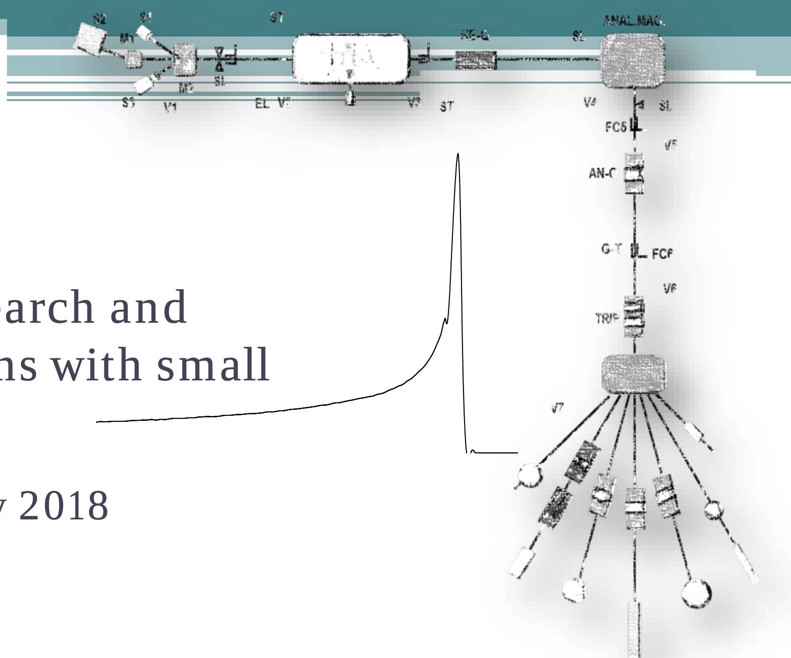
Fundamental and applied radiobiological research using low-energy accelerated particle beams

Lorenzo Manti

Radiation Biophysics Laboratory

Physics Department "E. Pancini", University of Naples Federico II

and INFN, Naples Section

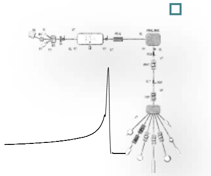


Workshop on basic research and interdisciplinary applications with small accelerators

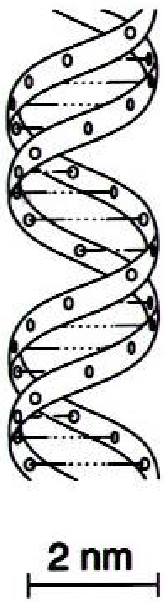
Naples, 17-18 January 2018

Outline

- Particle radiobiology
- Past research carried out at the Naples Tandem Accelerator
  - Ion type- and track structure-dependence of the radiobiological effectiveness of accelerated ion beams
  - Modulation by UMTS signals of the acute and long-term cellular effects from alpha particles at energies typical of radon exposure
- Current & future research using low-energy accelerated particles
  - Hadrontherapy-related particle fragmentation
  - Towards proton-boron capture therapy

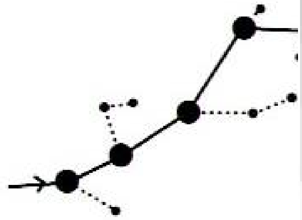


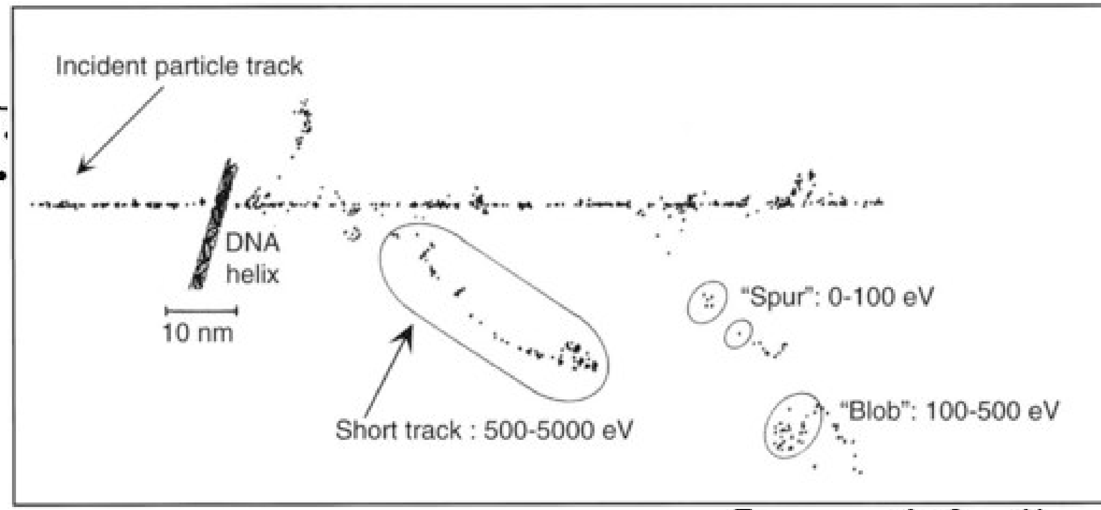
Physics governs cellular response



Parts of:

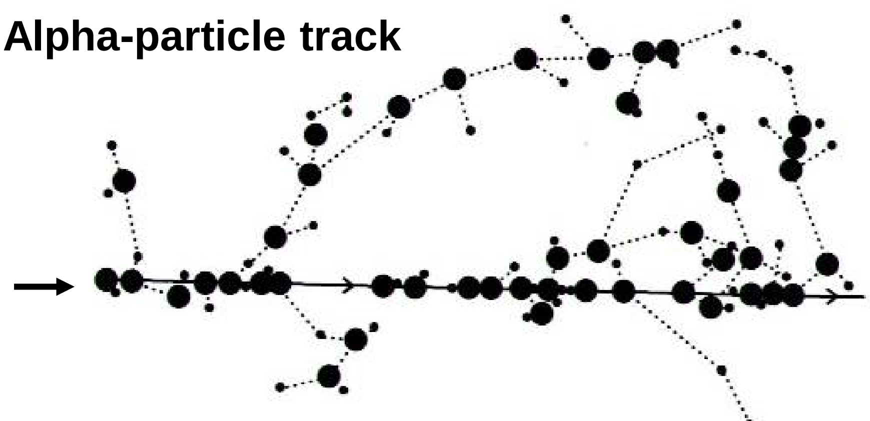
Electron track





+

Alpha-particle track



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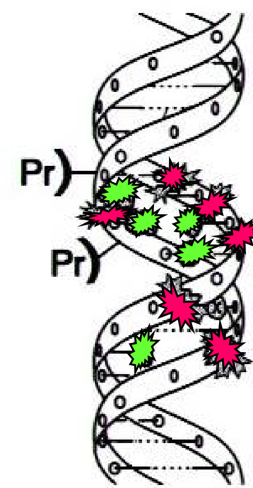
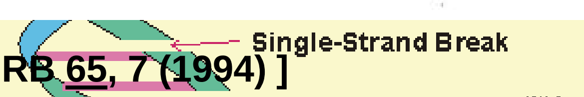
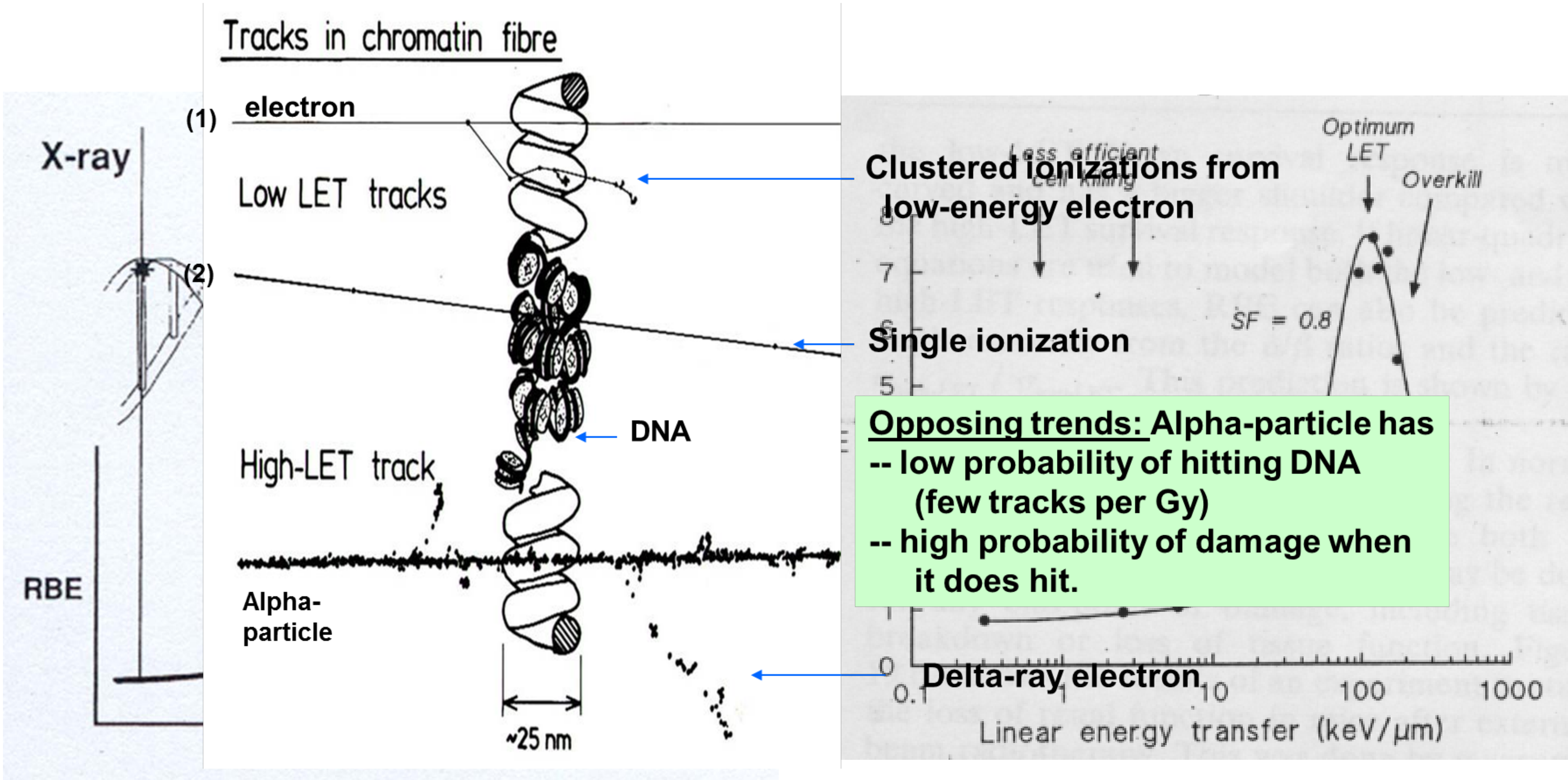




