ponte) e del midollo spinale;
- Sarcomi del distretto cervico-cefalico, paraspinali, retroperitoneali e pelvici;
- Sarcomi delle estremità ad istologia radioresistente (osteosarcoma, condrosarcoma);
- Meningiomi intracranici in sedi critiche (stretta adiacenza alle vie ottiche e al tronco encefalico);
- Tumori orbitari e periorbitari (es. seni paranasali) incluso il Melanoma oculare;
- Carcinoma adenoideo--cistico delle ghiandole salivari;
- Tumori solidi pediatrici;
- Tumori in pazienti affetti da sindromi genetiche e malattie del collageno associate ad un'aumentata radiosensibilità;
- Recidive che richiedono il ritrattamento in un'area già precedentemente sottoposta a radioterapia;

Radioimmunotherapy – a new frontier



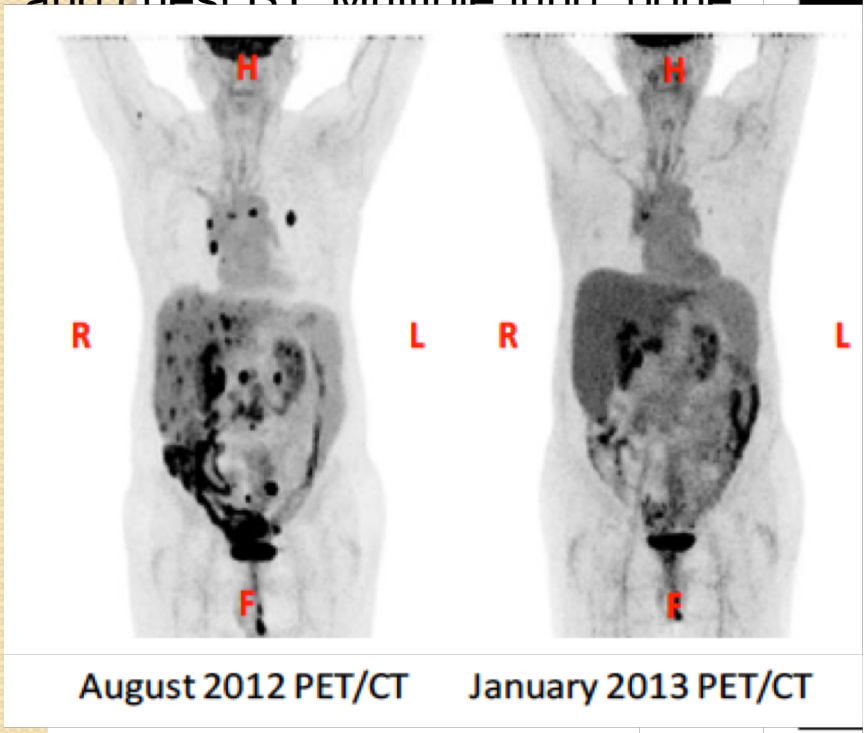
Durante *et al.*, *Trends Mol. Med*. 2013



Formenti *et al., JAMA Oncol*. 2015

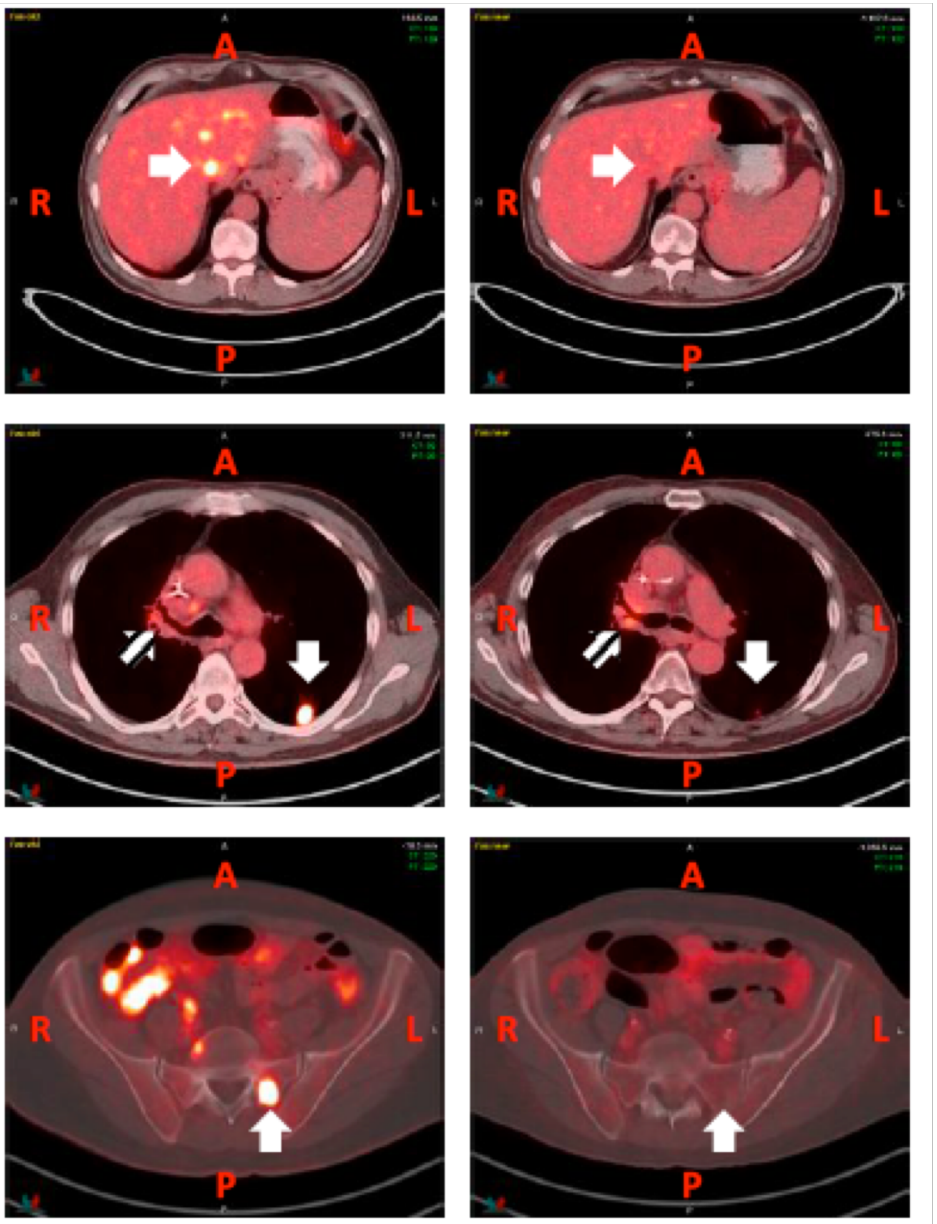
Combined radiotherapy and immunotherapy in the clinics: lung cancer trial

NSCLC progressing after 3 lines of
and chest RT: Multiple lung, bone



August 2012 PET/CT January 2013 PET/CT

RT to one liver met 6 Gy X 5 (TD 30 GY)
Ipilimumab, 3 mg/Kg, after first RT q3 weeks, X 4 cy



August 2012 PET/CT January 2013 PET/CT

Does Heavy Ion Therapy Work Through the Immune System?

