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STUDIECENTRUM VOOR KERNENERGIE
CENTRE D'ETUDE DE L'ENERGIE NUCLEAIRE

The impact of different radiation qualities on cancer cells

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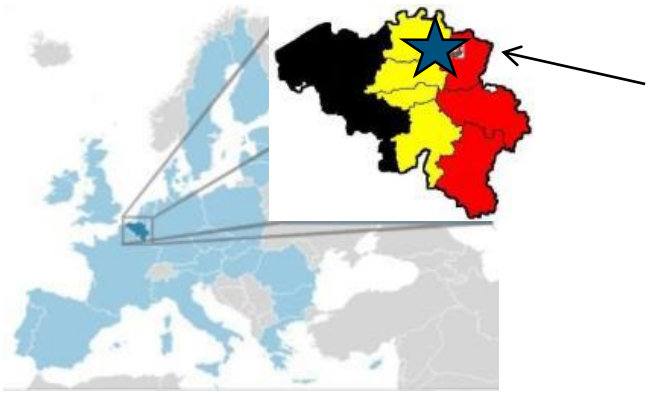
Radiobiology Unit, SCK•CEN, Belgium

XXth Colloque GANIL – Session 10, Amboise, France – Oct 19, 2017

The Belgian Nuclear Research Center

- 65 years of experience in nuclear science & technology



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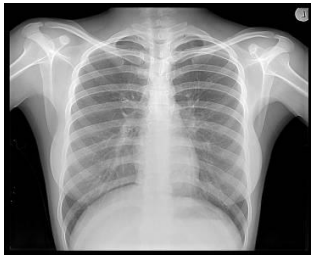
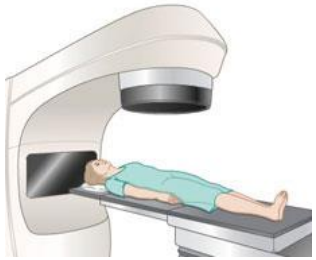
- Develop peaceful industrial & medical applications of radioactivity
  - Nuclear materials and systems (MYRRHA - ISOL@MYRRHA)
- Study impact of ionizing radiation on man and the environment
  - Radiobiology Unit, …