[Goodhead, IJRB 65, 7 (1994)]

Radiation quality and biological response to IR

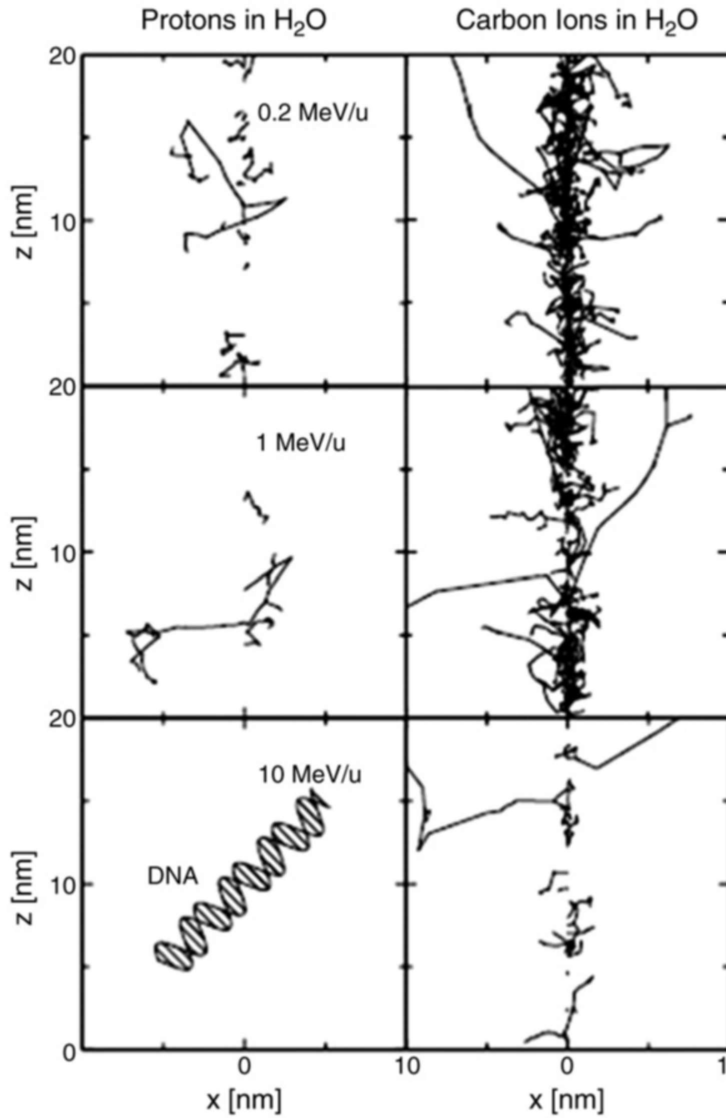


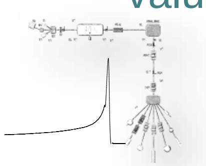
Track structure

- LET alone not a predictor of cellular response to particle radiation

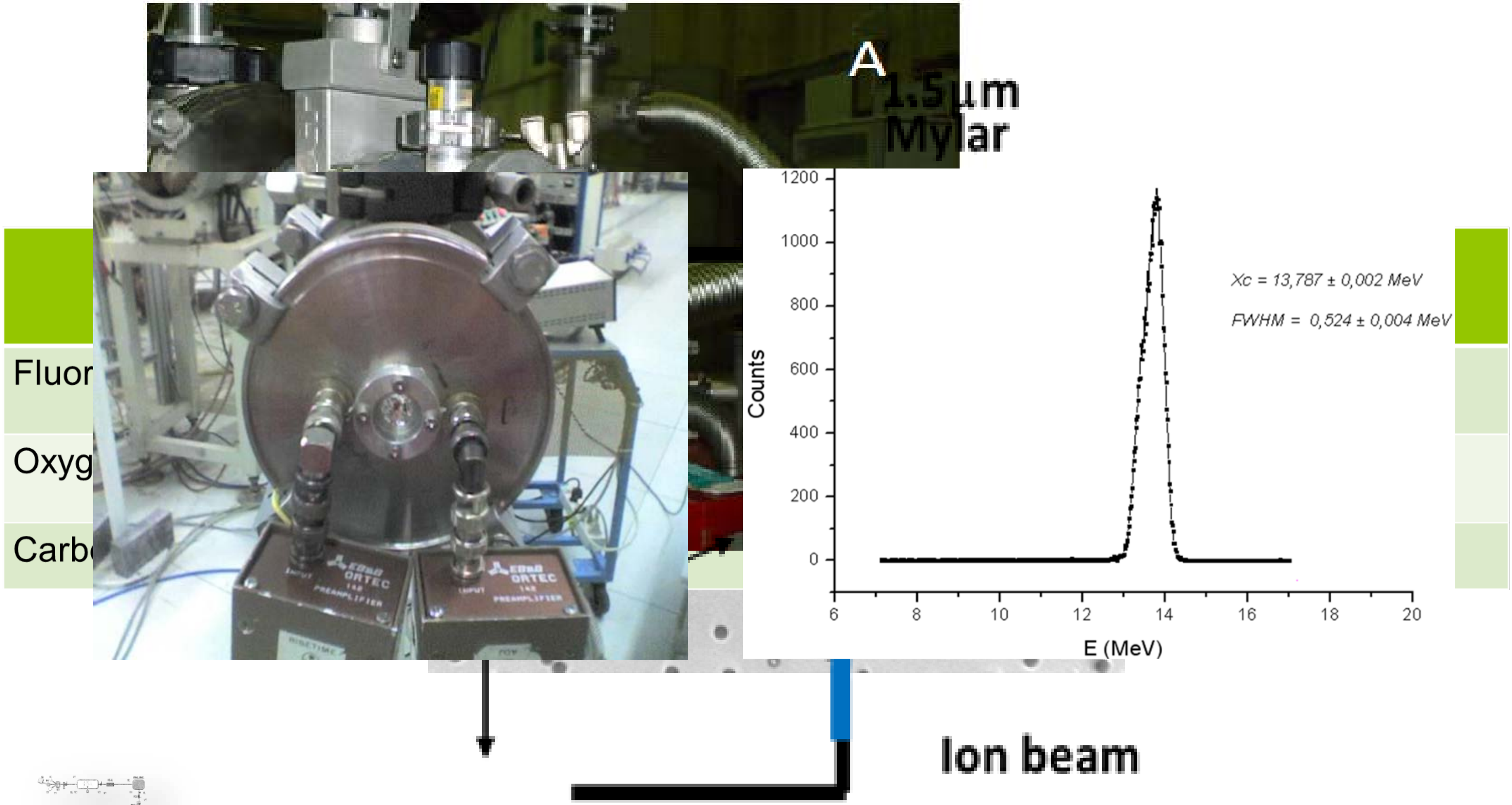
- Role of ion track structure
  - Energy deposited differently according to the ion mass and initial energy
  - Track diameter not proportional to LET, depends on particle velocity and, at a given energy, on ion Z

- Highly inhomogeneous damage clustering within and around the track for various ions of the same LET
  - Protons and carbon ions of similar LET values have different RBEs

