Introduction to Proton Therapy

JAI Octoberfest, 3rd October 2014

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The Particle Therapy Cancer Research Institute is a member of OXFORDMARTIN SCHOOL

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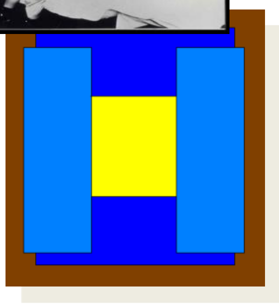
Introduction to Radiotherapy and Proton Therapy

The Evolution of External Beam Radiation Therapy

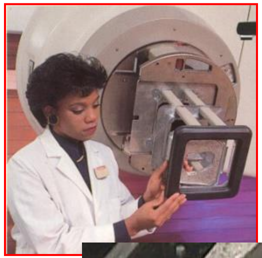
1950's

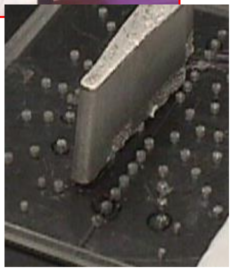
The First Cobalt Therapy Unit and Clinac



Standard Collimator

1970's

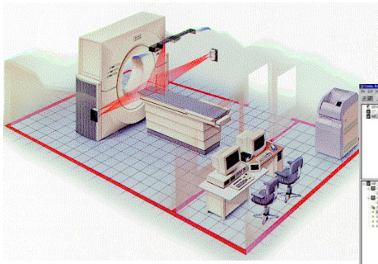


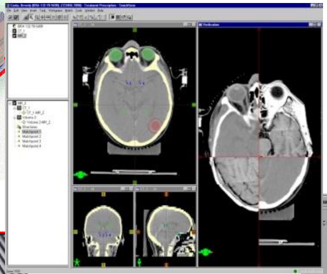


Cerrobend Blocks
Electron Therapy

1980's

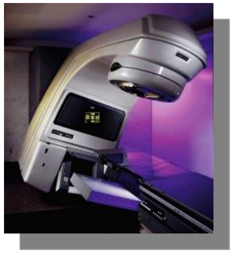
Computerized 3D CT Treatment Planning

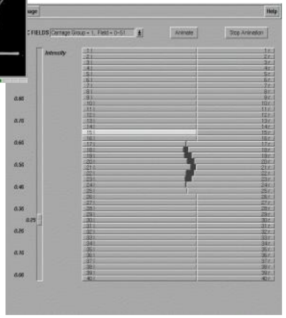




Multileaf Collimator

1990's

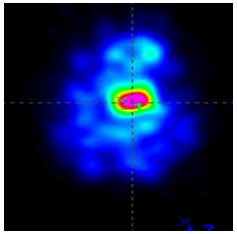




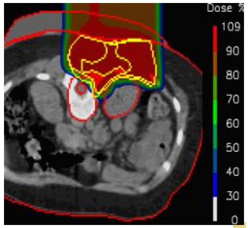
Dynamic MLC and IMRT

High resolution IGRT

2000's?



