VI Scuola Nazionale "Rivelatori ed Elettronica per Fisica delle Alte Energie, Astrofisica, Applicazioni Spaziali e Fisica Medica

INFN Laboratori Nazionali di Legnaro, 23-27 Marzo 2015

Charged particles in therapy and space











Charged particles from physics to biology and medicine



Cucinotta and Durante, Lancet Oncol. 2006

γ-rays





Live cell imaging of heavy ion traversals

High energy Fe-ions

-10.0 sec

Low energy Ni-ions, human cells, **GFP-APTX**



Jakob et al., Proc. Natl. Acad. Sci. USA 2009



GFP-NSBS1



GFP-XRCC1

Heavy ion tracks in euchromatin and heterochromatin: dangerous curves





Salvador Dali', 1932

Recruitment of XRCC1 to heterochromatin and euchromatin after exposure of mouse embryo fibroblasts to heavy ions









X-ray repair complementing defective in Chinese

hamster cells 1 (SSB and βexcision repair pathways)

Jakob et al., Nucl. Acids. Res. 2011



From DNA to chromosomes: heavy-ion induced rearrangements



46,XX T(1'q-5aq)(5'aq-1q) CAB 2\2\2; T(4'q,5bq)(5'bq-4q) CAB 2\2\2; Ti (20'p-9q) CAB 2\2\2





Why are we interested in energetic charged particles?





THE ROUGH GUIDE to The Moon & Mars

Health in Deep Space



- 2. Psychosocial and behavioural problems
- 3. Physiological changes caused by microgravity





% Risk of Cancer Death

Durante & Cucinotta, Nature Rev. Cancer (2008)



- A 501-day "free-return" Mars flyby 0 passing within a hundred miles of the surface
 - Only small correction maneuvers are needed during transit
- Simple mission architecture lowers 0 risk
 - No entry into Mars atmosphere
- An exceptionally quick free return 0 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 0
 - http://www.youtube.com/watch?v=IBGIY Nd2tmA









April, 3, 2013

- First flight scheduled 0 for 2013
- Man-rated design 0
- 53,000 kg to LEO 0
- 10,000 kg to Mars 0 for this mission
- Free-return 0 trajectory enables upper stage to stay attached for shielding

Graphic courtesy SpaceX

ECLSS Test Facility



The New Hork Eimes

Space & Cosmos

WORLD	U.S.	n.y. / region	BUSINESS	TECHNOLOGY	SCIENCE	HEALTH	SPORTS	OPINION
					ENVI	RONMENT \$	PACE & CO	SMOS

Data Point to Radiation Risk for Travelers to Mars



Estimated dose for Inspiration Mars = 1.8 mSv/day x 501 days = 0.9 Sv

But in 2018 we expect Solar Min.....

Measurements of Energetic Particle Radiation in Transit to Mars on the Mars Science Laboratory

C. Zeitlin, ¹* D. M. Hassler, ¹ F. A. Cucinotta, ² B. Ehresmann, ¹ R. F. Wimmer-Schweingruber, ³ D. E. Brinza, ⁴ S. Kang, ⁴ G. Weigle, ⁵ S. Böttcher, ³ E. Böhm, ³ S. Burmeister, ³ J. Guo, ² J. Köhler, ³ C. Martin, ³ A. Posner, ⁶ S. Rafkin, ¹ G. Reitz⁷

31 MAY 2013 VOL 340 SCIENCE



Phobios passing demios in Martian Sky – movie from Curiosity's Mars camera

Launched 26.11.2011, landed 5.8.2012 (253 days)



Particle therapy in oncology





- About 100,000 patients treated with H and 10,000 with C-ions
- >30 particle therapy facilities in operation (6 with heavy ions)
- Many more are under construction or planned

Potential advantages

High tumor dose, normal tissue sparing Effective for radioresistant tumors

Effective against hypoxic tumor cells

Increased lethality in the target because cells in radioresistant (S) phase are sensitized