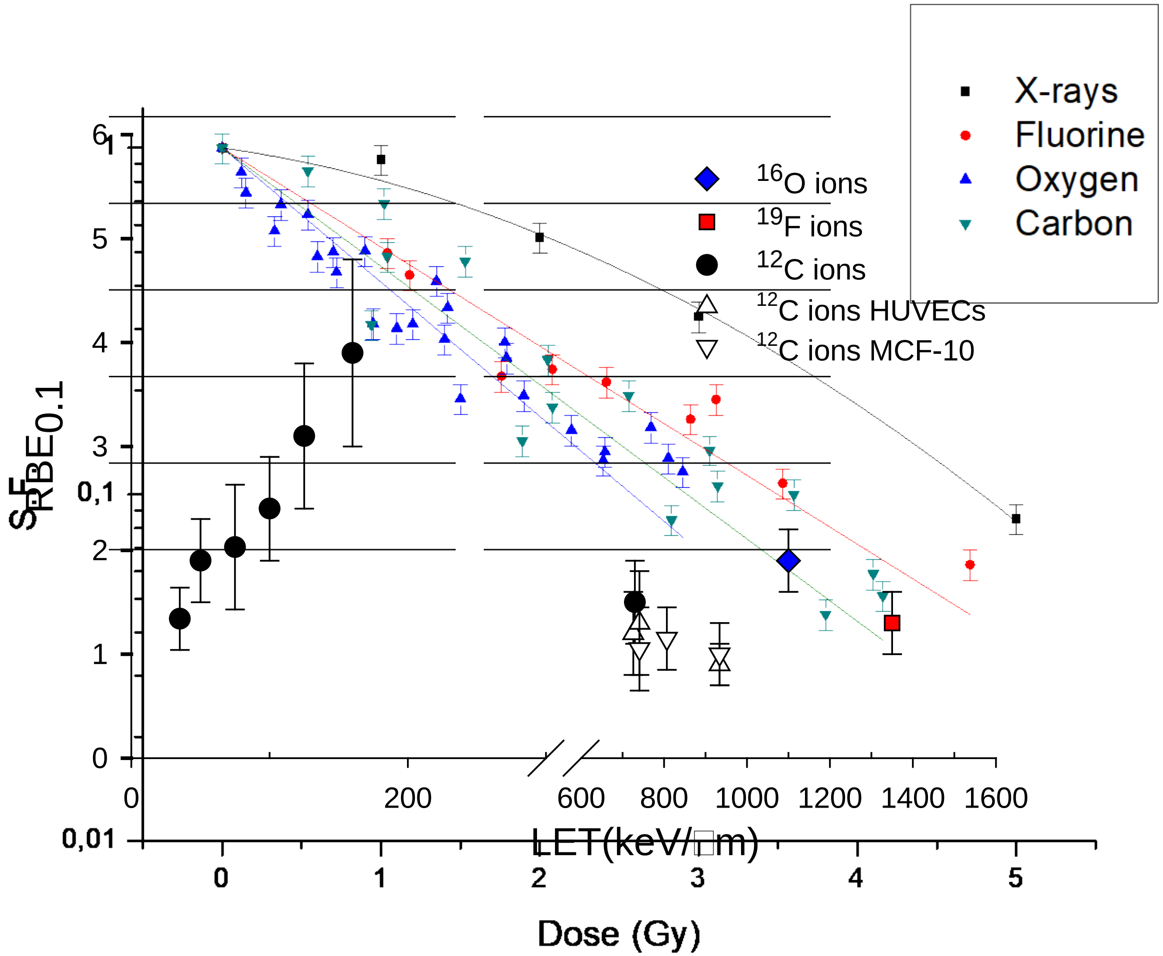


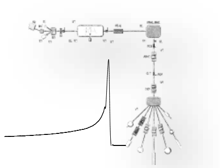


Irradiation set up at Naples Tandem

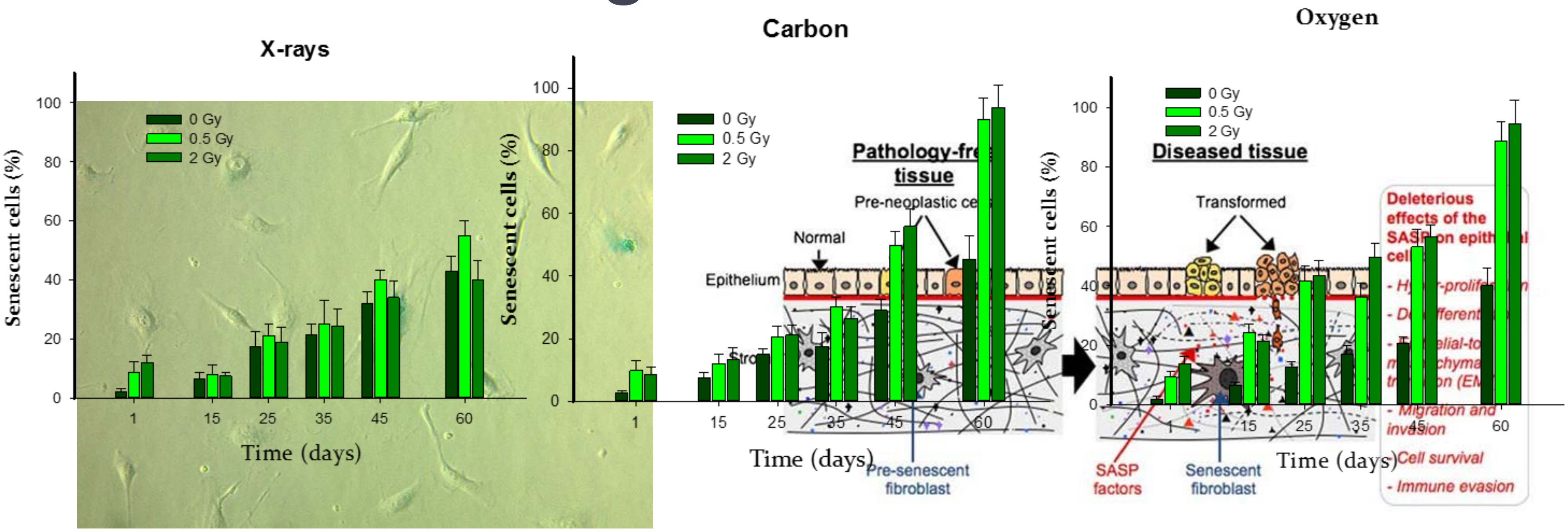


Survival following very-high LET ions

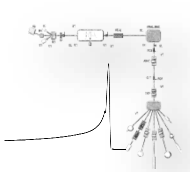




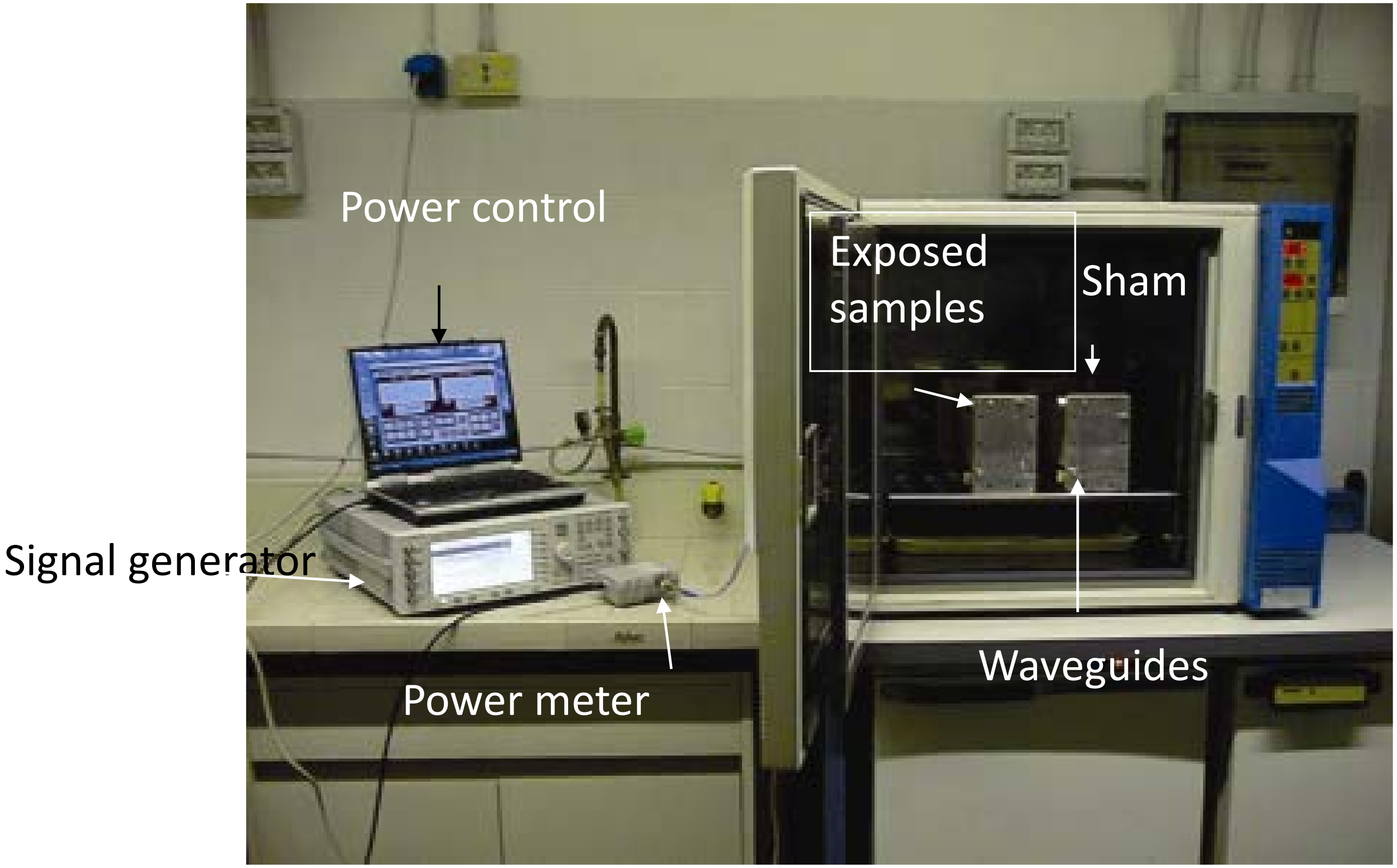
Cellular senescence following very-high LET ions



Ion	Incident energy (MeV)	Incident LET (keV/µm)	Residual range in water (µm)
^{12}C	5.9	934	8
^{16}O	15.5	1,120	15

