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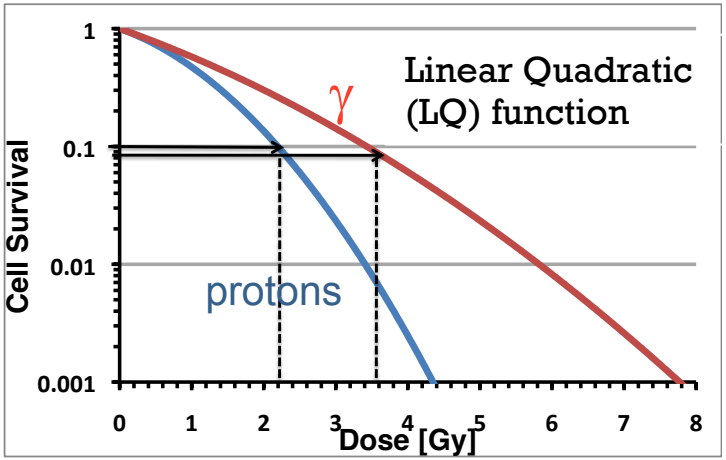
THE NEXT GENERATION OF RADIOBIOLOGY EXPERIMENTS

Content

1. Why we (still) need Radiobiological experiments
2. What we have learned from previous experiments
3. Rationale for new experiments
4. Radiobiological experiments: the next generation

The concept of RBE…
(Relative Biological Effectiveness)

In-vitro radiobiology



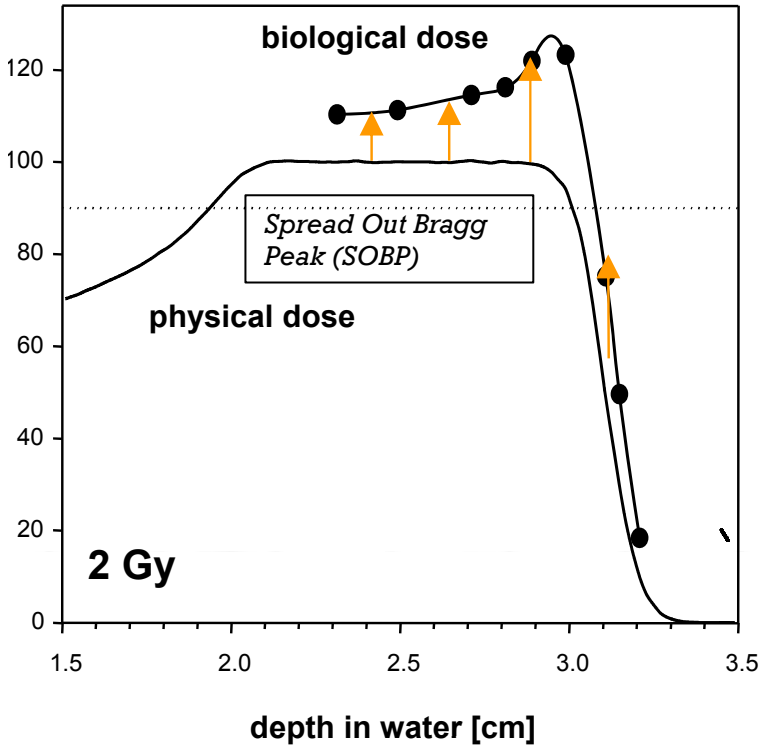
$$RBE = \frac{D}{D_{protons}} \langle effect \rangle$$

- Based on the *clonogenic assay*:
  - Growing cells in the incubator;
  - Counting them (density);
  - Plating them;
  - Irradiating them;
  - Re-plating them;
  - Leaving them in the incubator (for approx. 2 weeks) to grow further;
  - Counting the number of cells which have generated colonies (visually);
- Repeating the process for different dose levels