Fractionation spares normal tissue more than tumor

Reduced angiogenesis and metastatization

Physical gain: reduced intergral dose to the normal tissue, sparing of OARs

C-ions, 2 fields

IMRT, 9 fields

Courtesy of Oliver Jäkel, DKFZ, Heidelberg

In silico comparison of Carbon to SBRT

- Patient treated at Champalimaud Foundation, Lisbon (TrueBeam)
- 24 Gy single fx SBRT
 Photons

Carbon

In silico trial MSKCC/Champalimaud/ GSI

Courtesy of C. Anderle

Radiotherapy for Breast Cancer

- About 200,000 new cases per year in U.S
- Most affected at the most productive part of life
- Most patients survive (> 2 millions survivors)
- Increased risk of cardiac toxicity and second malignancies
- "Horror" stories from side effects of radiation leads many women to choose mastectomy over radiotherapy

Darby et al. N Engl J Med. 2013 Mar 14

Particle therapy for breast cancer? IMRT --- Proton = Difference

Andrew Chang, Presentation at the 2013 Proton Breast Cancer Workshop, Phoenix, AZ

Post-mastectomy radiation to IMN, SCV, Axilla and reconstructed breast

Protons with implants

Norm:Dose(5040.0 cGy = 100%)

Photons

Photon/Electron

Proton(IMPT)

MacDonald et al, Int. J. Radiat. Oncol. Biol. Phys. 2013 July 1

1. Particle therapy contributing to space research

Light flashes in space

Reports/experiments in space

- Unusual flashes of light have been first reported from the Apollo 11 crew (July 1969)
- following Apollo flights (12-17, to the Moon)
- Skylab missions (1973)
- Apollo Soyuz (1974)
- MIR (late 90s)
- ISS (2002-today)
- Shuttle flights

Experiments on ground

- many in the 70's

Heavy ions and/or protons? What/where is the target in the eye/optical nerve/brain?

Pinsky et al., Science 1974, 1975 Casolino et al., Nature 2003

Cosmic Flash, proposed project for the cultural utilisation of the ISS, Tim Otto Roth. Artist's impression. 2005

ALTEA - Space: the launch and set up

STS121: July 4, 2006

Courtesy of Livio Narici, University of Rome Tor Vergata

ALTEA-HIT

A controlled approach on patients at GSI

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

(recorded on 8 treatment days) $\Delta t = 0.3 - 0.8$ s from slice start Evidence that phosphenes are caused by direct energy deposition by charged particles in the retina (Schardt et al., Brain Stimul. 2012)

Phosphene

No phosphene

2. Space research contributing to particle therapy

Radiotherapy and SMN

- Cancer survivors represent about 3.5% of US population
- Second primary malignancies in this high-risk group accounts for about 16% of all cancers
- Three possible causes: Continuing lifestyle;Genetic predisposition:Treatment of the primary cancer

- CCSS study, St. Jude et al. 2008-2012
- Retrospective cohort of 14,000 survivors of childhood cancer diagnosed between 1970 and 1986
- Standardized incidence ratio
 (SIR) of observed to expected
 SMN was 6.38
- Highest SIR for breast, bone, and thyroid SMN
- Patients suriving Hodgkin's lymphoma are at greatest risk

New treatment modalities

Eric J. Hall, Int. J. Radiat. Oncol. Biol. Phys. 2006

Protontherapy in paediatric oncology

Courtesy of Jeffrey Dihn, MD Anderson, Houston, TX

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

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Protons (PSI)

La Tessa et al. Radiother. Oncol. 2012

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

Low-energy neutrons inside the phantom

La Tessa et al. Phys. Med. Biol. 2014

Distance from PTV (mm)

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 Boost field Total treatment	3.0 ^a 2.2 ^b	1.4 1.0	15 5 20	66 16 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.

<u>Total dose < 0.3 mSv</u>

Very low stray radiation reduced risk of secondary cancers or teratogen effects

Münter et al., Fertil Steril. 2010

GERMAN CANCER RESEARCH CENTER IN THE HELMHOLTZ ASSOCIATION

Radiation Absorbed Dose

Risk of SMN Incidence

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.

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

MDAnderson Cancer Center

Making Cancer History*

Thank you very much!

Trento Institute for Fundamental Physics and Applications