Marco Durante, PhD,* David J. Brenner, PhD,† and Silvia C. Formenti, MD‡

*Trento Institute for Fundamental Physics and Applications-National Institute for Nuclear Physics, University of Trento, Trento, Italy; †Center for Radiological Research, Columbia University Medical Center, New York, New York; and ‡Department of Radiation Oncology, Weill Cornell Medical College, New York, New York

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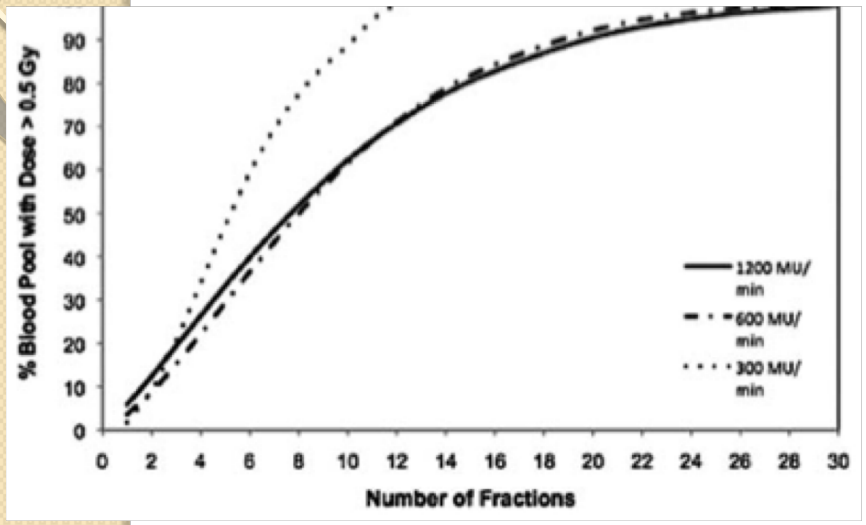
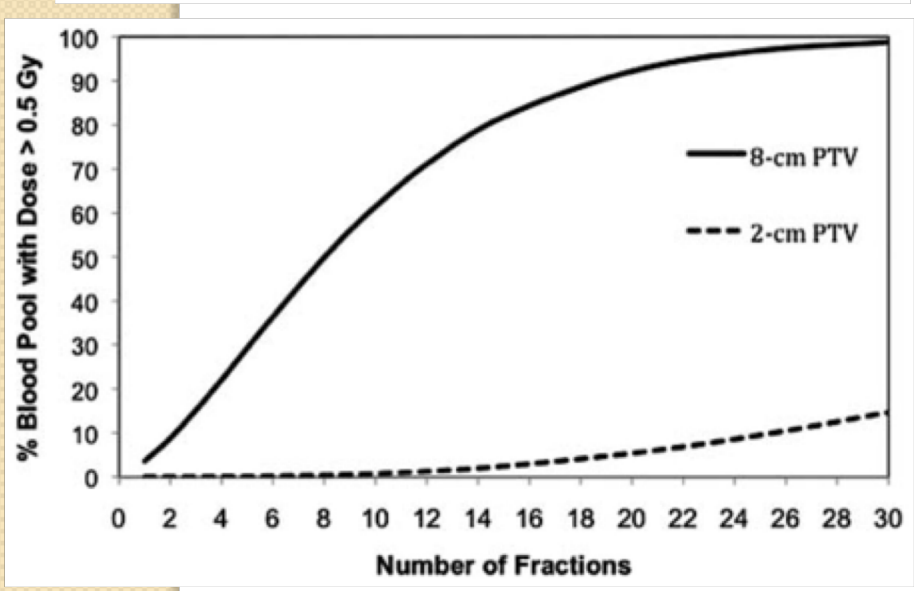
International Journal of Radiation Oncology biology • physics

www.redjournal.org

Radiotherapy (and chemotherapy) compromise the immune system





A single radiation fraction delivered 0.5 Gy to 5% of circulating cells,

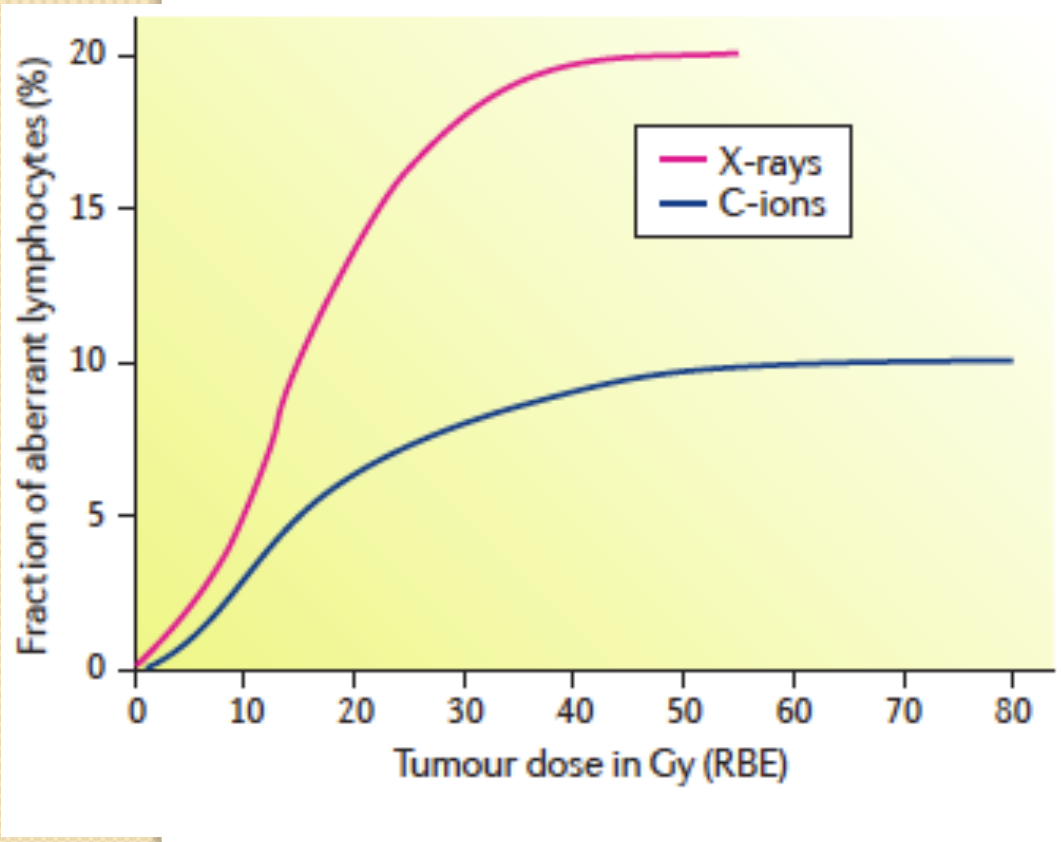
after 30 fractions 99% of circulating blood had received ≥0.5 Gy

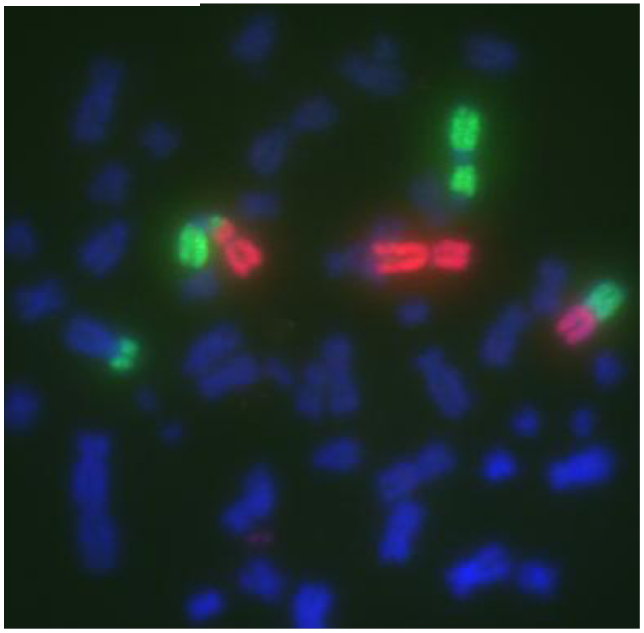
Circulating lymphocytes : D10 = 3 Gy
D50 = ~2 Gy
D90 = ~.5 Gy

Need:
- High dose-rate
- Hypofractionation
- Reduced integral dose

Yovino *et al Cancer Invest.* 2013

Physical advantages of particle therapy for immunology: chromosome aberrations in lymphocytes from patients during the treatment for uteus cancer by either X-rays or C-ions





M. Durante *et al., Nat. Rev. Clin. Oncol*. 2017

Particle therapy: beyond cancer

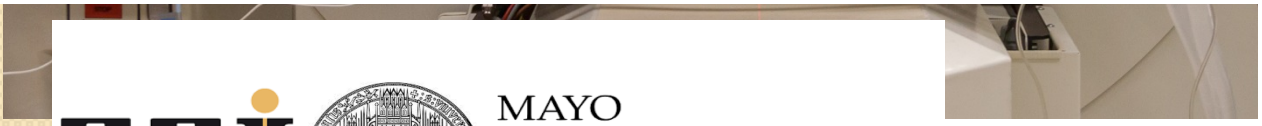
SCIENTIFIC REPORTS

OPEN

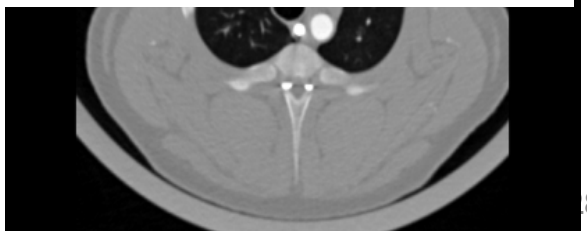
Feasibility Study on Cardiac Arrhythmia Ablation Using High-Energy Heavy Ion Beams