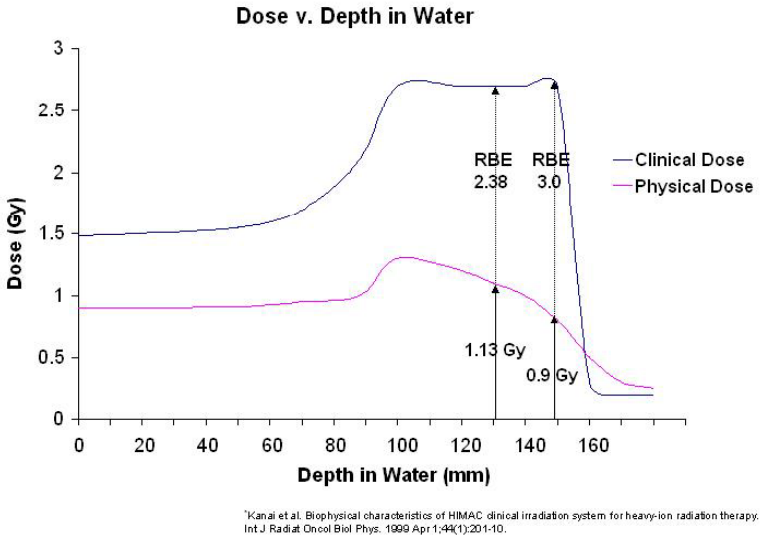
N.A.P. Franken, H.M. Rodermond, J. S, J. Haveman and C. van Bree, Clonogenic assay of cells in vitro, Nature Protocols, Vol.1, No.5 2006, pp. 2315-19.

… and its implications for treatments…

RBE effect for protons



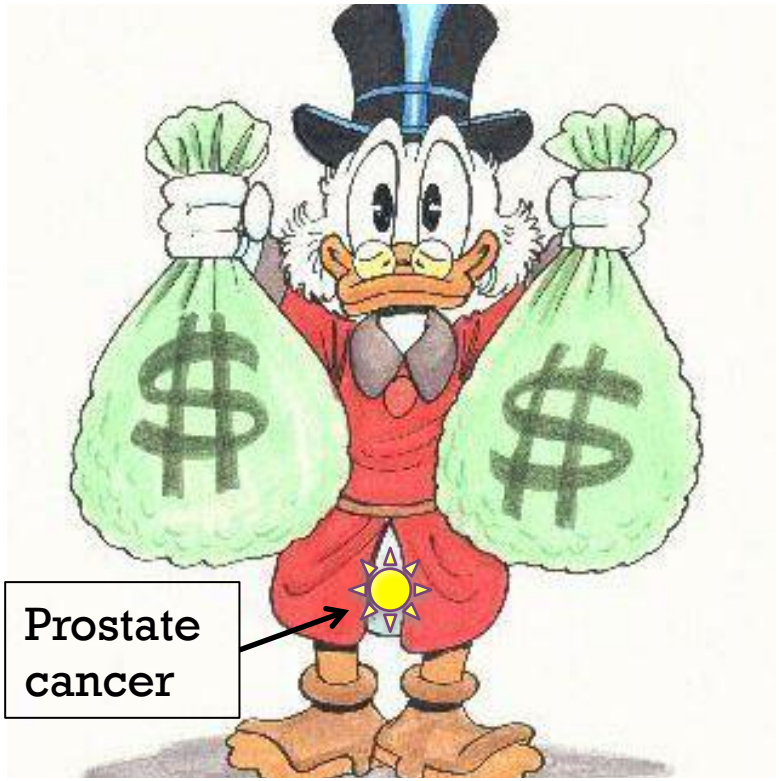
Example of flat SOBP for C-12



*Kanai et al. Biophysical characteristics of HIMAC clinical irradiation system for heavy-ion radiation therapy. Int J Radiat Oncol Biol Phys. 1999 Apr 1;44(1):201-10.