SCK•CEN Radiobiology Unit



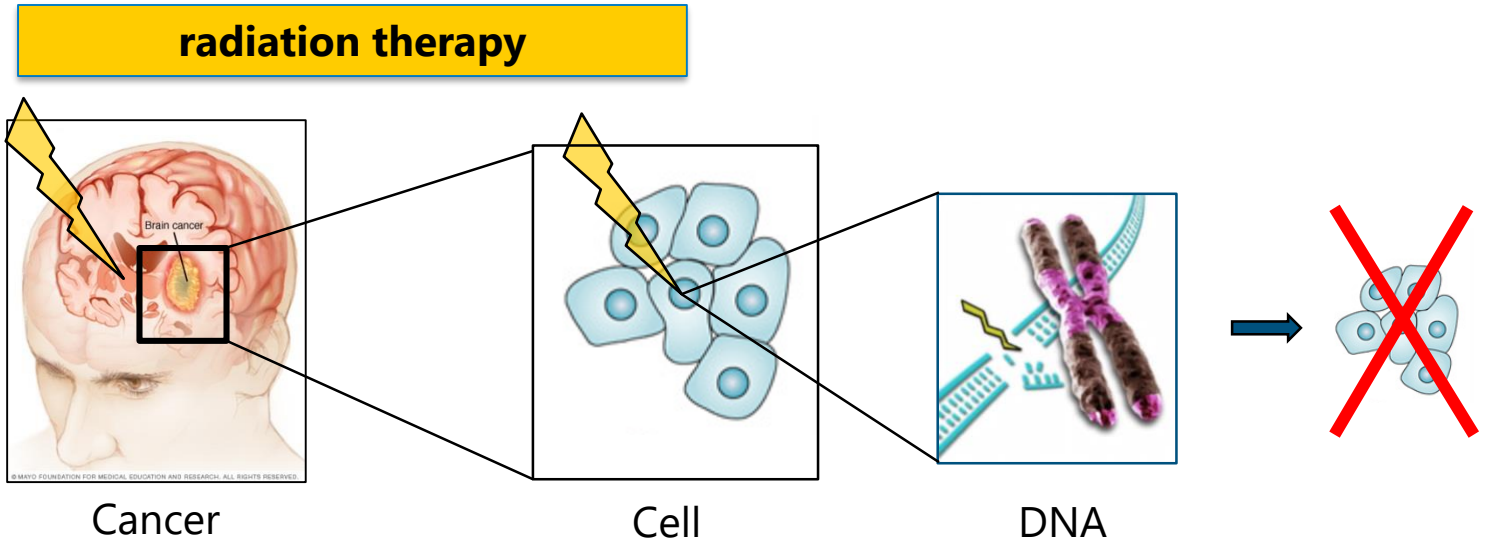


Evaluation of the **potential risks** of **ionising radiation on humans**

To provide the **scientific background** for **radiation protection, radiotherapy and nuclear medicine**

How physics is used to treat cancer

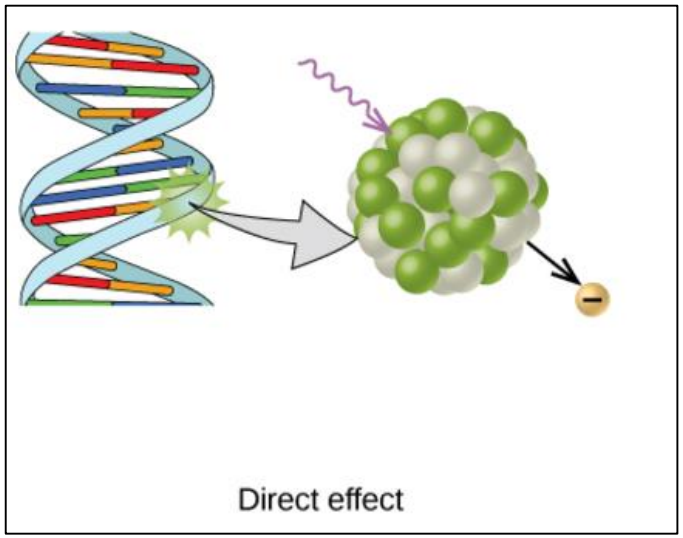
- Radiotherapy uses ionizing radiation with high energy that is transmitted to cancer cells

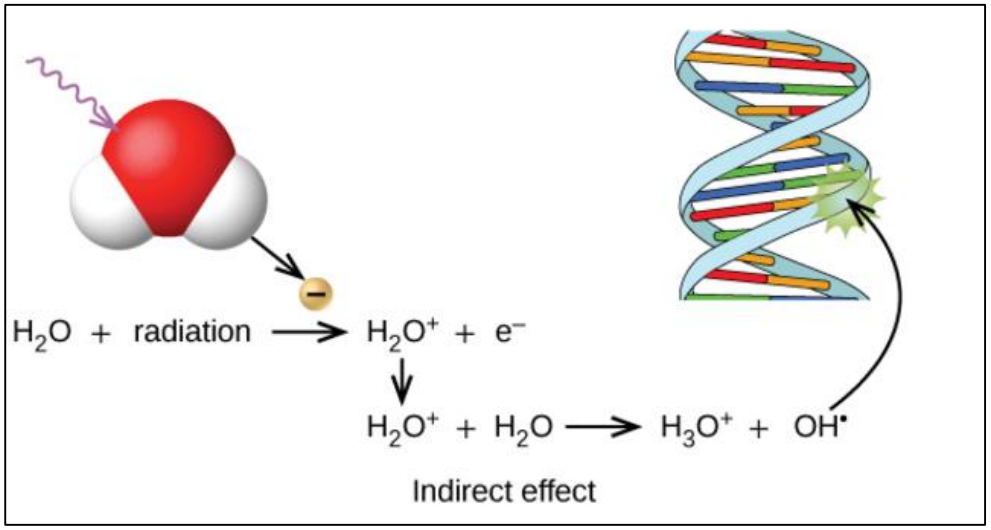


- Typical dose varies between 60 – 80 Gy (2 Gy/ fraction)