Functional Imaging



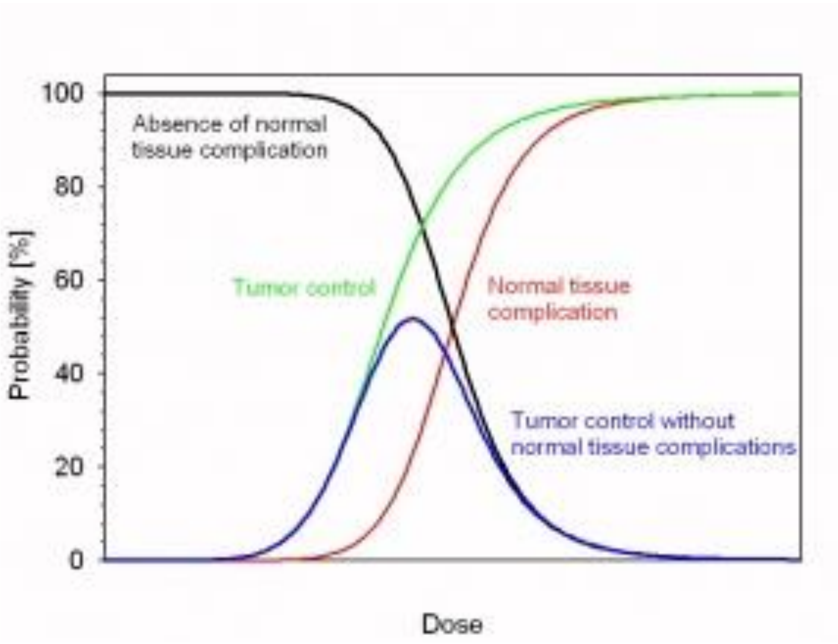
Particle Therapy

Slide courtesy of Prof. Gillies McKenna

Goal of RT

Maximise Tumour Dose

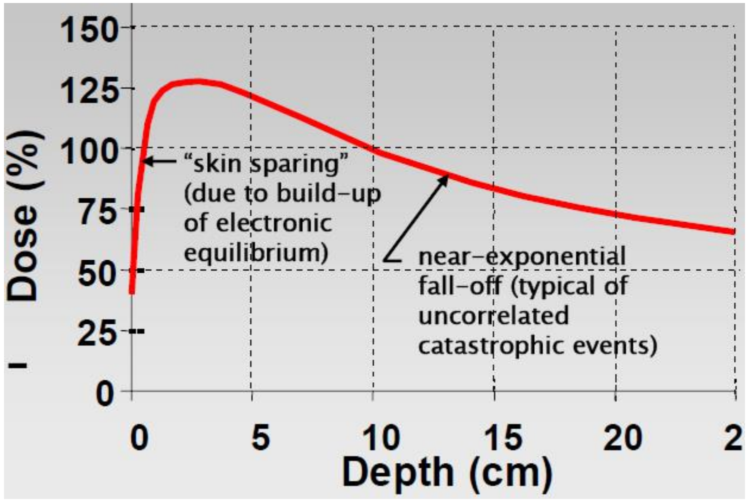
Minimise Normal Tissue Dose



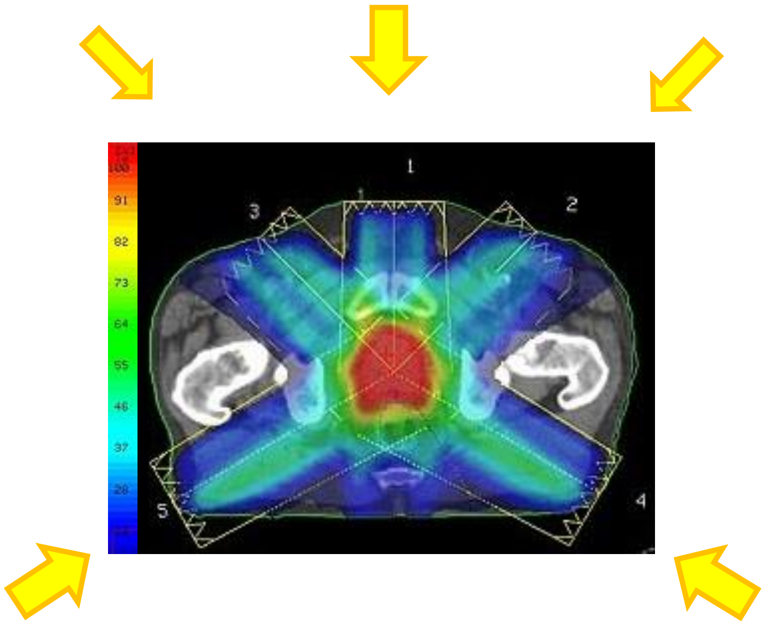
- **Radiation Induced Toxicity:**
  - **Central Nervous System:** blindness, deafness, paralysis, confusion, dementia
  - **Bowel:** colostomy, chronic bleeding.
  - **Lung:** shortness of breath, pneumonias
  - **Kidney:** renal failure and hypertension
  - **Reproductive organs:** sterility
  - **Everywhere:** severe scarring in medium to high dose regions, possible increase in induced cancers in low-medium dose regions