Received: 08 August 2016
Accepted: 09 November 2016
Published: 20 December 2016

H. Immo Lehmann[1,*], Christian Graeff[2,*], Palma Simoniello[2], Anna Constantinescu[2], Mitsuru Takami[1], Patrick Lugenbiel[3], Daniel Richter[2,4], Anna Eichhorn[2], Matthias Prall[2], Robert Kaderka[2], Fine Fiedler[5], Stephan Helmbrecht[5], Claudia Fournier[2], Nadine Erbeldinger[2], Ann-Kathrin Rahm[3], Rasmus Rivinius[3], Dierk Thomas[3], Hugo A. Katus[3], Susan B. Johnson[2], Kay D. Parker[2], Jürgen Debus[6], Samuel J. Asirvatham[1], Christoph Bert[2,4], Marco Durante[2,7] & Douglas L. Packer[1]



GSI MAYO CLINIC



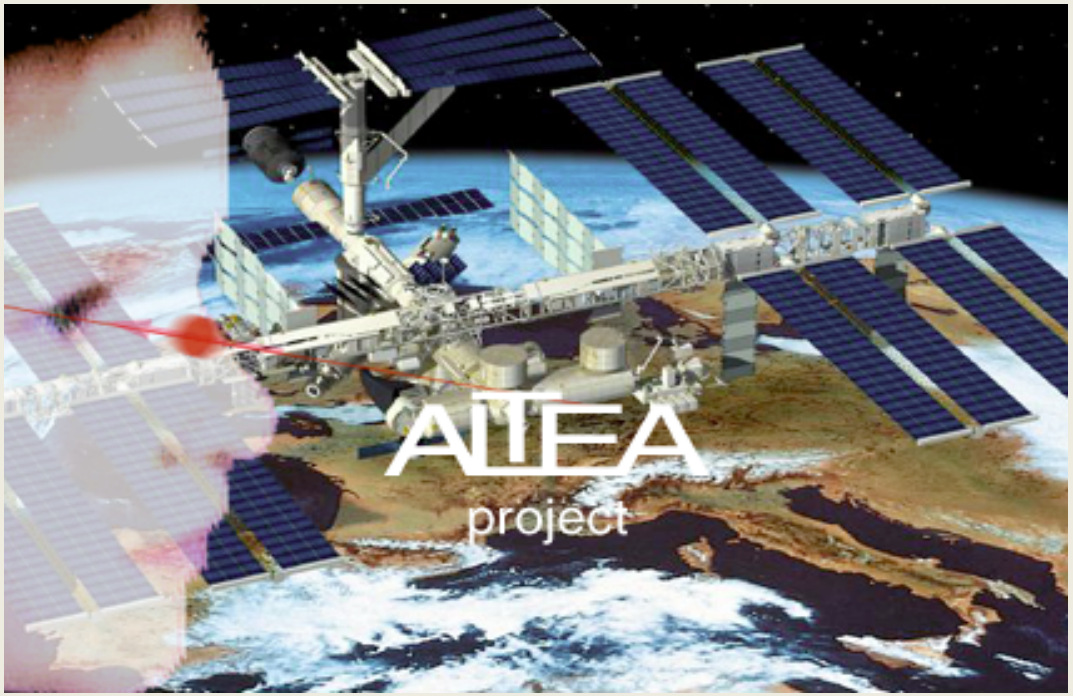
1. Particle therapy contributing to space research

Heavy ion effects on the Central Nervous System: ground and space investigations: the ALTEA program

University of Rome "Tor Vergata"

INFN

NASA



ASI

Alenia SPAZIO LABEN

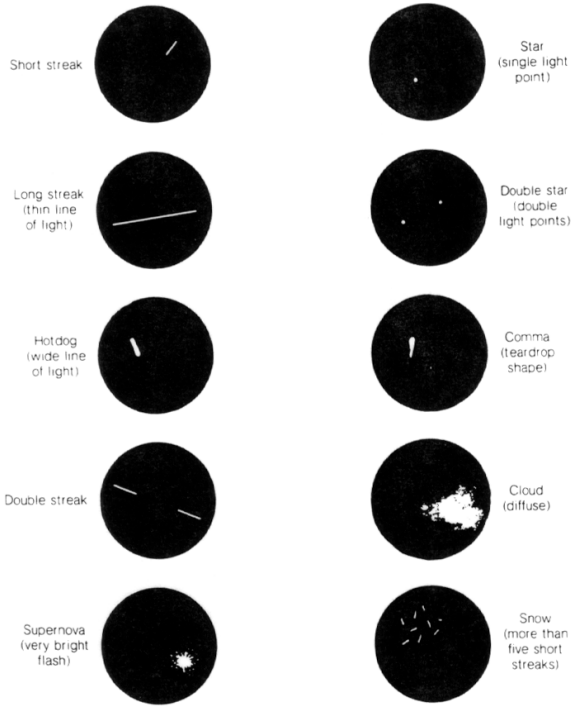
GSI

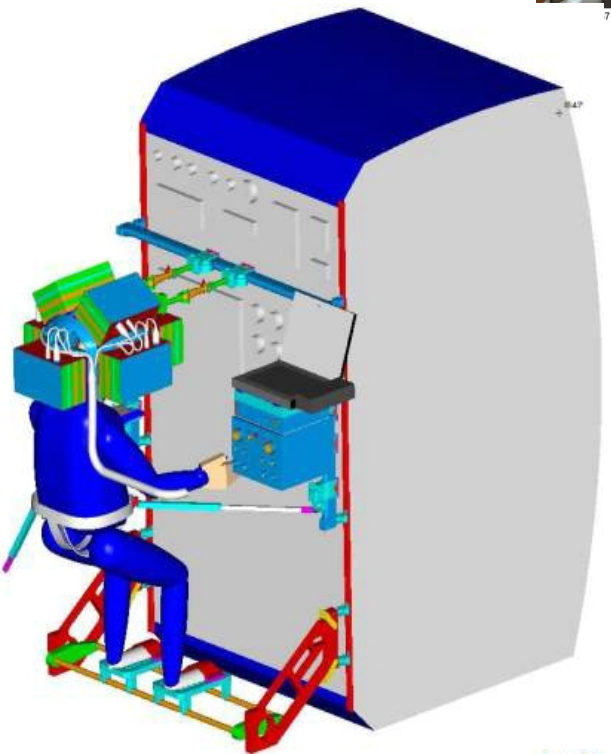
ИМБП

PI: Livio Narici
Department of Physics, University of Rome and INFN
'Tor Vergata' Rome, Italy