How physics is used to treat cancer

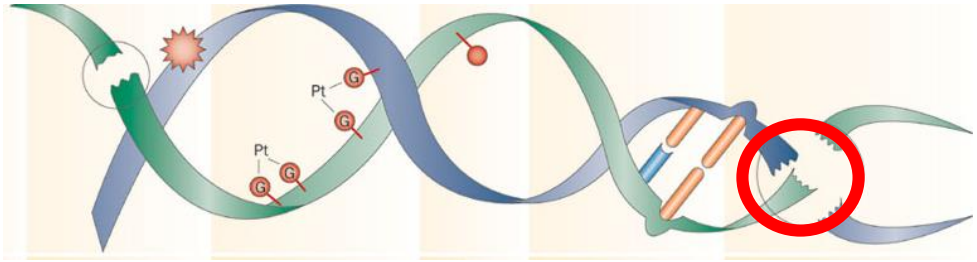
- Ionizing radiation can induce cell damage in two ways



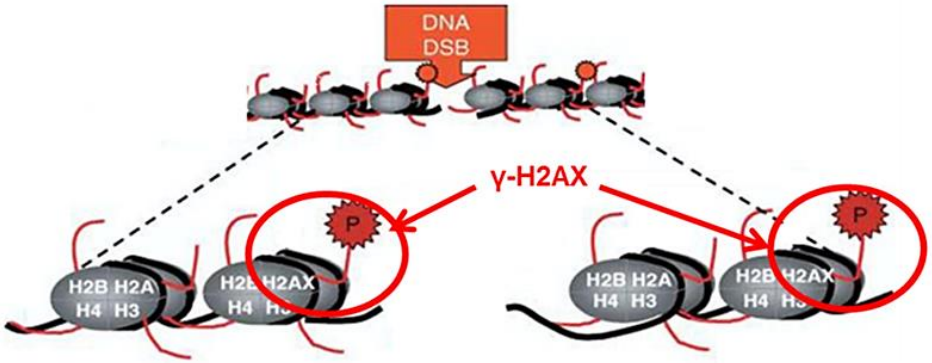


How physics is used to treat cancer

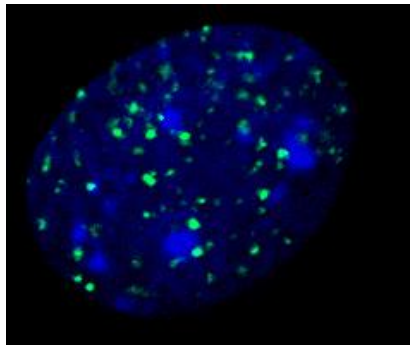
- Ionizing radiation induces a large spectrum of DNA lesions