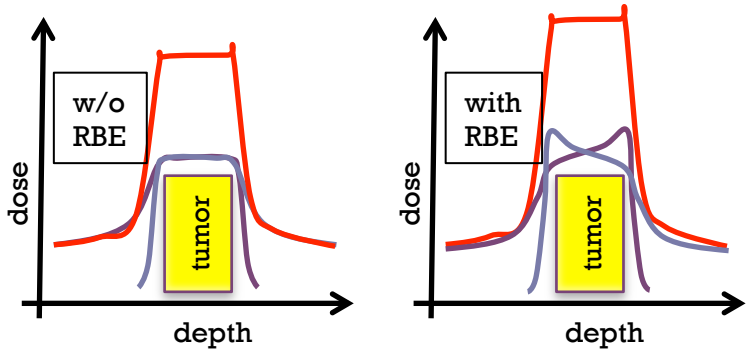
… with some exceptions

Ideal Proton Therapy Patient in the US



Treatment Modality

- 2 opposite fields:



- RBE effect is practically cancelled due to field compensation!
- Unfortunately not every case is as simple as this one…

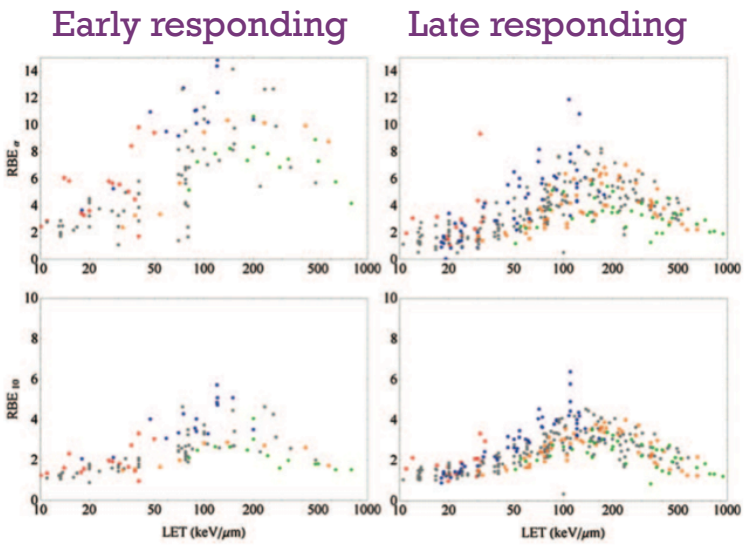
The PIDE*

(Particle Irradiation Data Ensemble)

What is it?

- It's a database containing results of more than 800 cell survival experiments from different laboratories all over the world, using different cell types and different ions at various energies.
- It only includes publications for which the LQ parameters of the response to photons as reference radiation were available or derivable

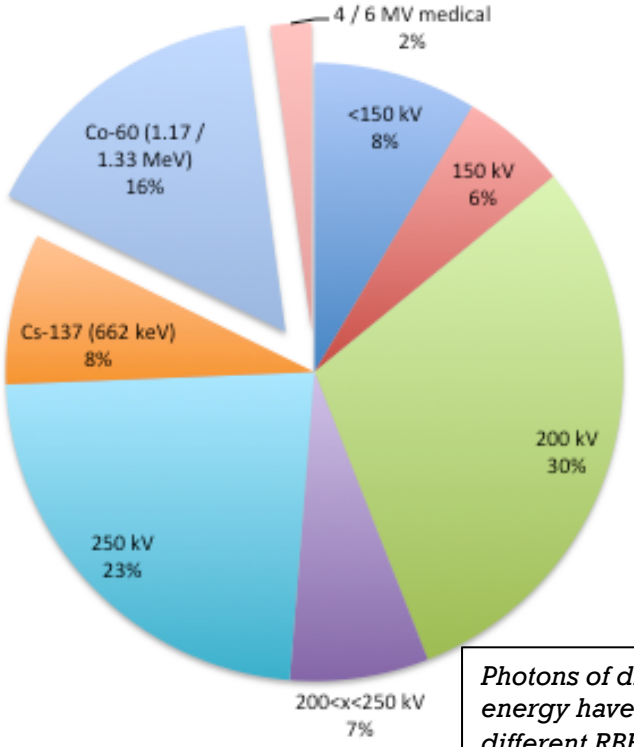
Overview of the results…



* T. Friedrich, U. Scholz, T. Elsässer, M. Durante and M. Scholz, Systematic analysis of RBE and related quantities using a database of cell survival experiments with ion beam irradiation, *Journal of Radiation Research*, 2012, pp 1–21