ALTEA - space: the launch and set up

STS121: July 4, 2006



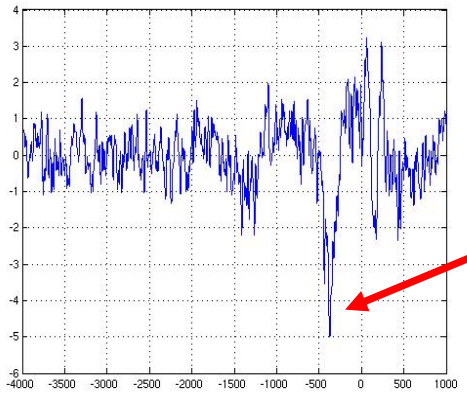


Light flashes seen by astronauts in space

A controlled approach on patients at GSI

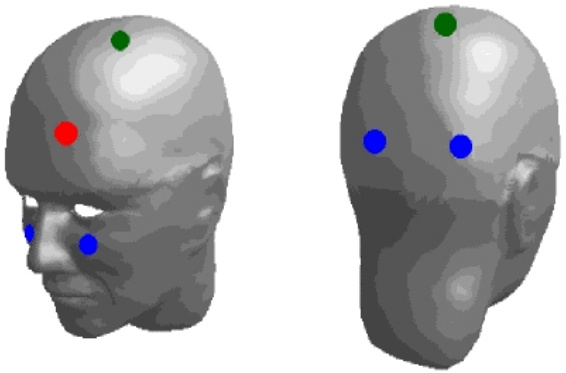
ALTEA-HIT

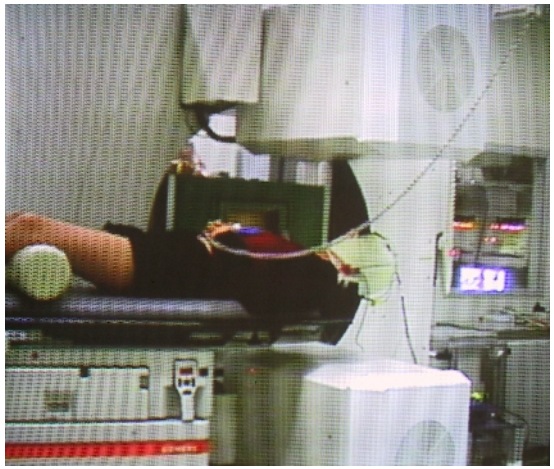
- LF perceived by several patients during the therapy
- Use the high precision in beam time/site localisation to search for the interaction site
- Electrophysiology during the treatment

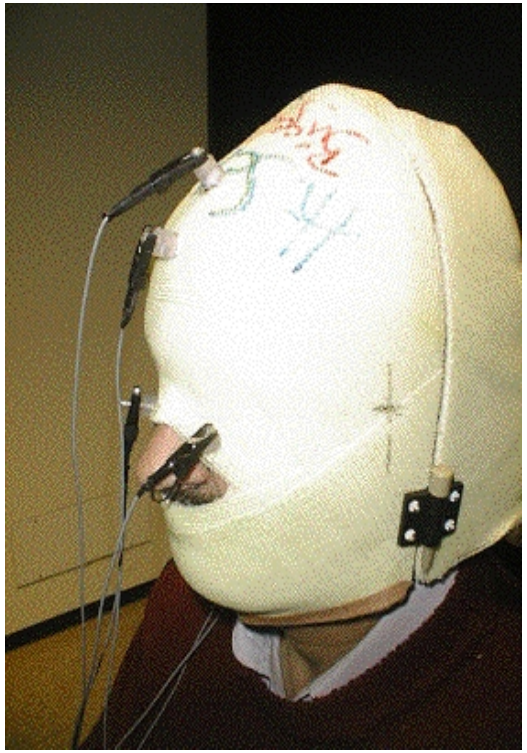


- Particle Evoked Responses?

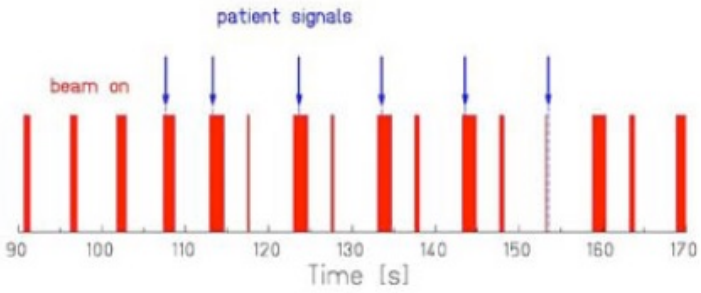
A candidate for an electrophys. averaged ion response