Double Strand Break (DSB)
=
Principal **cytotoxic** lesion



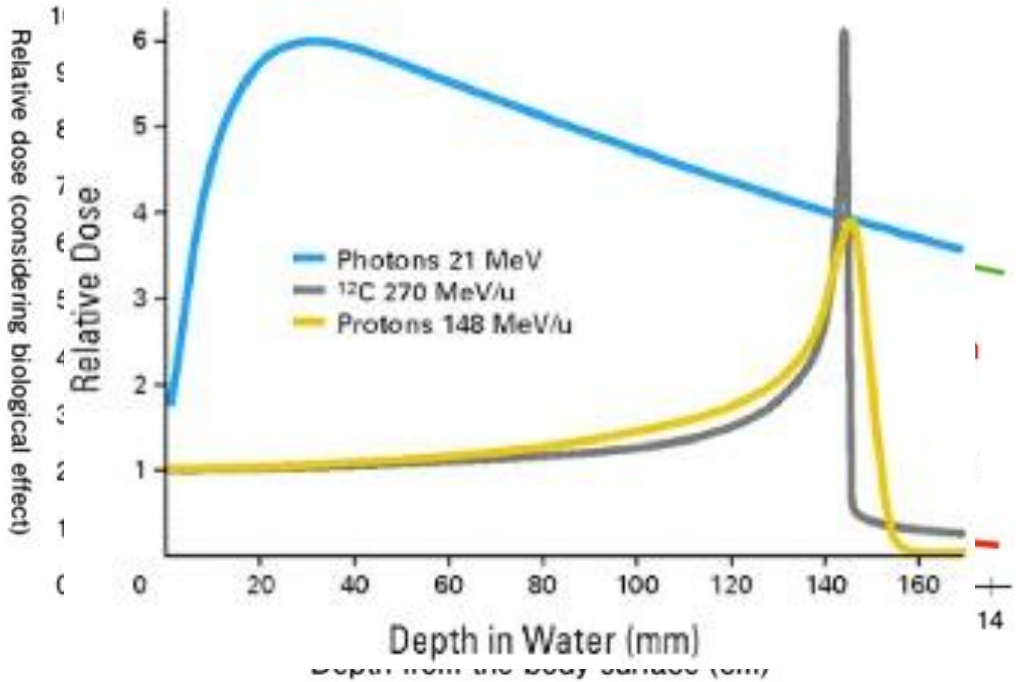
Huang and al., 2005

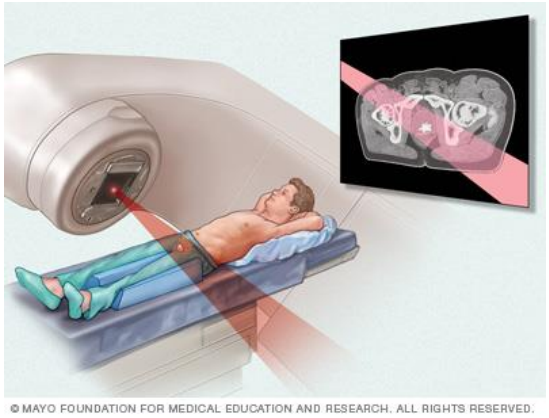


- nucleus (blue)
- yH2AX foci ~ DSB (green)

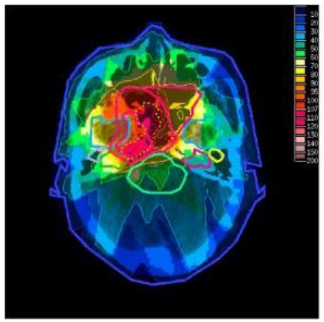
Radiotherapy: how physics is used to treat cancer

- Conventional (>99%): photon RT
- Advanced: hadron therapy
  - Particle accelerators: proton, carbon

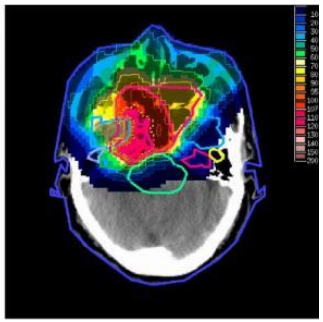




IMRT



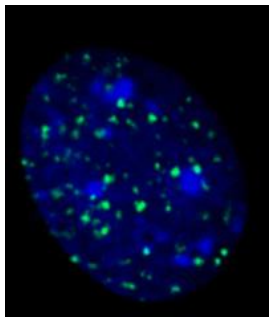
Particle therapy



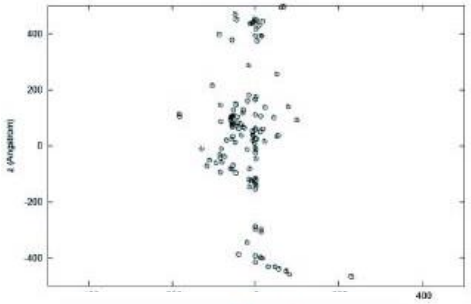
Particles: unique biological properties

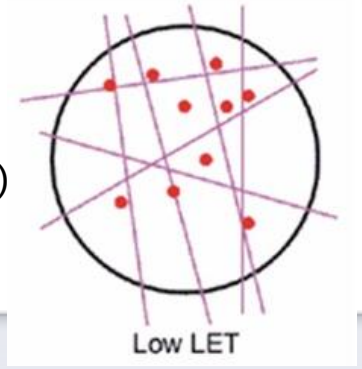
- Particles → (dense) ionization tracks
- Higher number of DNA lesions
  - More complex: mixture of 'clustered' DNA lesions
  - More difficult to repair ~ enhanced cell killing

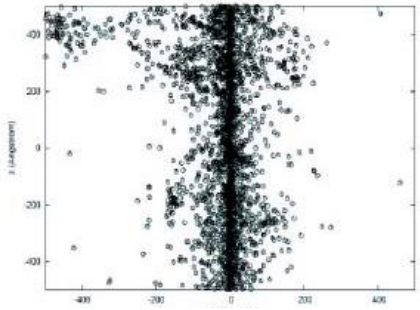
Photons

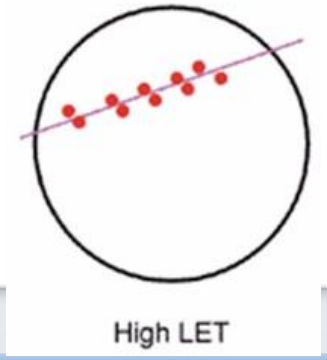


- yH2AX foci ~DSB (green)