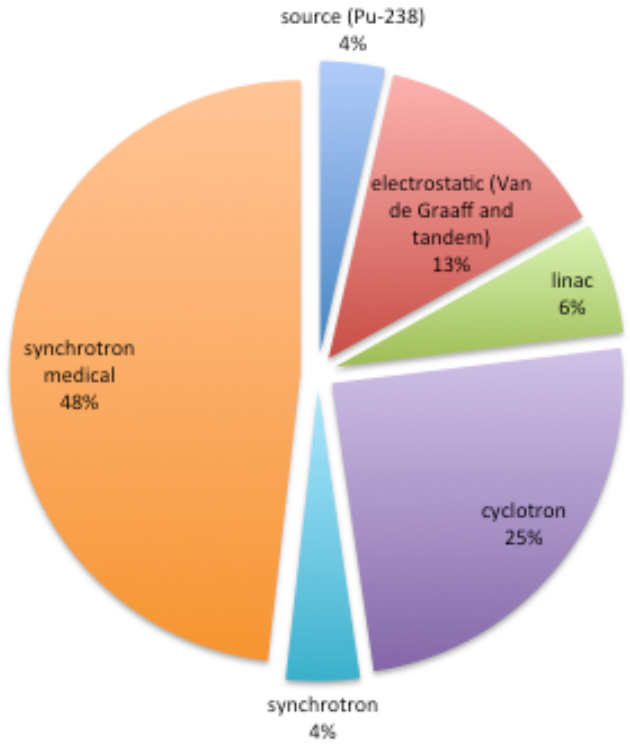
Statistics about source of radiation in PIDE…

Photons



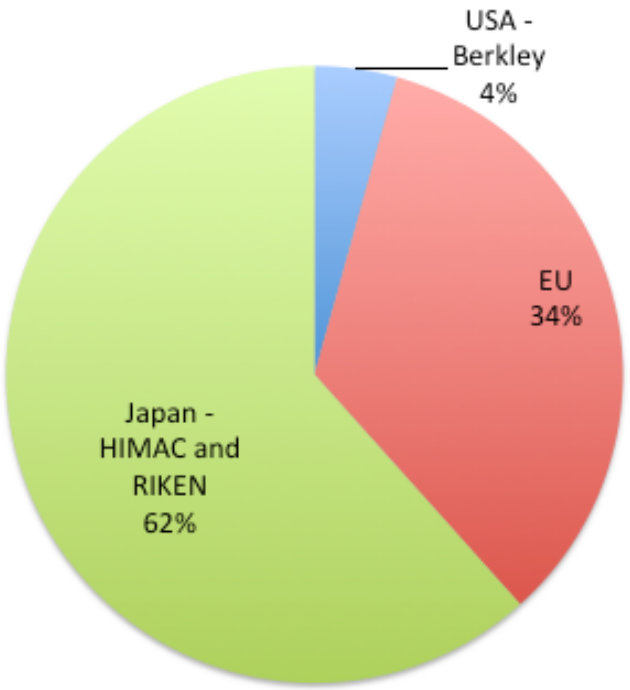
Photons of different energy have different RBE