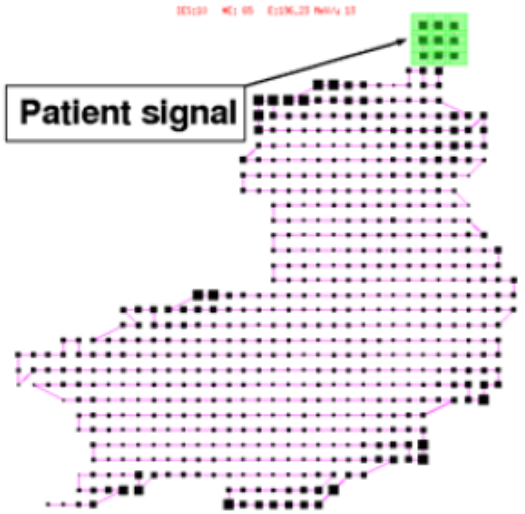


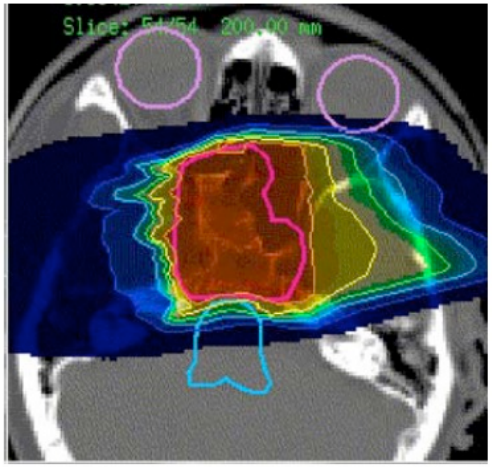




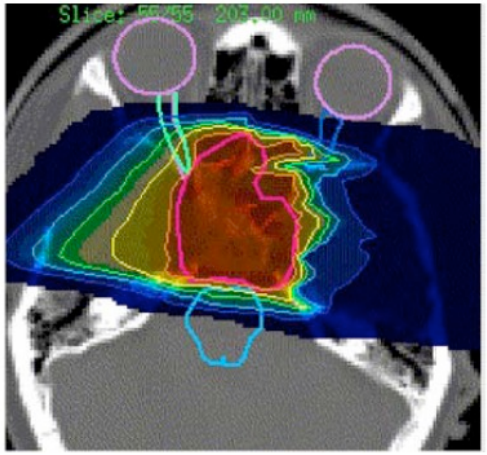
Patients' experiments at GSI







Phosphene

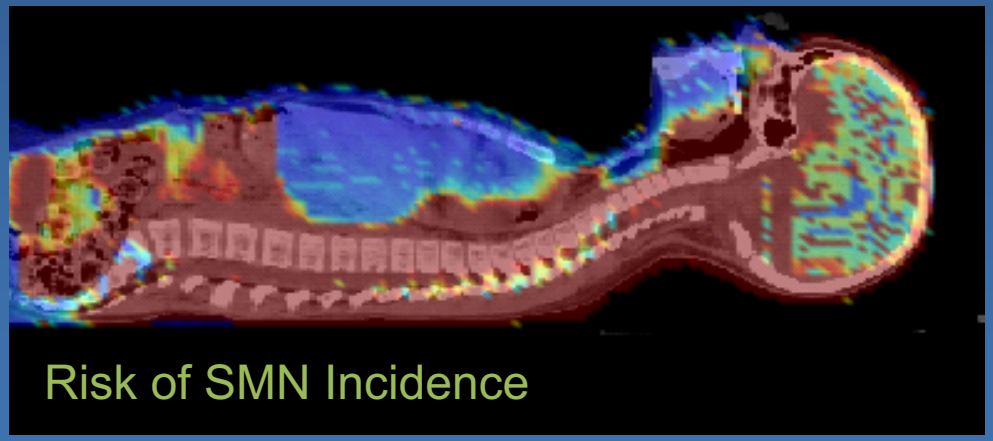


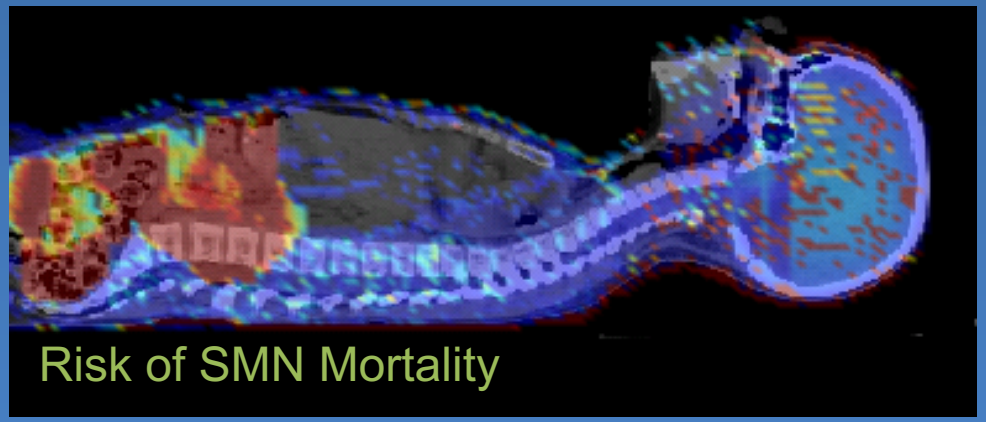
No phosphene

Phosphenes are correlated to dose deposition within the eye

Schardt *et al.*, *Brain Stimul.* 2012

2. Space research contributing to particle therapy





Secondary Malignant Neoplasms (SMN) in particle therapy

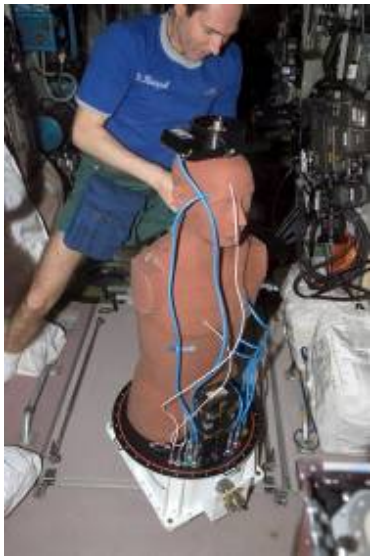
Comparison of relative radiation dose distribution with the corresponding relative risk distribution for radiogenic second cancer incidence and mortality. This 9-year old girl received craniospinal irradiation for medulloblastoma using passively scattered proton beams. The color scale illustrates the difference for absorbed dose, incidence and mortality cancer risk in different organs.

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

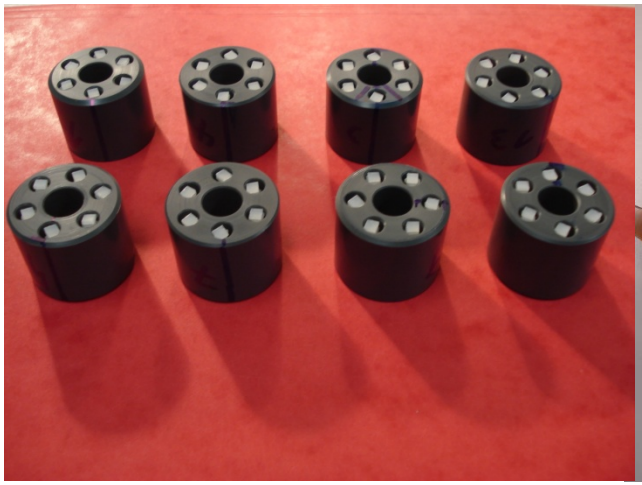
Newhauser & Durante, *Nat. Rev. Cancer* 2011

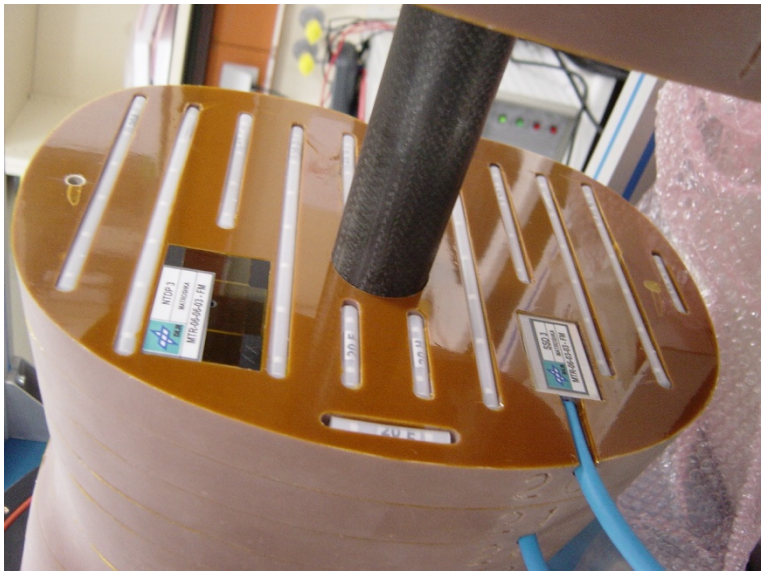
The MATROSHKA facility

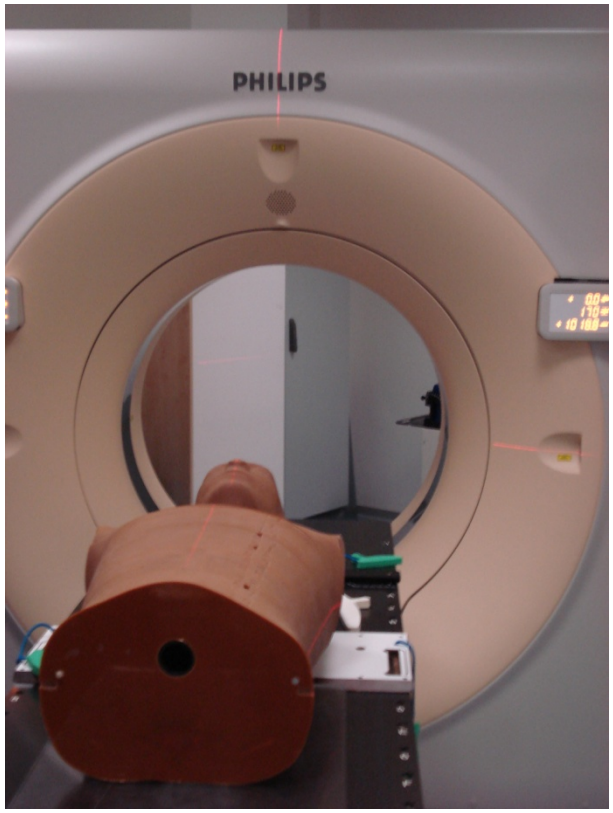
- Standard RANDO phantom of property of DLR (German Aerospace center)
- 850 mm high divided into 34 slices
- Holders for detectors in several slices
- Currently used for space radiation dosimetry inside the ISS