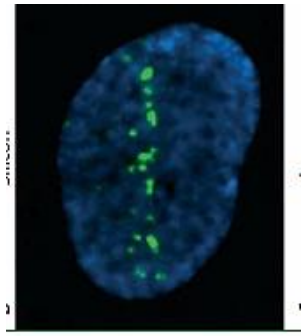








Particles



- yH2AX foci ~DSB (green)

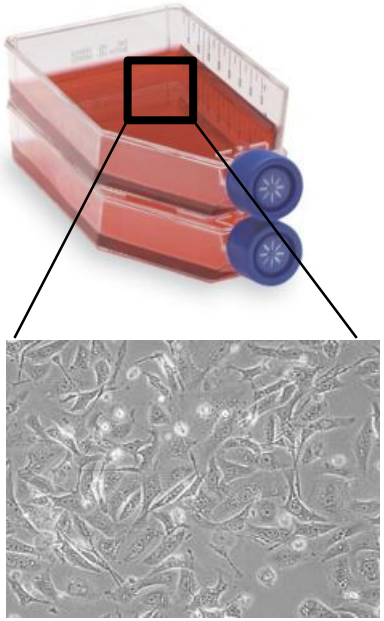
Particle therapy: what we (do not) know …

- Positive clinical outcome – increased use during next years
  - Published data based on a **small number** of patients
  - **No or limited data** of **long-term follow-up** studies (secondary malignancies, metastasis)
  - Many biological uncertainties
- Research is needed in all parts of radiation oncology
  - Clinical - physics- **radiobiology**

Hadron therapy research at SCK•CEN

- Compare biological actions of photons vs. particles in cancer cells

In vitro



Human cancer cell lines
- Prostate cancer
- Colon cancer
- Peadiatric brain cancer
- Breast cancer

X-rays (SCK•CEN, Belgium)
C-ions (GANIL, Caen, France)
Protons (iThemba LABS, South-Africa)

Cancer cell survival

DNA damage & repair

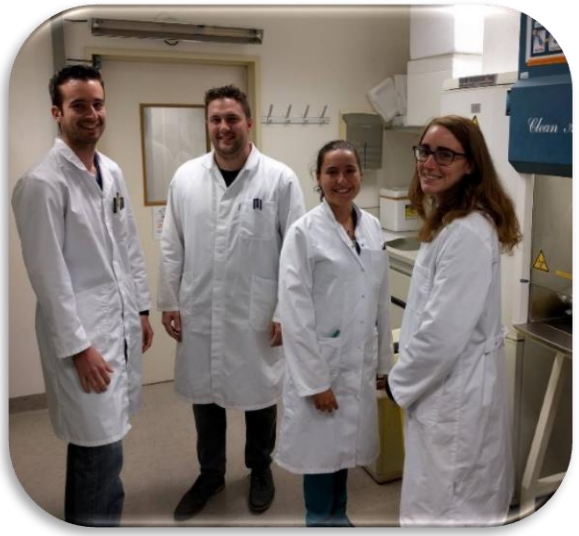
Gene expression

Cell migration

^{13}C beam @GANIL

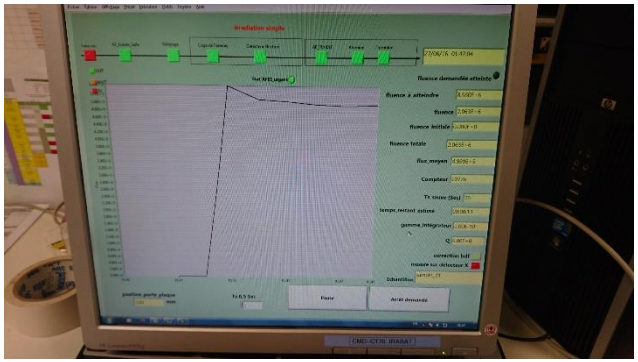
- iPAC GANIL: five ^{13}C beam times (2011- 2017)
  - P911-H + P1006-H
  - Transport cells from Belgium to LARIA, GANIL