Ions

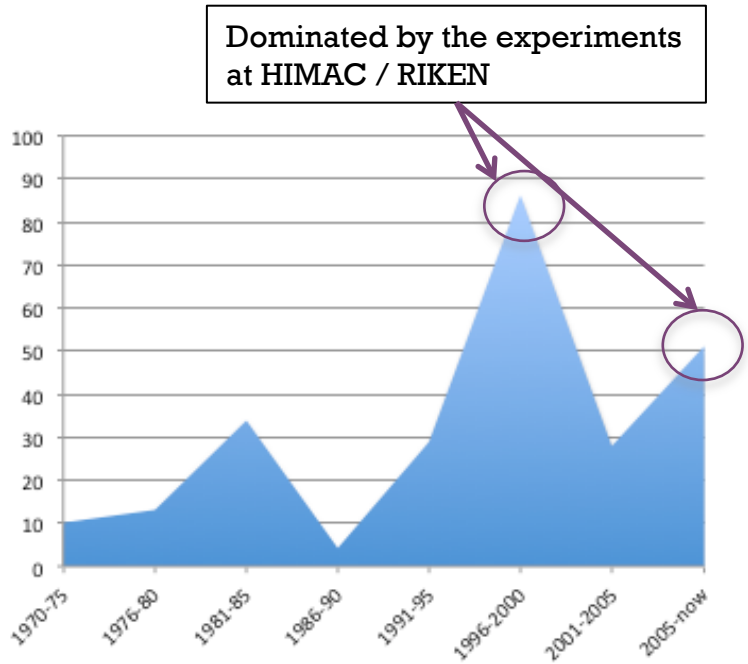


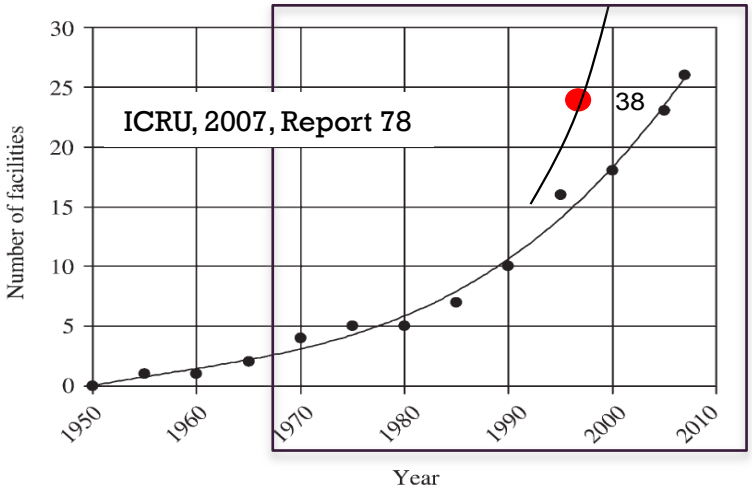
… and region and year

Region



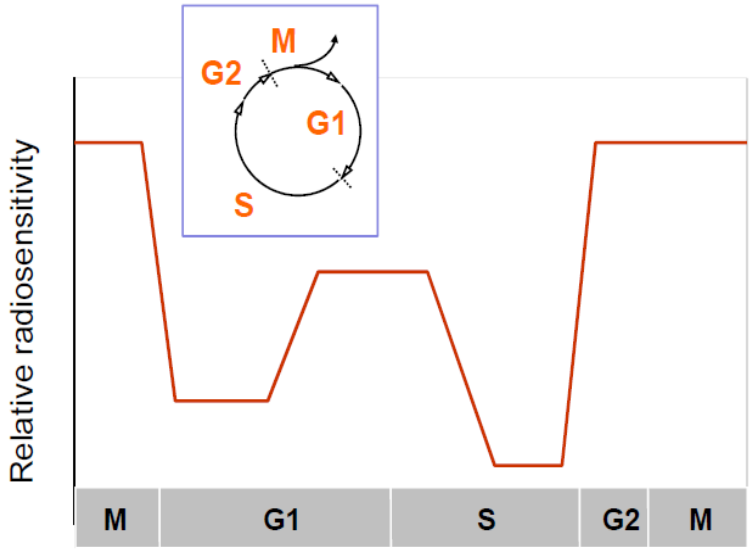
Year





Challenges (1/2): *Heterogeneities*

Cell cycle

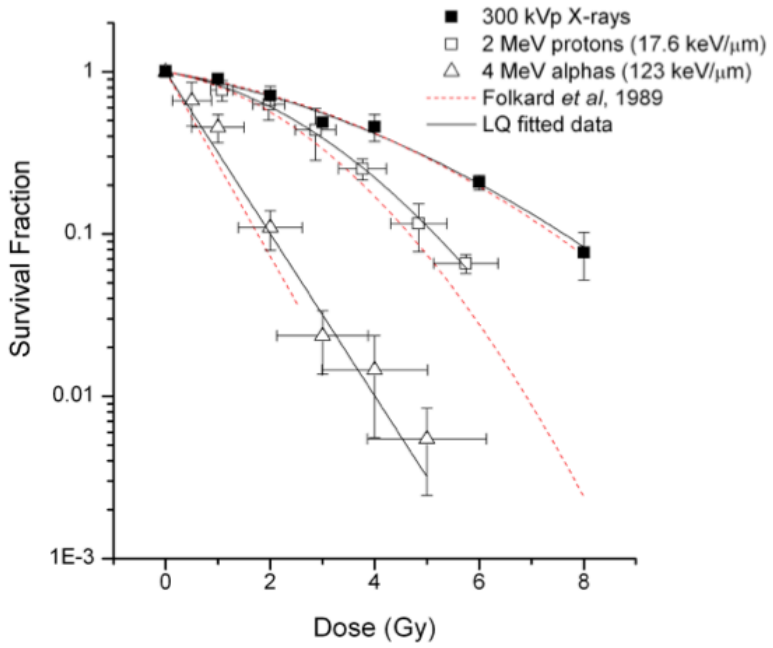


ESTRO Conference – W. Dörr

Types of cells

- 80 different cell lines investigated. The same cell line may behave differently depending on experimental factors or age of the cell line.
- 44% human, 56% rodent
- 21% cancer, 79% normal

Challenges (2/2):
Dosimetry and Statistics



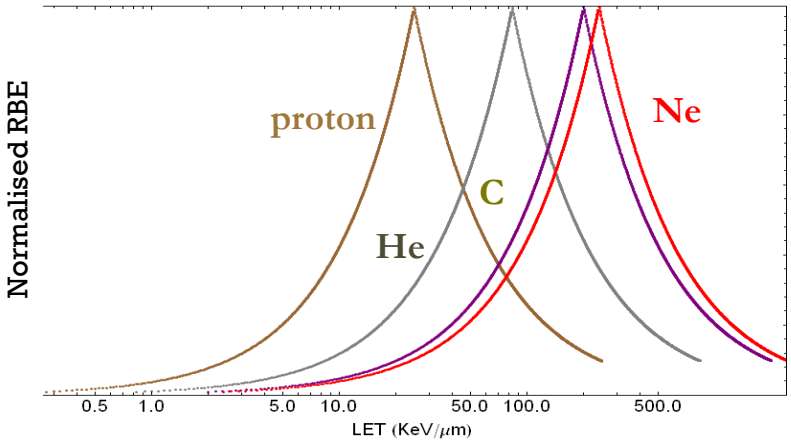