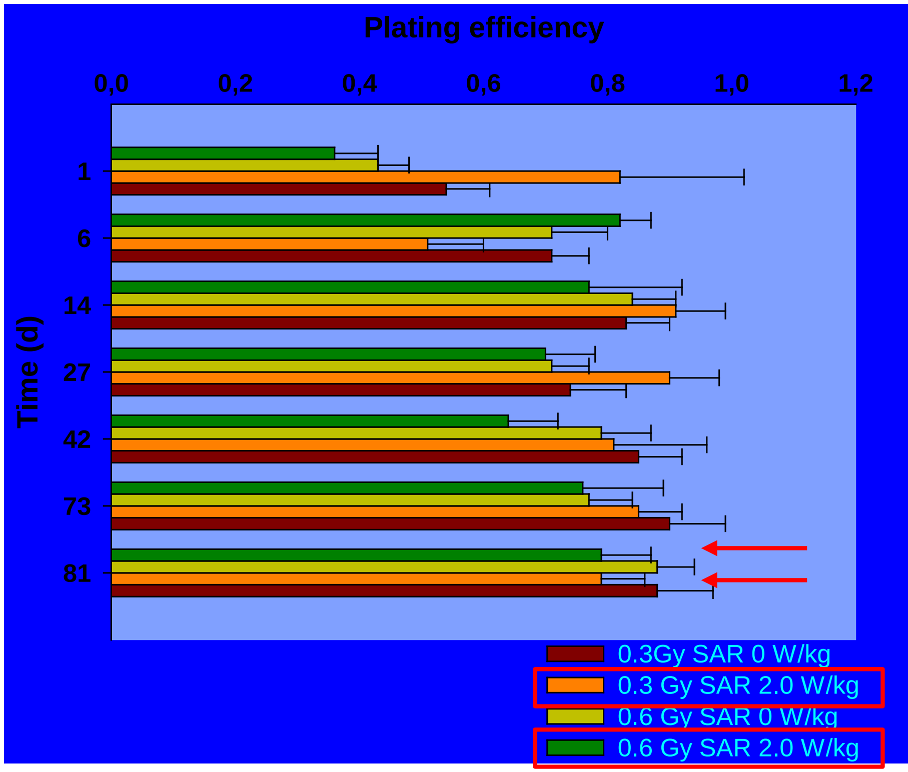


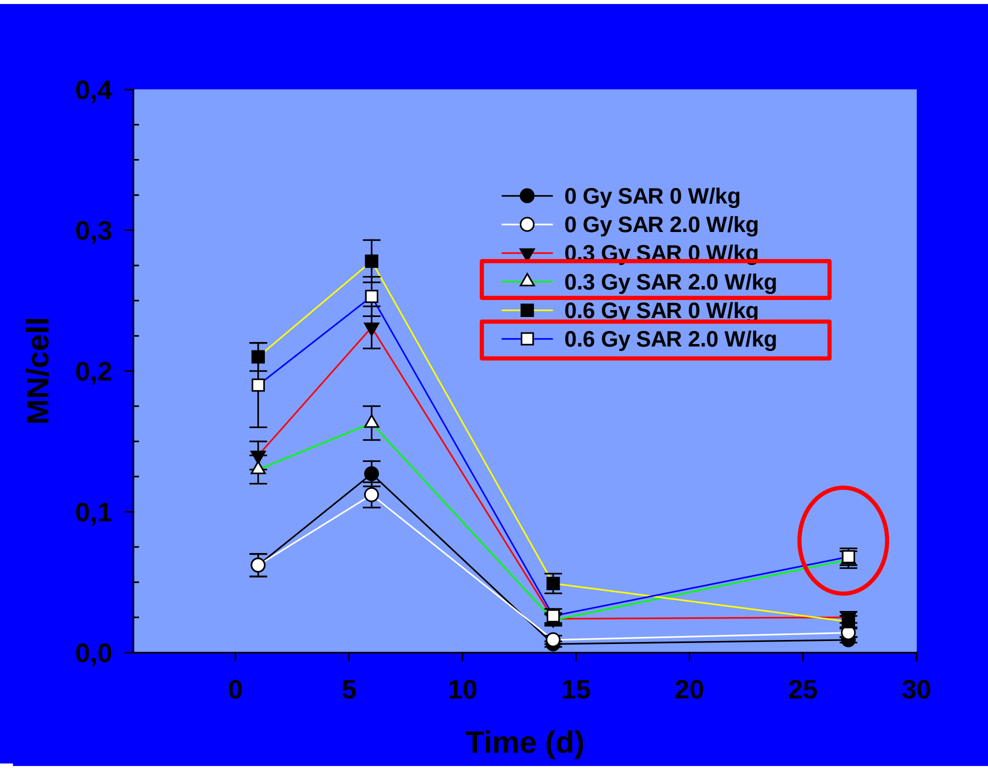
Combined exposures-1



- h-TERT human bronchial cells (HBEC-3kT) were co-exposed to high -LET low-fluence α-particles in the dose range 0-0.6 Gy (incident energy 5.5 MeV, LET = 120 keV/μ), produced at the 3-MV Tandem accelerator . Cells were subsequently incubated for 24 h in a thermostated waveguide fed by an UMTS signal (1.95 GHz, SAR = 2.0 W/kg).

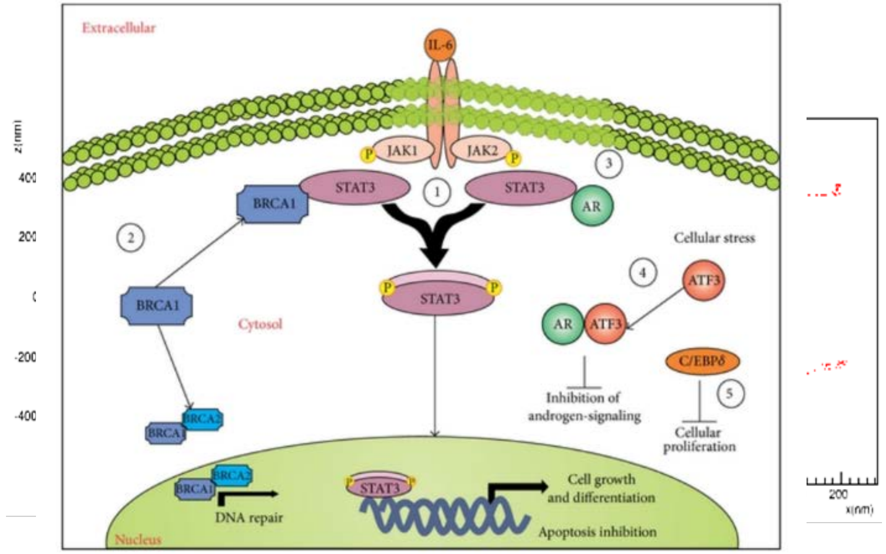
Combined exposures-2

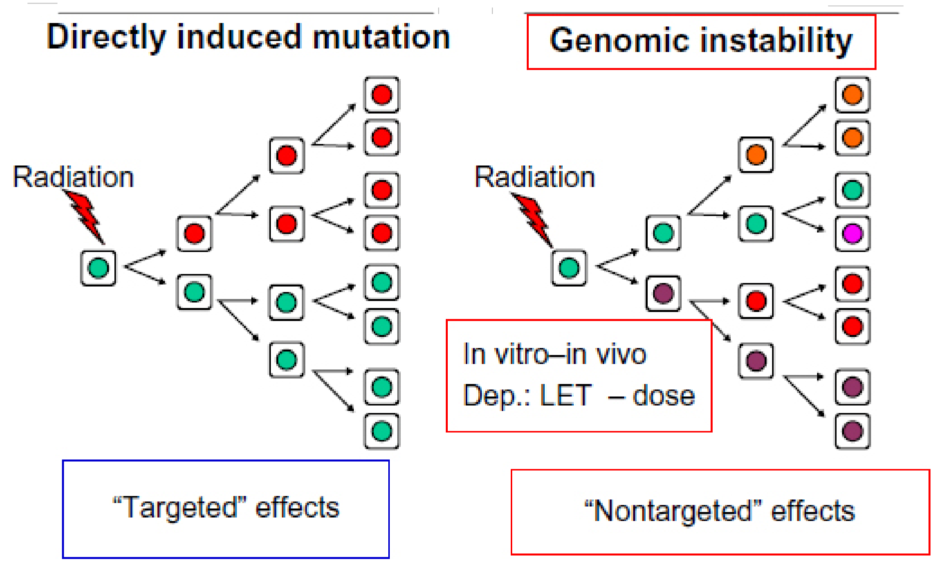




Main results

- Deviation from predicted RBE-LET dependence
- Exacerbation of high LET-induced genomic instability by RF signals





Naples Tandem output (2009-12)

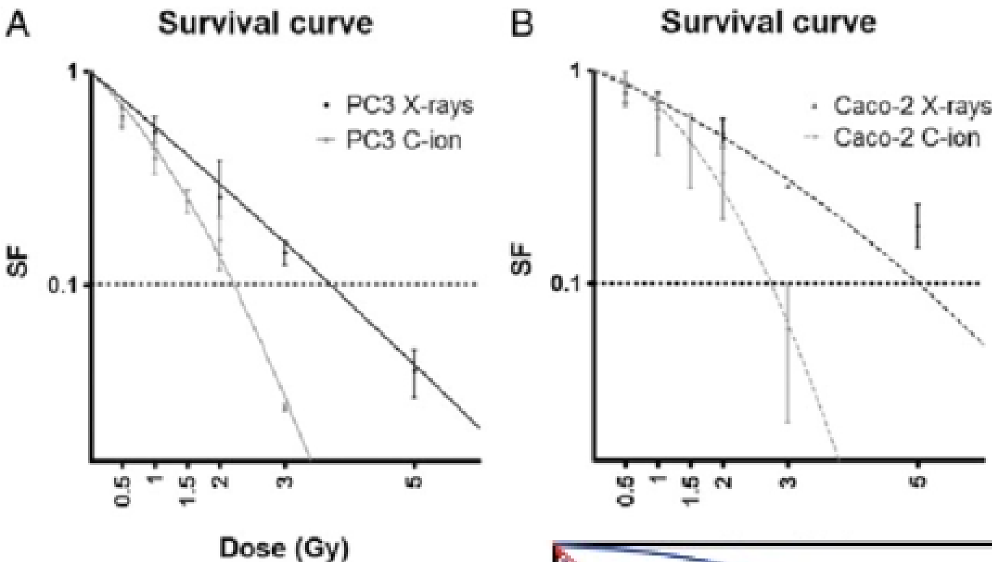
Papers & proceedings:

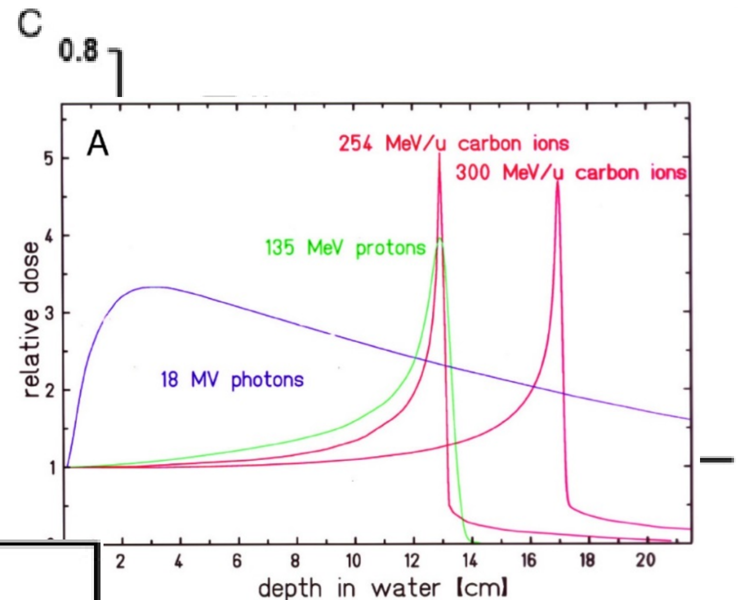
- Development of a low-energy particle irradiation facility for the study of the biological effectiveness of the ion track end. JOURNAL OF PHYSICS. CONFERENCE SERIES, Manti L. et al.,. vol. 373, p. 012019-012026, ISSN: 1742-6588, doi:10.1088/1742-6596/373/1/012019 (2012).
- BioEM2009 Joint meeting of The Bioelectromagnetics Society (BEMS) and the European BioElectromagnetics Association (EBEA). Effects Of UMTS Signal (1.95 GHz) On Cytogenetic Damage Induced By Ionising Radiation Of Varying Quality Radiation In Human Cells In Vitro. Manti L. et al., Davos, Svizzera, giugno 2009.
- 37th annual meeting of the European Radiation Research Society (ERRS). In Vitro effects of exposure to radiofrequency on DNA damage induced by high-LET ionising radiation. Manti L. et al., Praga, Rep. Ceca, agosto 2009.
- 38th annual meeting of the European Radiation Research Society (ERRS). Combined exposure of human cells to high-LET radiation and UMTS signal: acute damage and genomic instability.Manti L. et al.,Campajola. Stoccolma (Svezia) settembre 2010.
- XV Convegno Nazionale della Società per la Ricerche sulle Radiazioni (SIRR). Influenza del segnale UMTS (1.95 GHz) su danno citogenetico acuto ed instabilità genomica indotti in vitro da radiazione ionizzante ad alto LET. D’Arco A. et al.,Roma, ottobre 2010.
- 14th International Congress of Radiation Research, Irradiation of tumour cell lines with very high-LET particle beams accelerated at Naples Tandem facility. Manti L. et al., Varsavia (Polonia), agosto 2011.
- ION BEAMS '12 - Multidisciplinary Applications of Nuclear Physics with Ion Beams- Influence of the ion type on the radiobiological effectiveness of accelerated ion beams. Manti L. et al., Legnaro, LNL-INFN (Padova) , giugno 2012

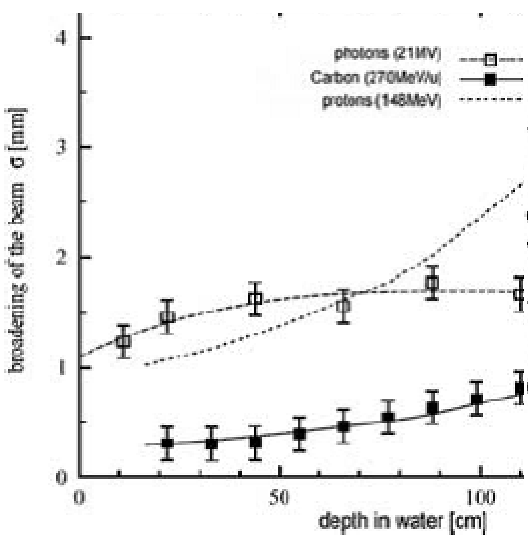
MSc Theses in Physics

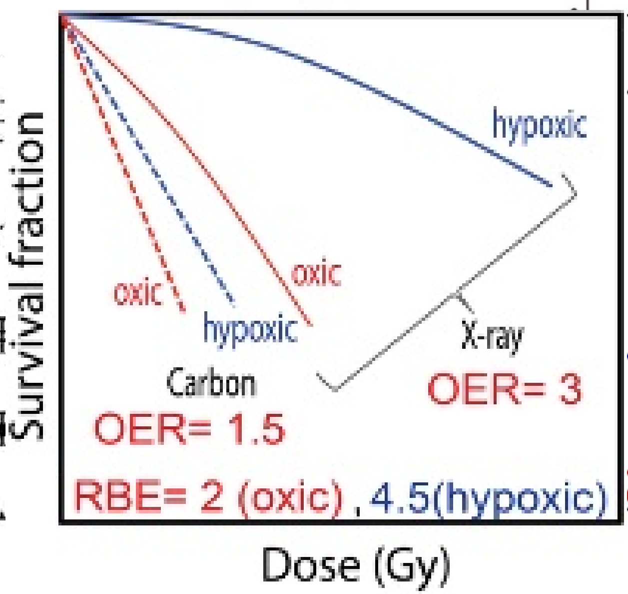
- Annalisa D'Arco, 2009-10, «Effetti combinati derivanti dall’esposizione in vitro di cellule umane alla radiazione ionizzante di vario LET ed a campi a radiofrequenza”
- Francesca Margaret Perozziello, 2011-12 “Caratterizzazione radiobiofisica di fasci di ioni carbonio, ossigeno e fluoro accelerati al Tandem TTT-3 del Dipartimento di Scienze Fisiche dell’Università di Napoli Federico II”
- Carla Maiorino, 2011-12 “Studio degli effetti subletali indotti da radiazioni ad alto LET e diverso Z nell’ambito del progetto MiMo-Bragg”
- Giuseppe Signore, 2012-13, “ Effetti radiobiologici di ioni su cellule umane: modellizzazione mediante il toolkit GEANT4 della perdita di energia”

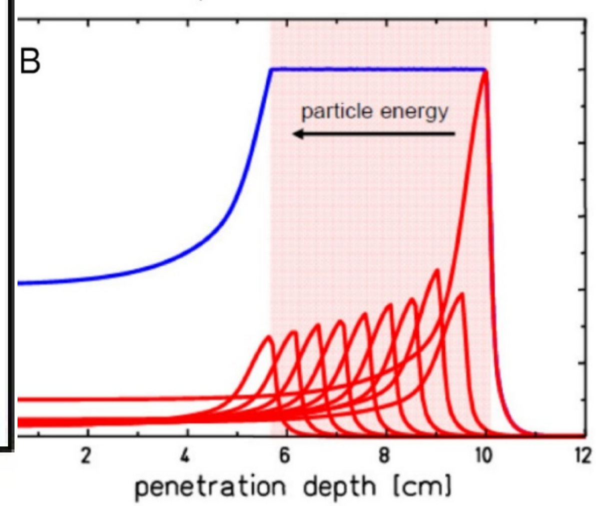
Therapeutic applications of charged particles: hadrontherapy