GANIL
GRAND ACCELERATEUR NATIONAL D'IONS LOURDS
LABORATOIRE COMMUN DSM/CEA-IN2P3/CNRS



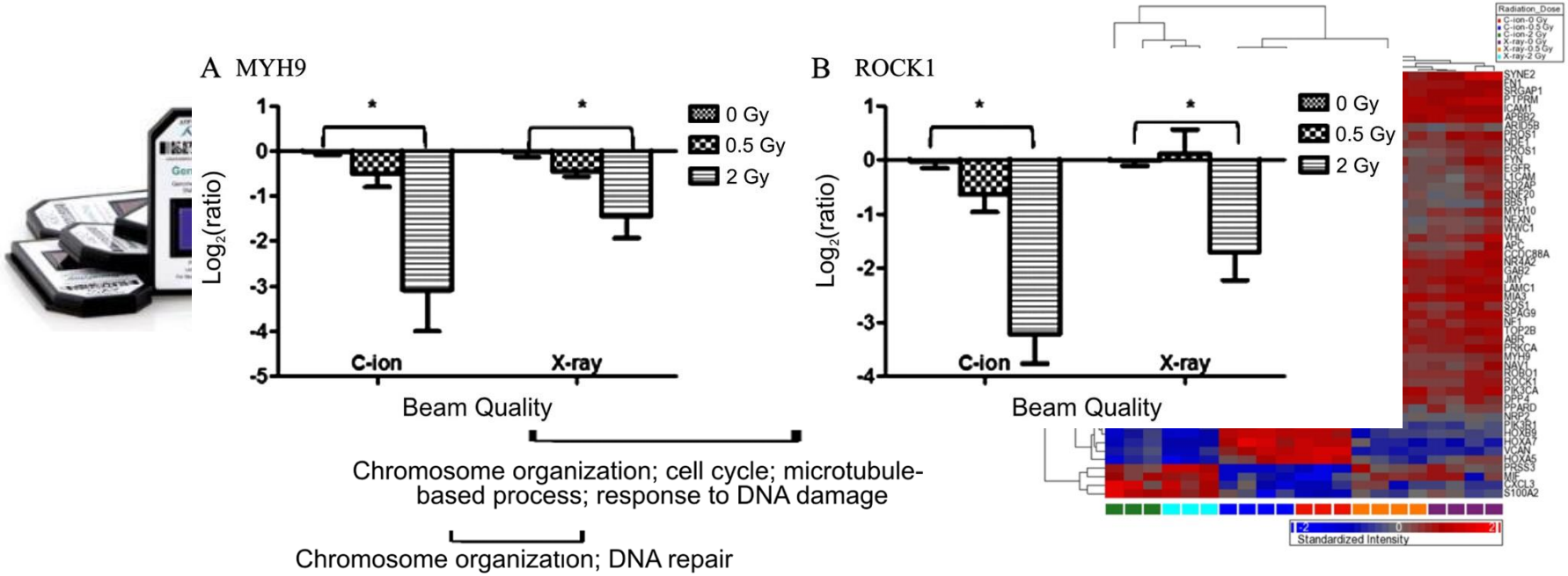
^{13}C beam @GANIL

- D1 beam line
- ^{13}C beam: 75 MeV/u – LET: 33,7 keV/µm
- Flux: 6,24x$10^{5}$$cm^{-2}$ sec-1
- Dosimetry performed by CIMAP group (Dr. A. Cassimi)



Carbon ion irradiation of the human prostate cancer cell line PC3: A whole genome microarray study

ANNELIES SUETENS[1,3], MARJAN MOREELS[1], ROEL QUINTENS[1], SABINA CHIRIOTTI[2,3], KEVIN TABURY[1], ARLETTE MICHAUX[1], VINCENT GRÉGOIRE[3] and SARAH BAATOUT[1,4]