J.C.G. Jeynes, *et al.*, High throughput hadron irradiation of mammalian cells using a vertical facility, Radiation and Environmental Biophysics, 0301-634X, 2013.

- Experimental data must be fitted with the LQ function
- Data show big error bars:
  - Hor.: *dosimetry*. The dose can be measured directly using RadioChromic Films previously calibrated for a specific LET or counting the number of particles and estimating the LET;
  - Ver.: *statistics*. The number of cells per sample which can be easily counted is approx. 50, the number of samples is limited to maintain the same experimental conditions throughout the whole curve.

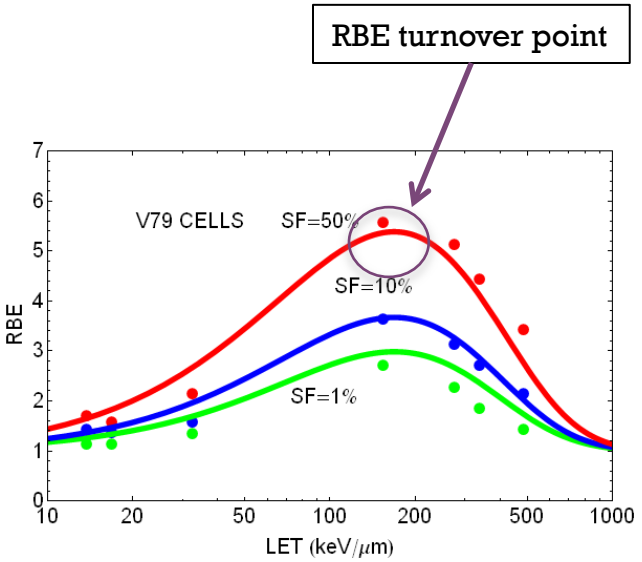
What have we learned from those experiments?