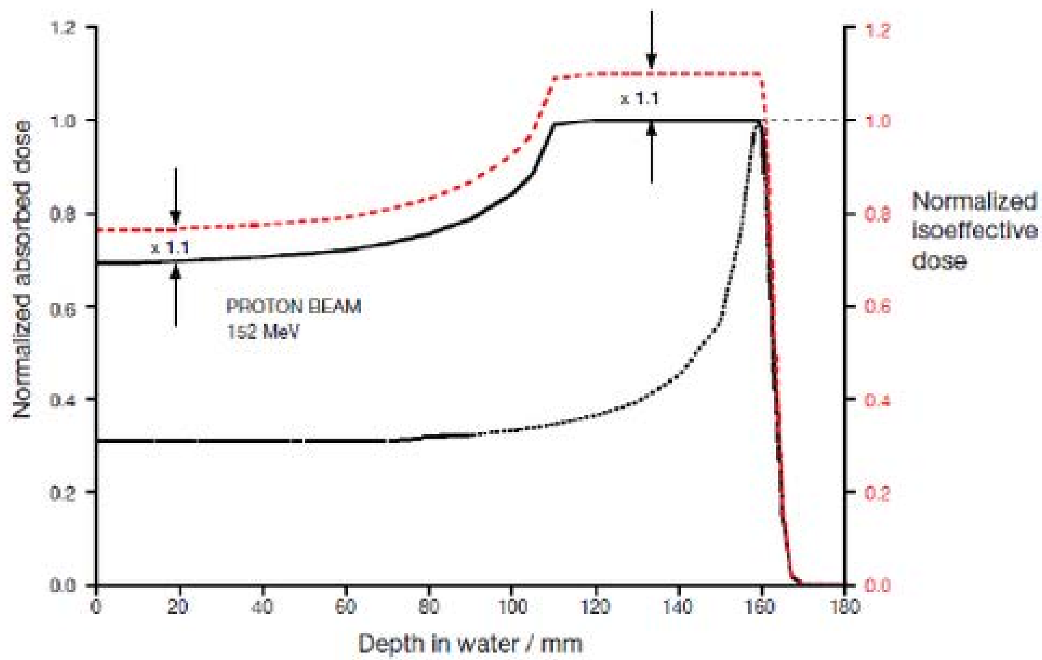


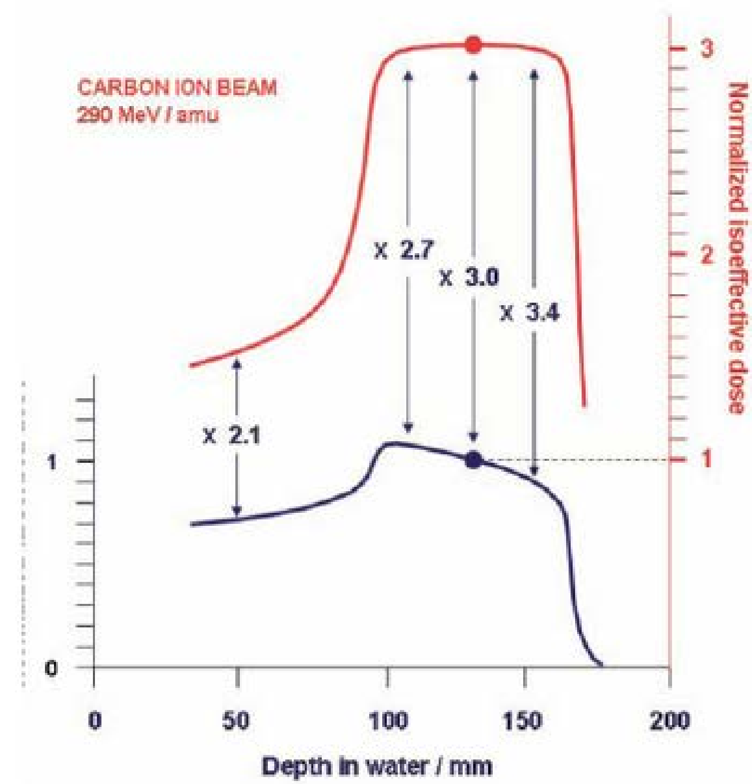






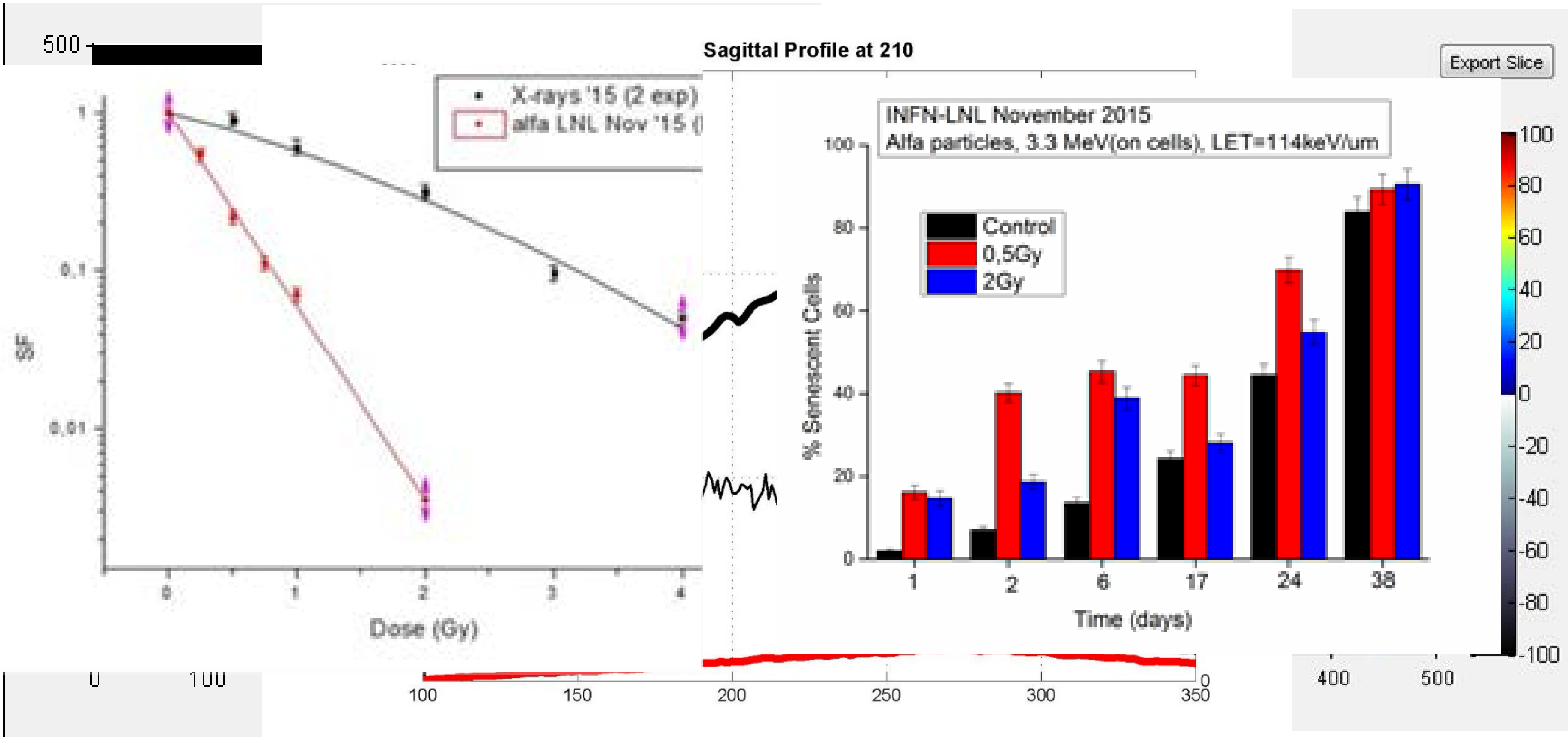
Enhancing protontherapy effectiveness





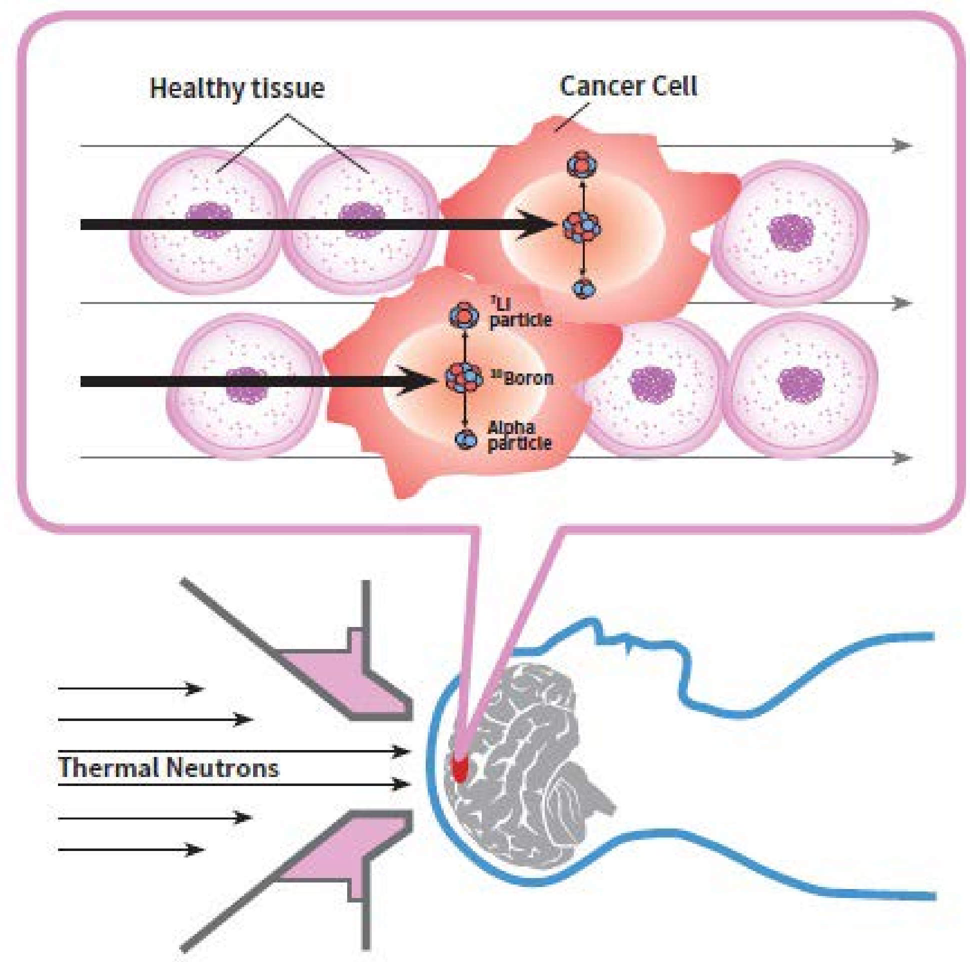
Paganetti H, Proton Beam Therapy, IOP publishing, 2017

Projectile fragmentation in ^{12}C ion hadrontherapy



Boron-Neutron Capture Therapy (BNCT)