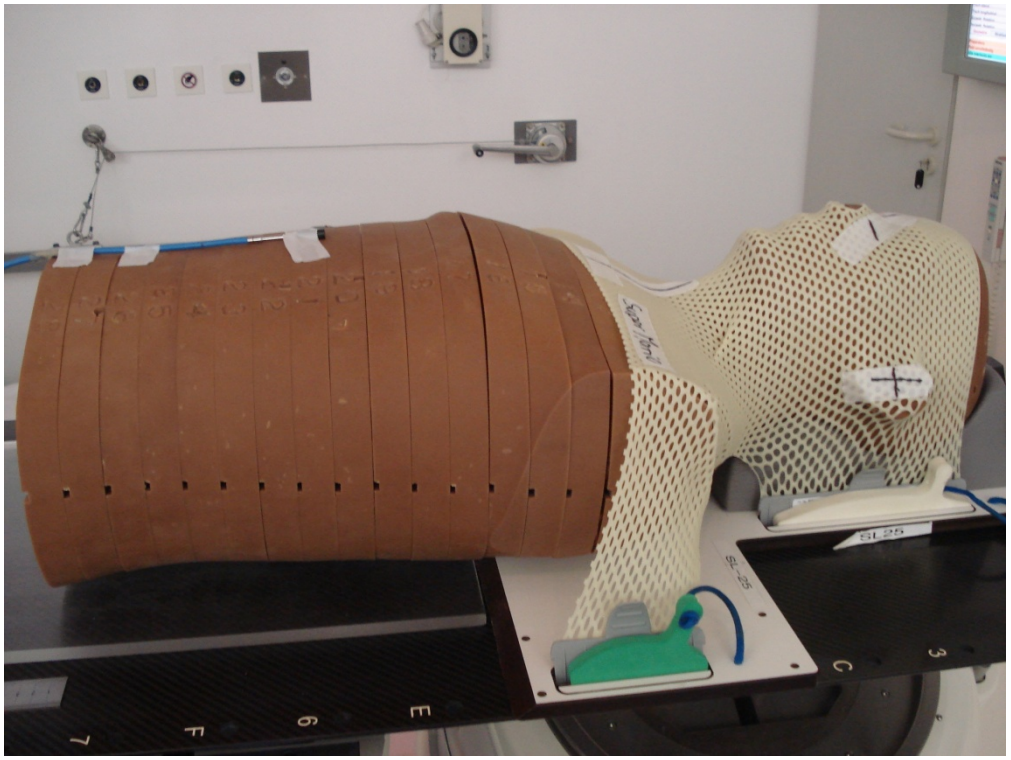


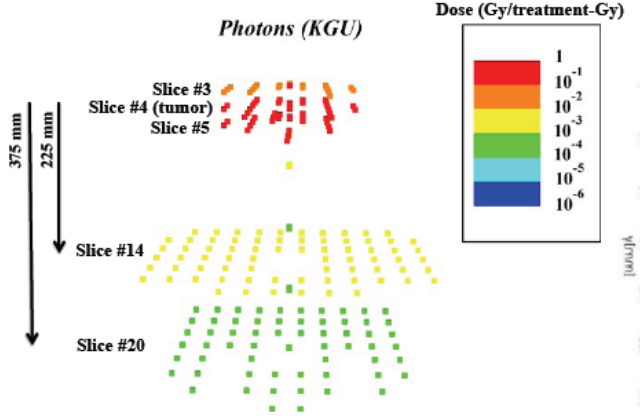
In collaboration with G. Reitz, T. Berger et al. (DLR)



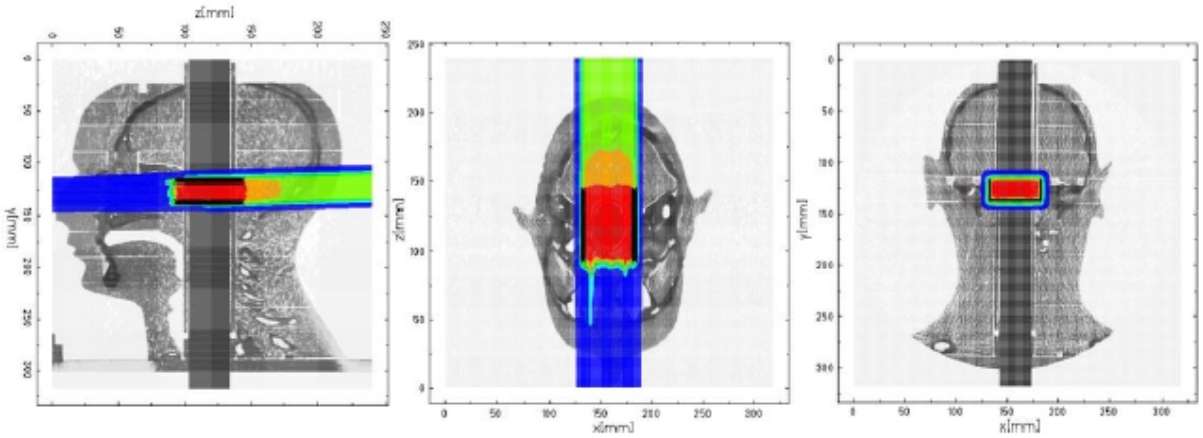


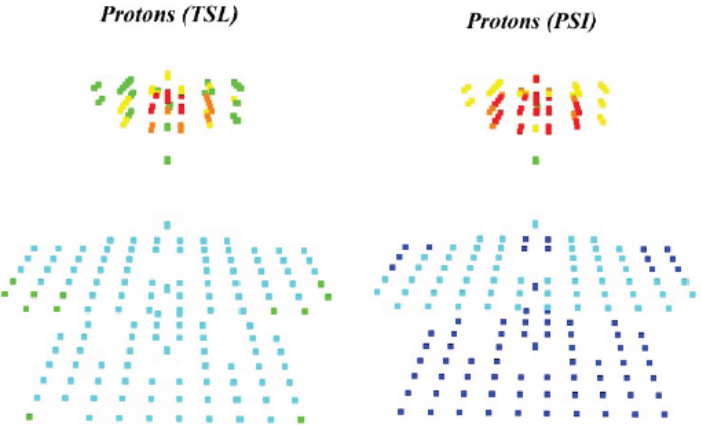

PHILIPS



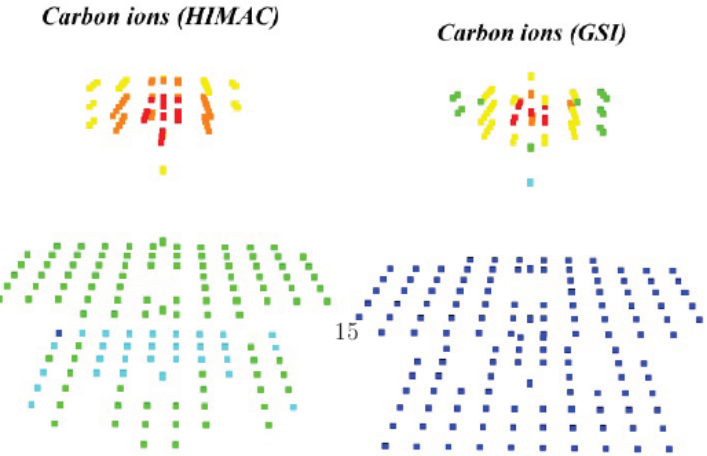

Photons (KGU)
Slice #3
Slice #4 (tumor)
Slice #5
375 mm
225 mm
Slice #14
Slice #20

Dose (Gy/treatment-Gy)
1
10-1
10-2
10-3
10-4
10-5
10-6

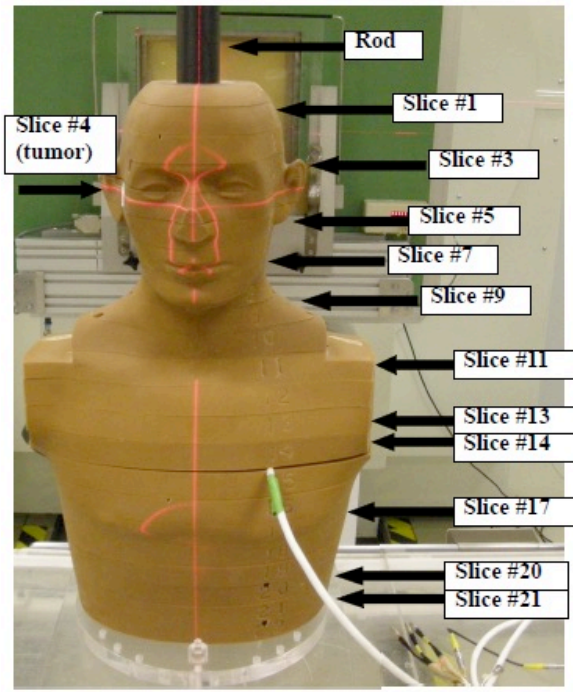

z[mm]
y[mm]
x[mm]
z[mm]
x[mm]
y[mm]
x[mm]

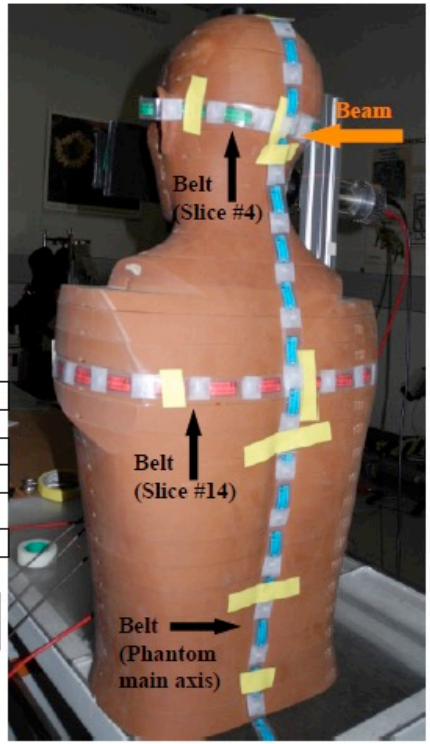

Protons (TSL)

Protons (PSI)


Carbon ions (HIMAC)