The RBE value depends:

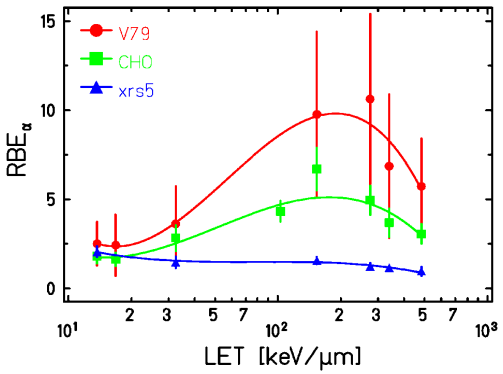
- On the dose level (survival fraction);
- On the cell type;
- On the mass and energy of the particles (LET value).

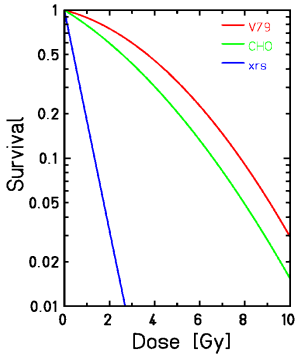


B. Jones, Preliminary analysis on PIDE data



W. Weyrather *et al.*, IJRB 1999; **75:**1357–64.





New generation of Radiobiological Experiments

Must have

- Experiments set up to prove a specific aspect of the RBE model, maintaining most of the parameters fixed
- Large database of response upon variation of all parameters
- Optimisation of experimental conditions

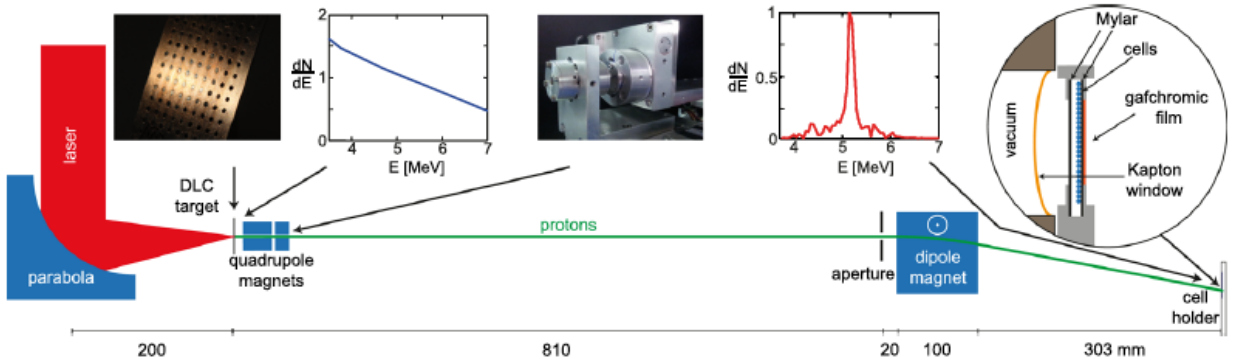
This can lead to only one solution:

- Accelerator totally dedicated to these experiments, and
- Located close or in the radiobiology departments, same as the photon irradiators

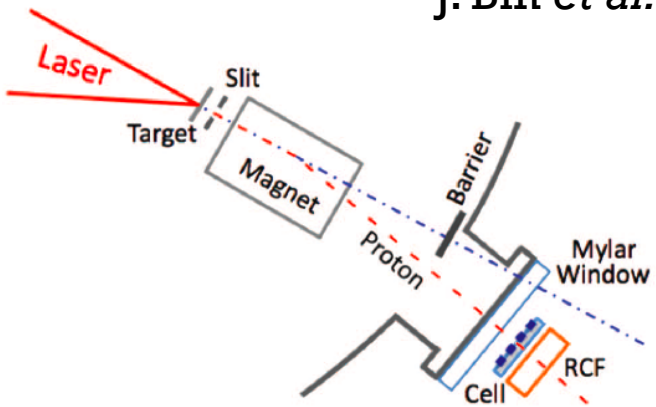
Possible solution

- A table-top (around 10 m^2) multi-TW Ti : Sapphire laser system:
  - Femtoseconds pulse length
  - Power density of ~10^{19} W/cm^2
  - Spot size of a few microns
  - Solid targets ~10 um thick
- Why? Because:
  - "Standard" equipment for the plasma groups working on laser-plasma particle acceleration
  - Strong interest from the community in developing such systems for various applications
  - Starting with a "medical" application could facilitate its development towards a proper particle therapy facility
  - 10 MeV protons are already available