^{10}B +



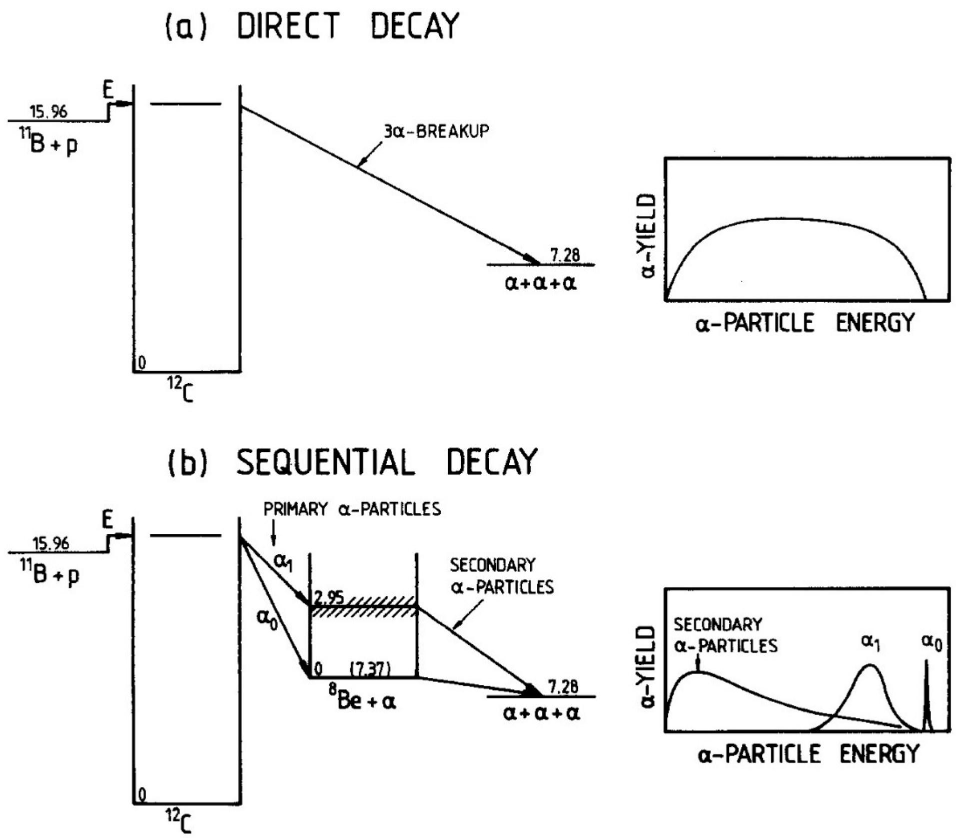
(6%)

(94%)

https://www.nccs.com.sg/Newsroom/NewsArticlesandReports/2015NewsArticlesandReports/Pages/Thenextbigthing.aspx

The proton-boron fusion reaction

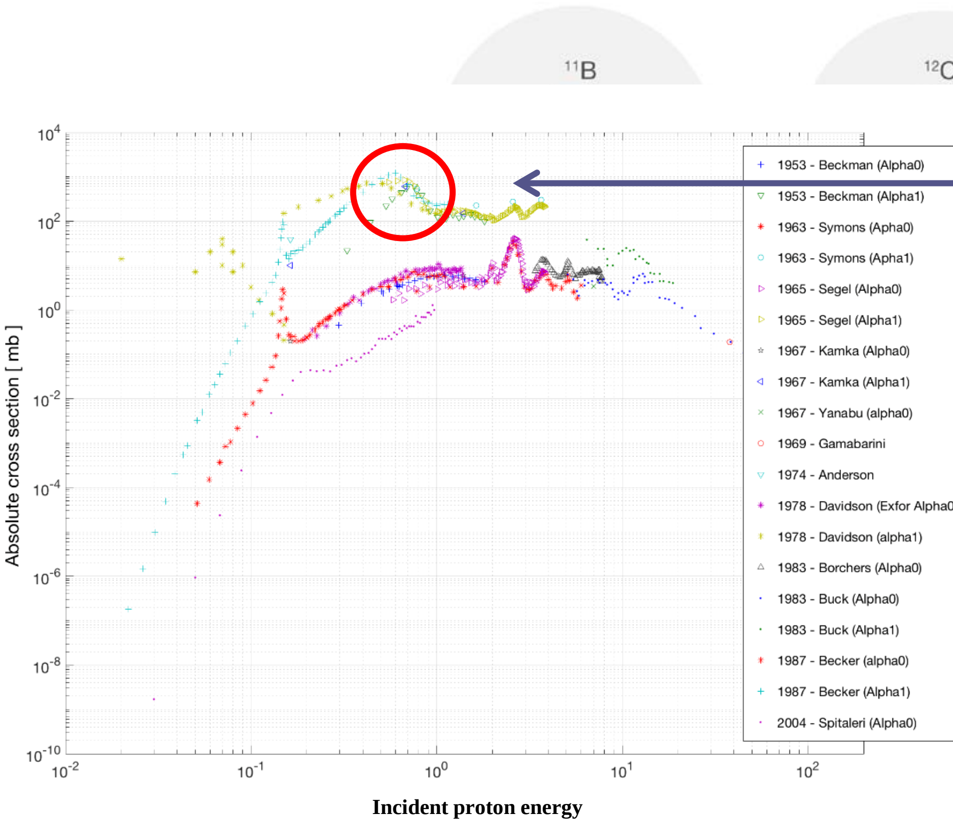
$^{11}B + p \rightarrow 3\alpha + 8.7\ MeV$

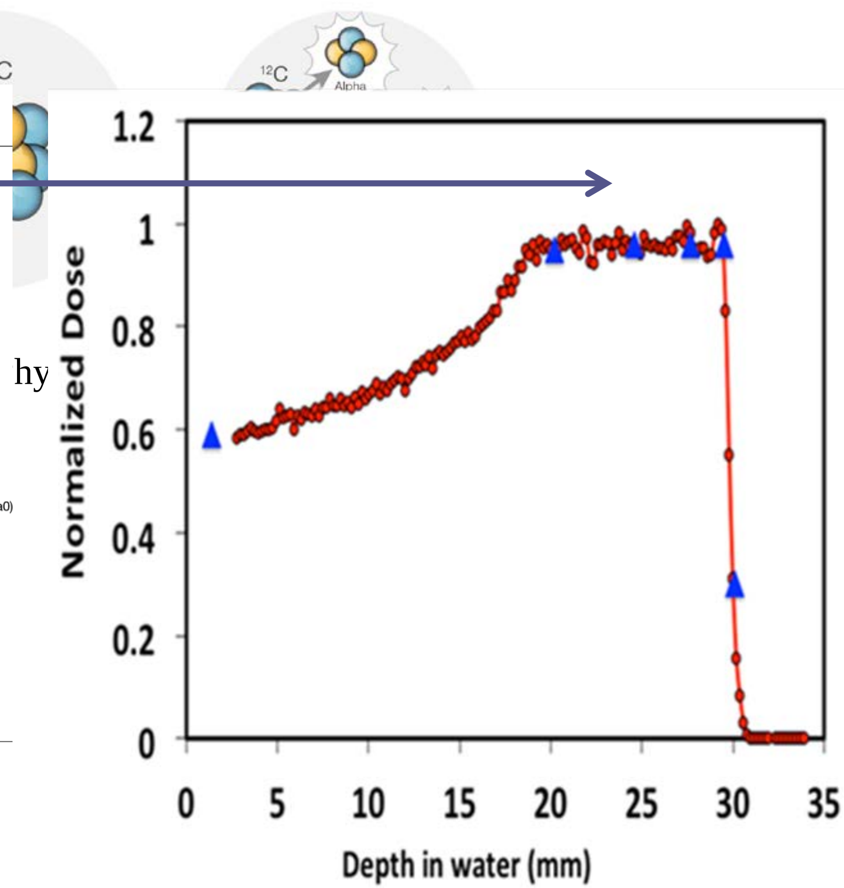


Rolfs C. and Trautvetter H.P. Z. Phys. A - Atomic Nuclei (1987)

(2011)

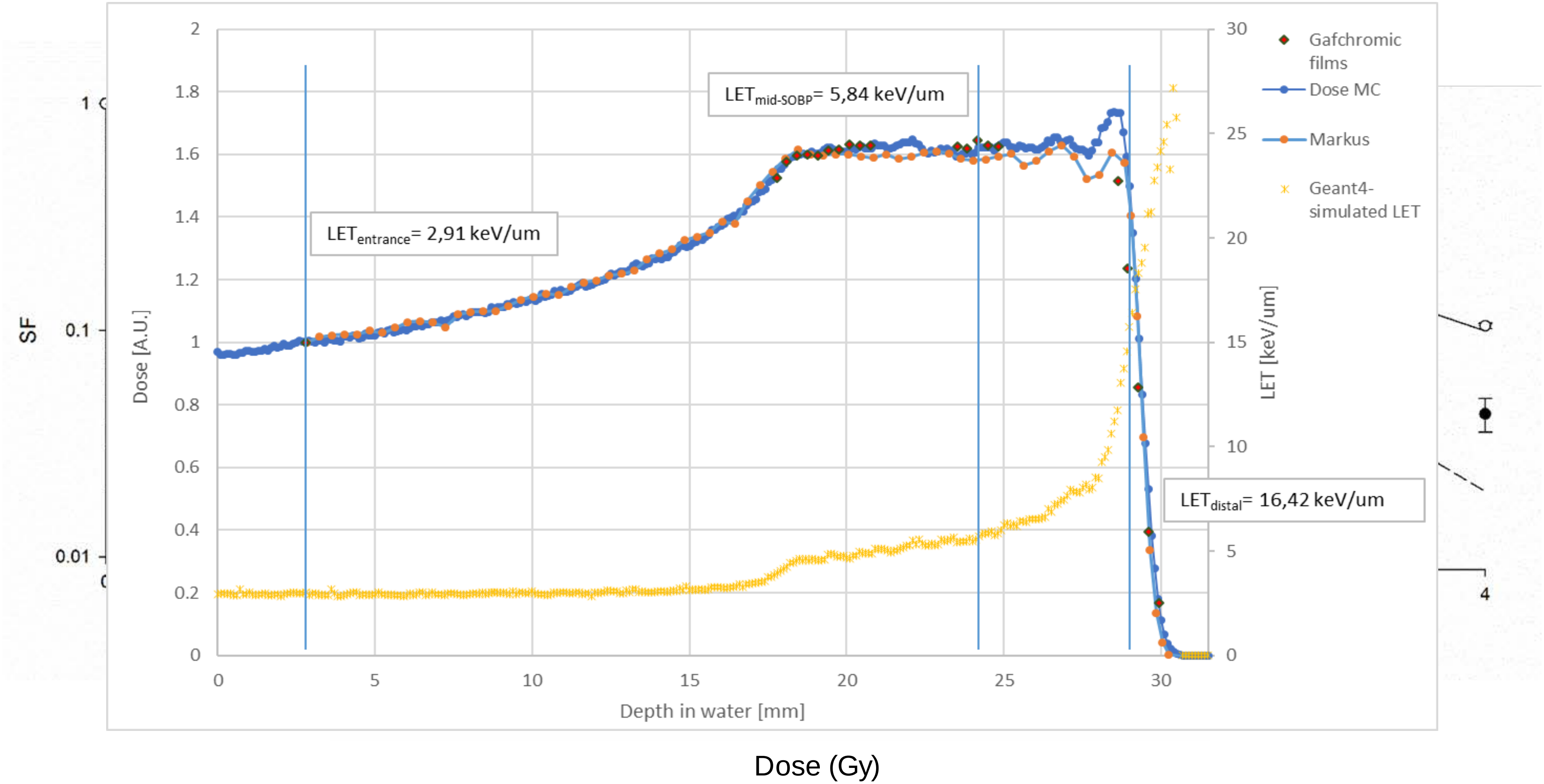
Towards Proton-Boron Capture Therapy (PBCT)-1