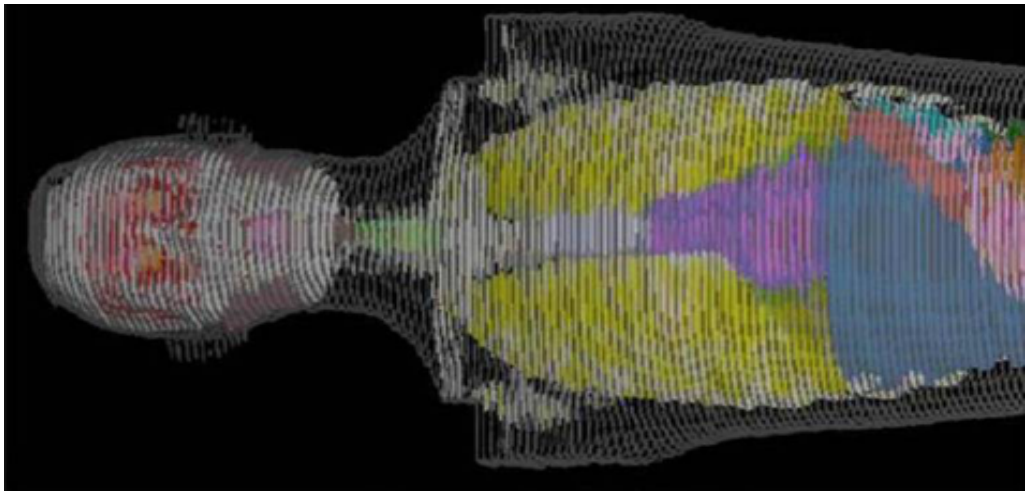
Carbon ions (GSI)


Rod
Slice #1
Slice #4 (tumor)
Slice #3
Slice #5
Slice #7
Slice #9
Slice #11
Slice #13
Slice #14
Slice #17
Slice #20
Slice #21

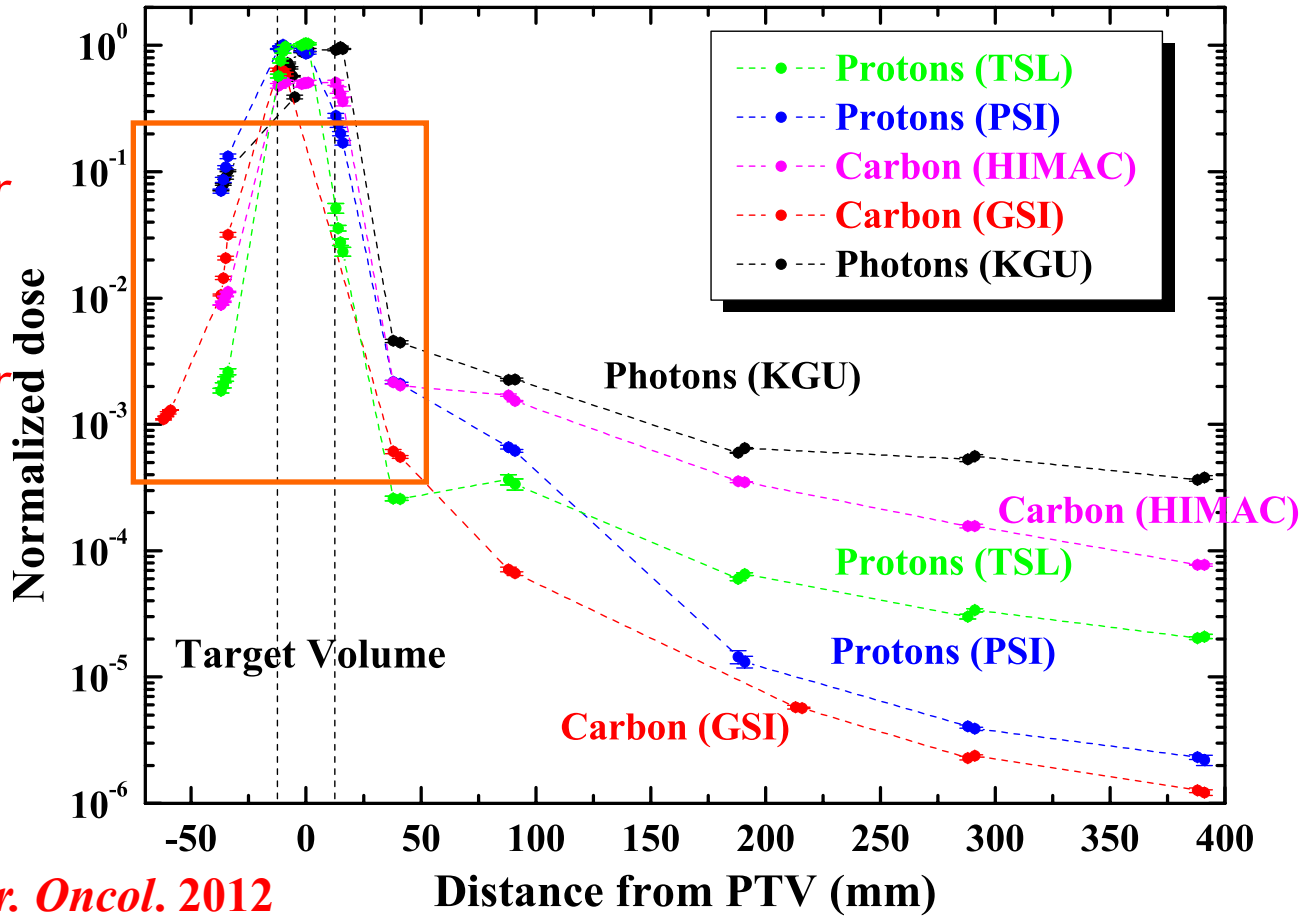

Beam
Belt (Slice #4)
Belt (Slice #14)
Belt (Phantom main axis)

Inner dose

TLD 700



- *Highest out-of-field dose for photons*
- *Higher lateral dose for passive modulation than scanning delivery*
- *Higher lateral dose for protons than carbon ions*
- *Collimator produces sharper field edges*



La Tessa *et al., Radiother. Oncol.* 2012

In patient dosimetry
(uterus dose for a pregnant woman)

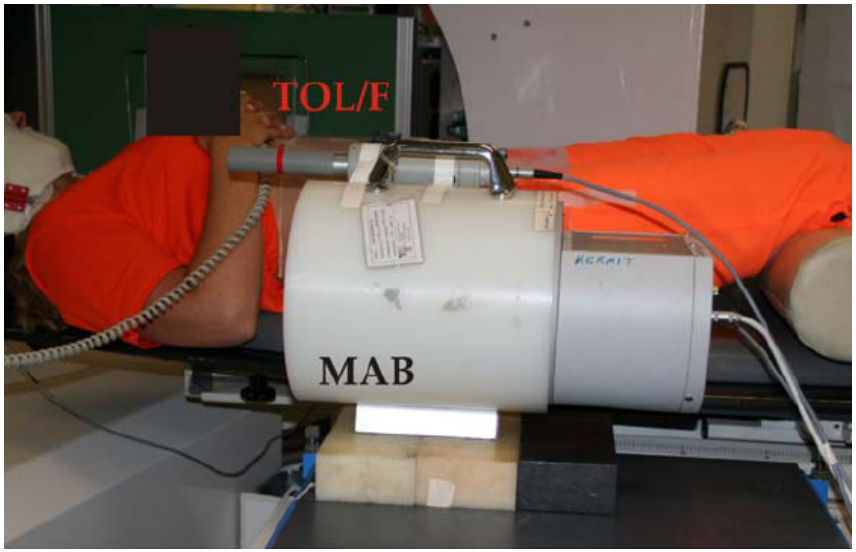


TABLE 1

Measured doses in the pelvic region during the treatment.

	Photon dose (μSv/fraction)	Neutron dose (μSv/fraction)	No. of fractions	Total dose (μSv)
Normal field	3.0[a]	1.4	15	66
Boost field	2.2[b]	1.0	5	16
Total treatment			20	82

[a] Calculated assuming a factor of 1.4 between normal and boost fields as in neutron dose.
[b] Measured by the TOL/F gamma dose rate meter. The passive thermoluminescence dosimeter films did not measure any significant dose above the normal background.

Münter. Heavy ion radiotherapy during pregnancy. Fertil Steril 2010.