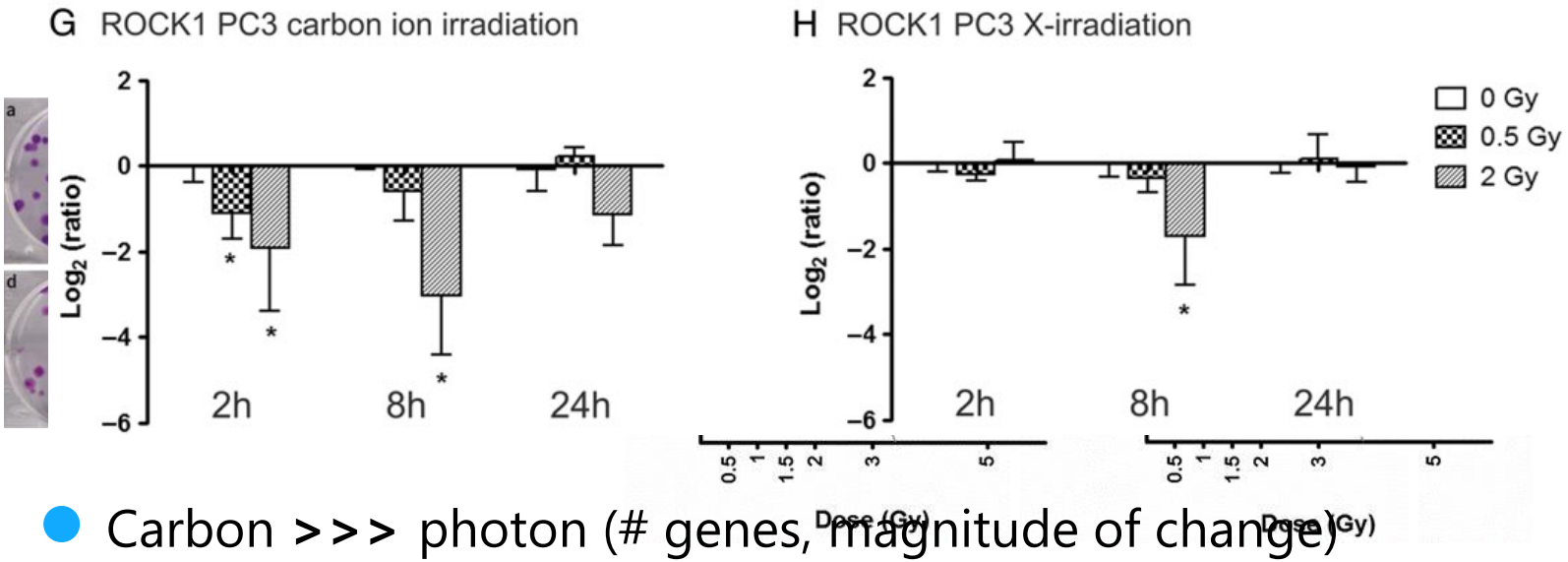


Suetens A., Moreels M et al. *Int J Onc, 2014; (44):1056-72*

Journal of Radiation Research, 2015, 56, 11–21
doi: 10.1093/jrr/rru070 Advance Access Publication 4 September 2014

Dose- and time-dependent gene expression alterations in prostate and colon cancer cells after *in vitro* exposure to carbon ion and X-irradiation

Annelies SUETENS[1,2], Marjan MOREELS[1], Roel QUINTENS[1], Els SOORS[1], Jasmine BUSET[1], Sabina CHIRIOTTI[2,3], Kevin TABURY[1], Vincent GREGOIRE[2] and Sarah BAATOUT[1,4,*]



- Carbon >>> photon (# genes, magnitude of change)

frontiers in Oncology

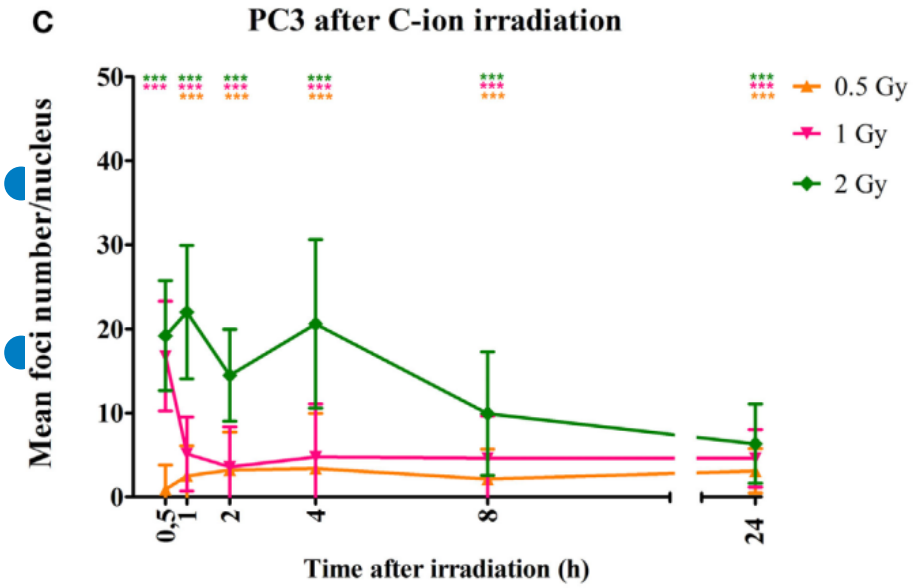
ORIGINAL RESEARCH
published: 13 April 2016
doi: 10.3389/fonc.2016.00087