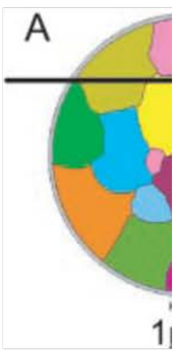
Courtesy of Cirrone G.A.P., INFN-LNS, Italy

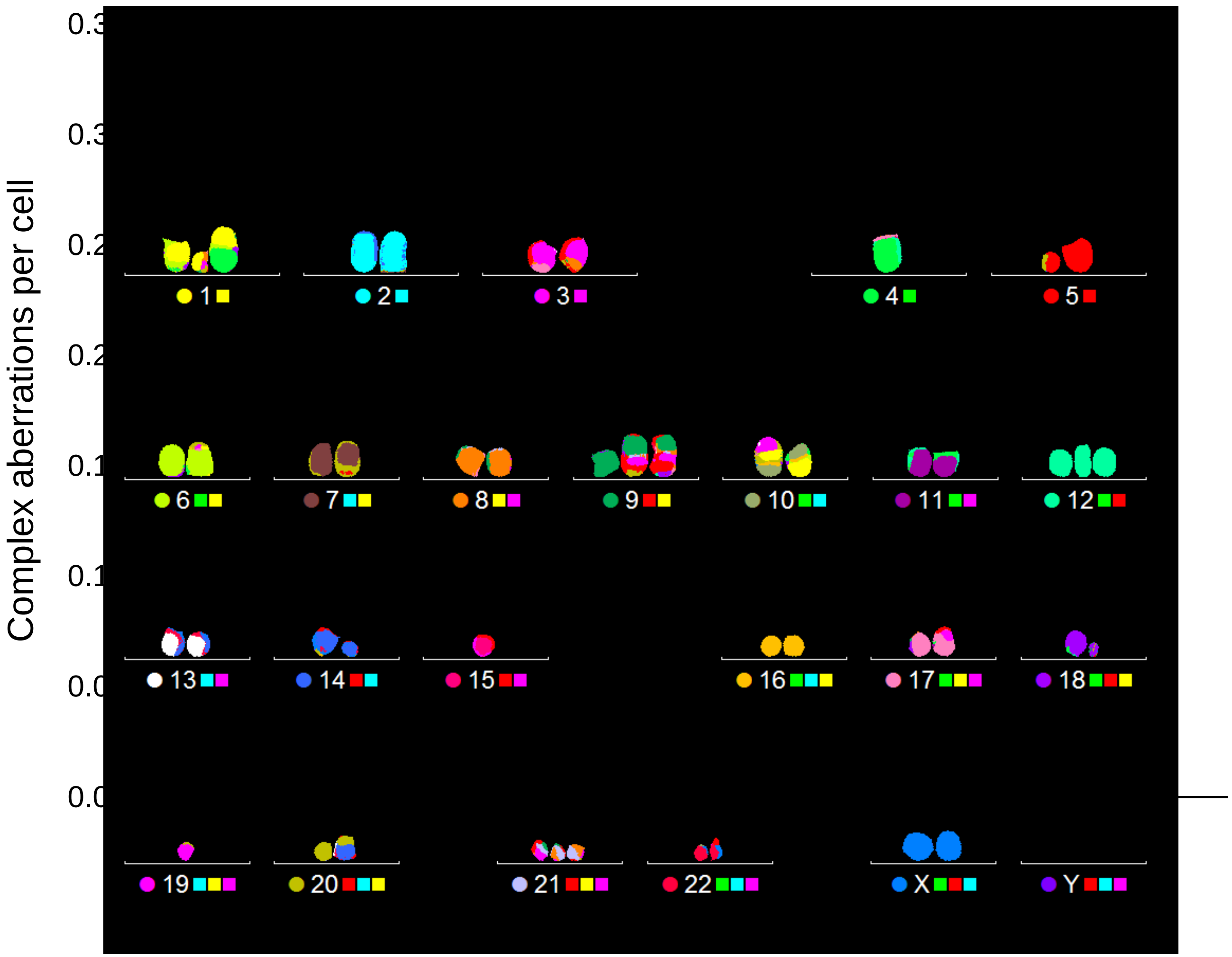
Towards Proton-Boron Capture Therapy (PBCT)-2

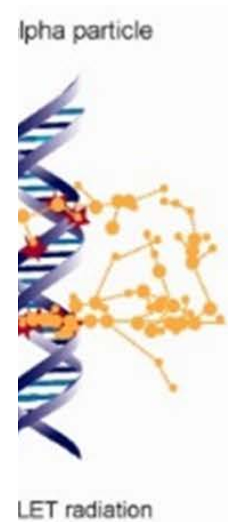


- *Cirrone et al., First experimental proof of Proton Boron Capture Therapy (PBCT) to enhance protontherapy effectiveness Sci Rep, in press*

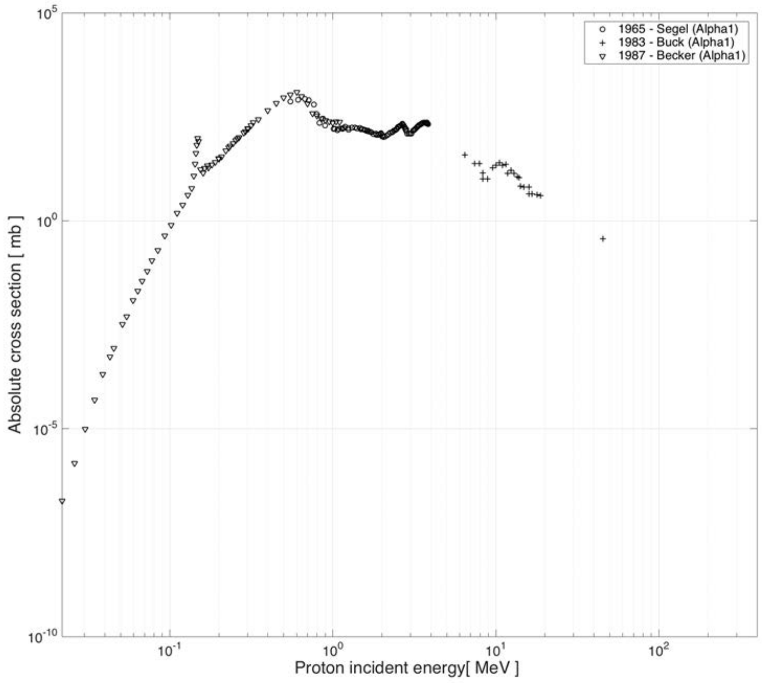
Chromosome aberration studies







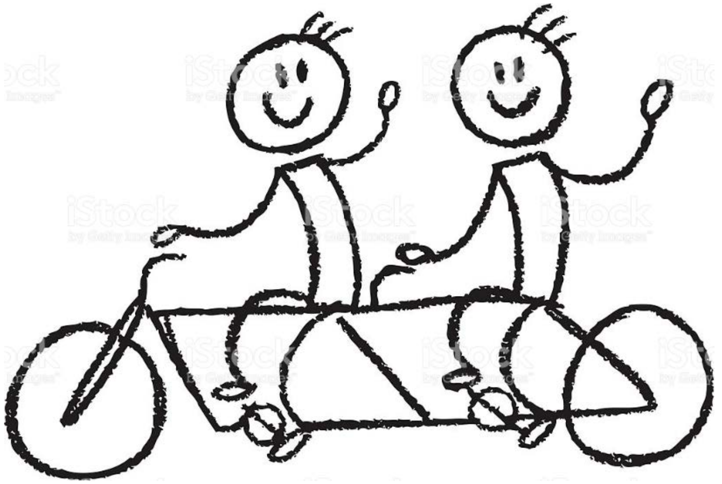
Validation of PBFT

- *In vitro* stuc  l beams
- *In vivo* pre-

- Low-energy proton irradiation

Conclusions

- Ion radiobiology may still greatly benefit from small accelerators
  - Fundamental research on basic radiation action (e.g. role of track structure, cellular repair mechanisms, etc.)
  - Clinically relevant applications (e.g. RBE of hadrontherapy-relevant fragmentation products, novel strategies employing nuclear fusion reactions, etc.)



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