Total dose < 0.3 mSv

Very low stray radiation

reduced risk of secondary

cancers or teratogen effects

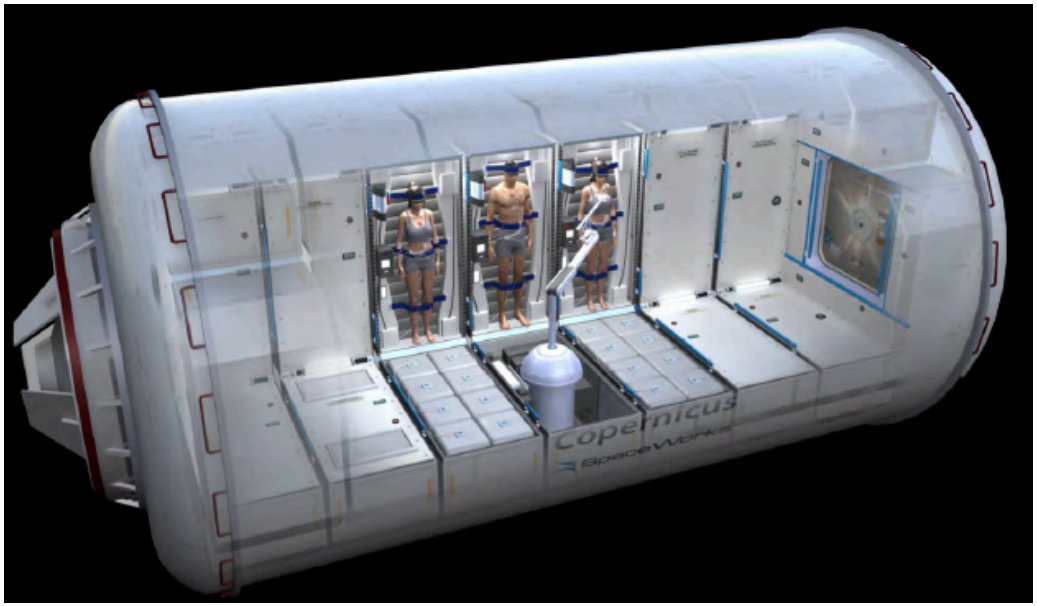
Münter *et al., Fertil Steril.* 2010

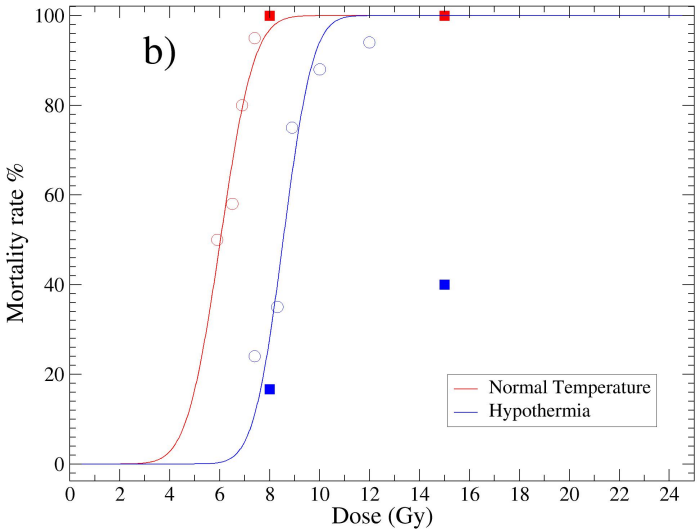
3. Hibernation: a futuristic view of space and therapy

Hibernation: space and therapy

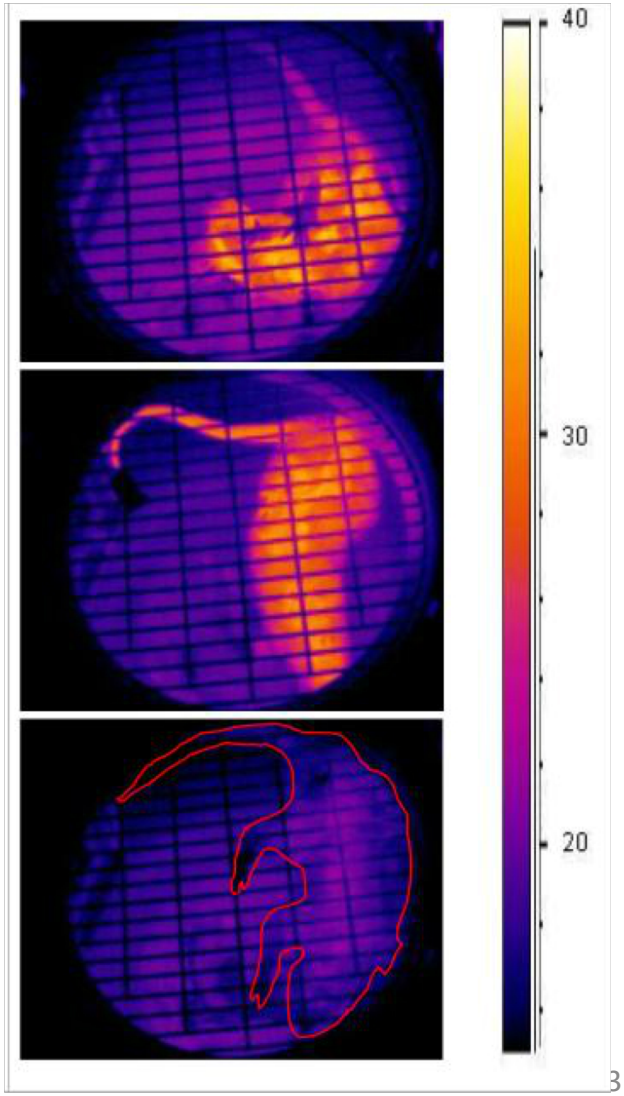
- Increased radioresistance in hibernation
- Reduced tumor growth
- Reduced organ motion
- Radiotherapy in hibernation?

Radiosensitivity in non-hibernating





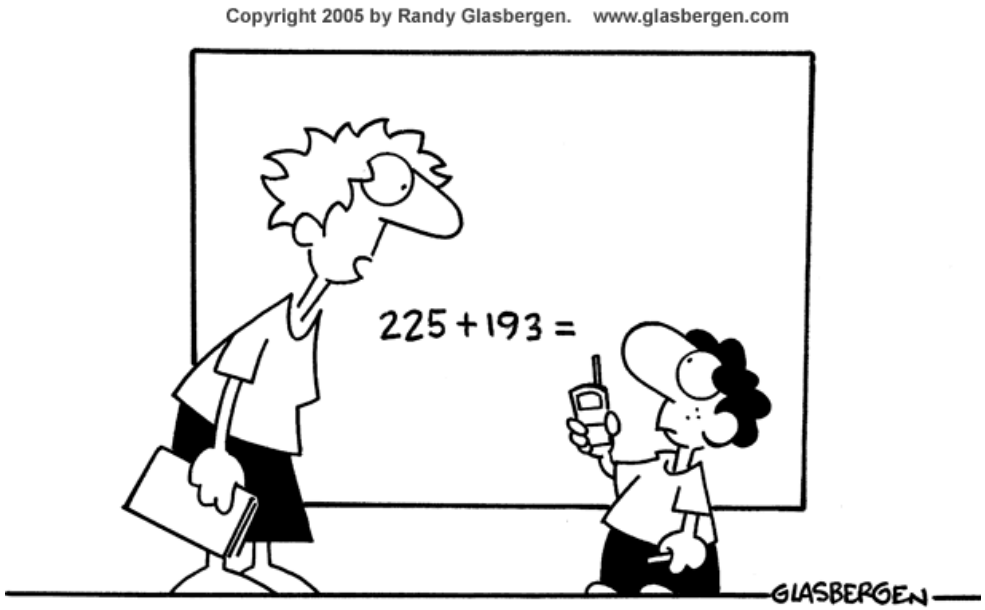
Cerri et al., Life Sci. Space Res. 2016



Conclusions

- Heavy ions are different in many facets from X-rays and other genotoxic agents
- Their „special“ radiobiological properties make them very effective in radiotherapy, but potentially dangerous for late effects, and therefore a major hazard in human space exploration
- Accelerator-based research in radiobiology is essential for improving radiotherapy and ensure protection in space: it should be increased, and can serve both medical and space research communities

Thank you for attention!



"You have to solve this problem by yourself. You can't call tech support."