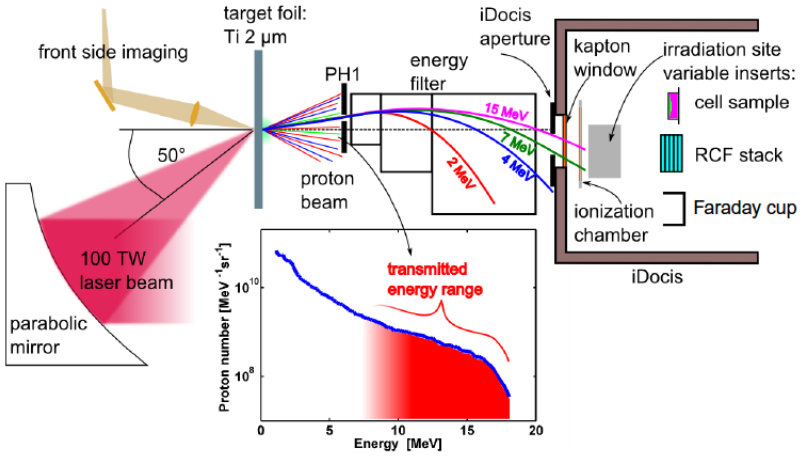
Radiobiological experiments with laser accelerated protons



J. Bin *et al.*, Munich (2012)

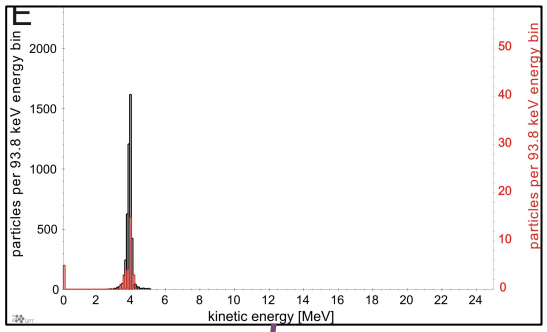


D. Doria *et al.*, Belfast (2012)

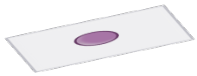


S.D. Kraft *et al.*, Dresden (2010)

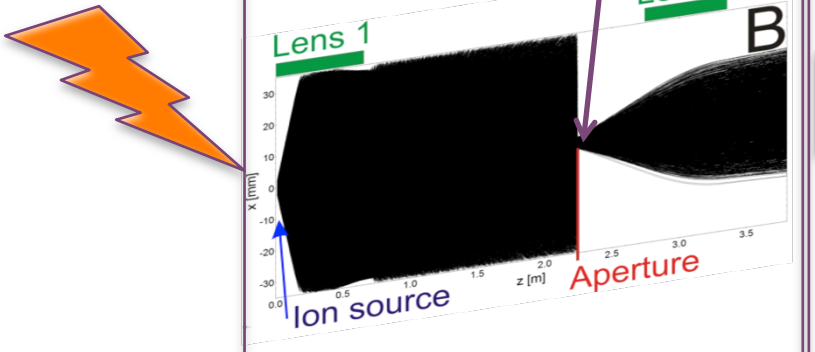
Proposal of Imperial College



cells



Ti-Sapphire laser



2 Gabor lenses

Permanent magnets 90 deg FFAG bend

Come to see our posters:

THPSM10
THPSM11
THPSM12
THPSM13

Thank you!

Patients who benefit most from hadron therapy

Acknowledgments

- Henry Tsang and Hugo Larose (UG students at Imperial College) for their hard work during a very hot summer
- Prof B. Jones (Oxford) for the fruitful discussions and material
- The CRUK centre in Hammersmith for their financial support