Higher Initial DNA Damage and Persistent Cell Cycle Arrest after Carbon Ion Irradiation Compared to X-irradiation in Prostate and Colon Cancer Cells

OPEN ACCESS

Edited by:
Marco Durante

Annelies Suetens[1,2†], Katrien Konings[1,3†], Marjan Moreels[1*], Roel Quintens[1], Mieke Verslegers[1], Els Soors[1], Kevin Tabury[1], Vincent Grégoire[2] and Sarah Baatout[1]



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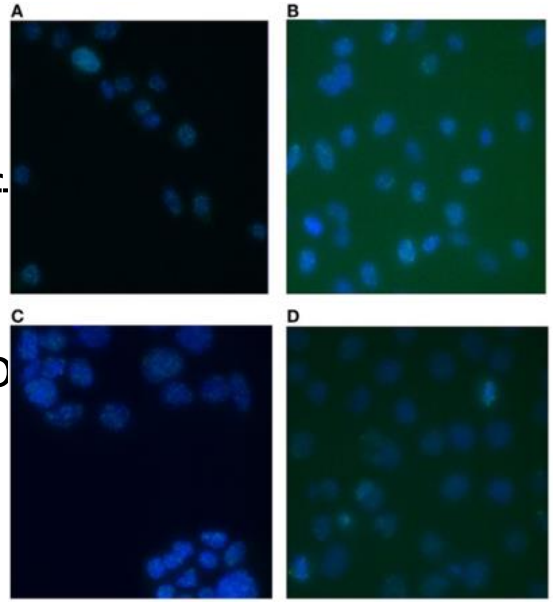
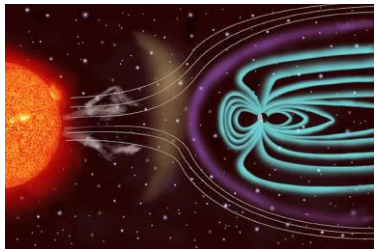
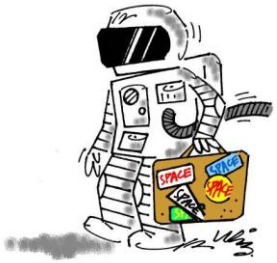


Ongoing Work & Outlook

- Data analysis of previous GANIL experiment
- iThemba LABS - proton beam time (April 2017)
  - Lab of Prof Dr J. Slabbert – Charlotte Vandevoorde
  - Compare photon – proton – carbon
- Knowledge relevant for space research (high-LET particles)





Take home message

- Photon and particle irradiation differ in the manner in which energy is deposited in a cell, even at the same LET
- Particles show unique molecular and cellular responses
- Still much to learn related to the biological effects
  - Beam time for radiobiological experiments is often limited
- Ultimately, the obtained knowledge will be important for both radiotherapy and radiation protection communities.

Acknowledgements

SCK•CEN (Mol, Belgium)

- Ms Katrien Konings
- Dr Annelies Suetens
- Ms Sabina Chiriotti
- Mr Kevin Tabury
- Ms Arlette Michaux
- Dr Emiliano d'Agostino
- Dr Roel Quintens
- Prof Dr Sarah Baatout

Lab of Experimental Radiotherapy (KU Leuven, Belgium)

- Prof Dr Karin Haustermans
- Dr Sofie Isebaert
- Ms Annelies Gonissen

Radiation Oncology Department (UCL, Belgium)

- Prof Dr Vincent Grégoire

GANIL (Caen, France)

- Dr A. Cassimi
- Dr Y. Saintigny
- Dr F. Durantel

federale overheidsdienst
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VEILIGHEID VAN DE VOEDSELKETEN
EN LEEFMILIEU

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