Photons/X-rays dose deposition

Depth-dose curve – single beam



RT dose plan – multiple beams beam



Multiple Beams:

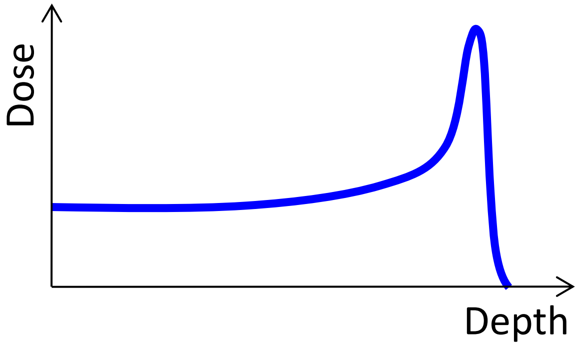
- Reduced dose to organs at risk
  - Fewer complications
- Increased tumour dose
  - Higher probability of tumour control
- However:
  - Large volumes of low-intermediate dose

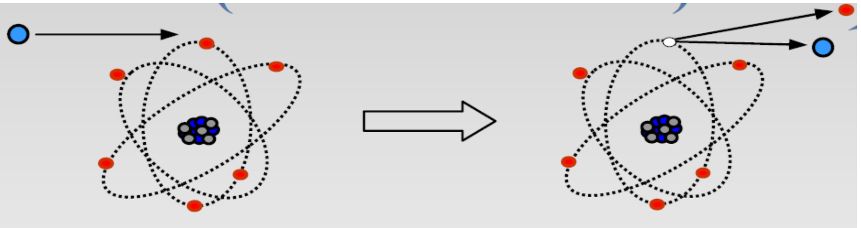
History of Proton Therapy

- 1946: Therapy proposed - Robert R. Wilson, Harvard Physics
- 1955: 1^{st} Proton Therapy - Lawrence Tobias University of California, Berkeley
- 1955-73: Single dose irradiation of benign CNS lesions - Uppsala, MGH, St Petersburg, Moscow

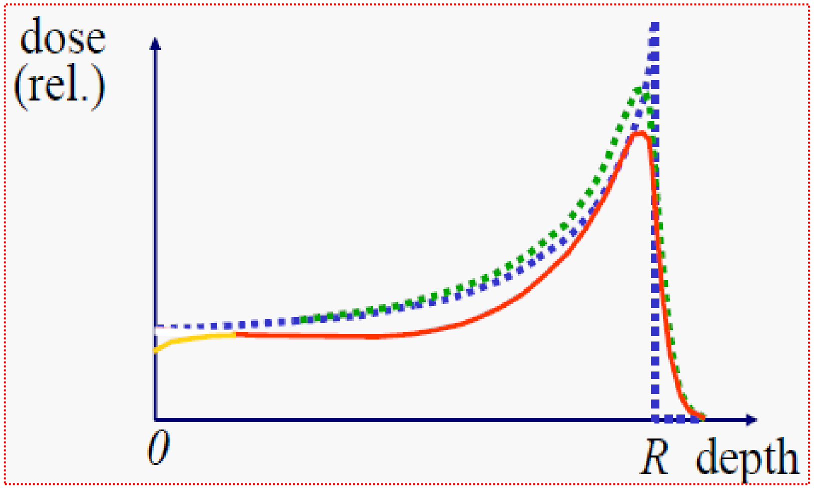
The Bragg Peak

- Components of the proton depth dose curve:
  - – Bethe-Bloch formula
    - Coulomb interactions with atomic electrons
  - – Scattering, energy spread and interactions with atomic nuclei

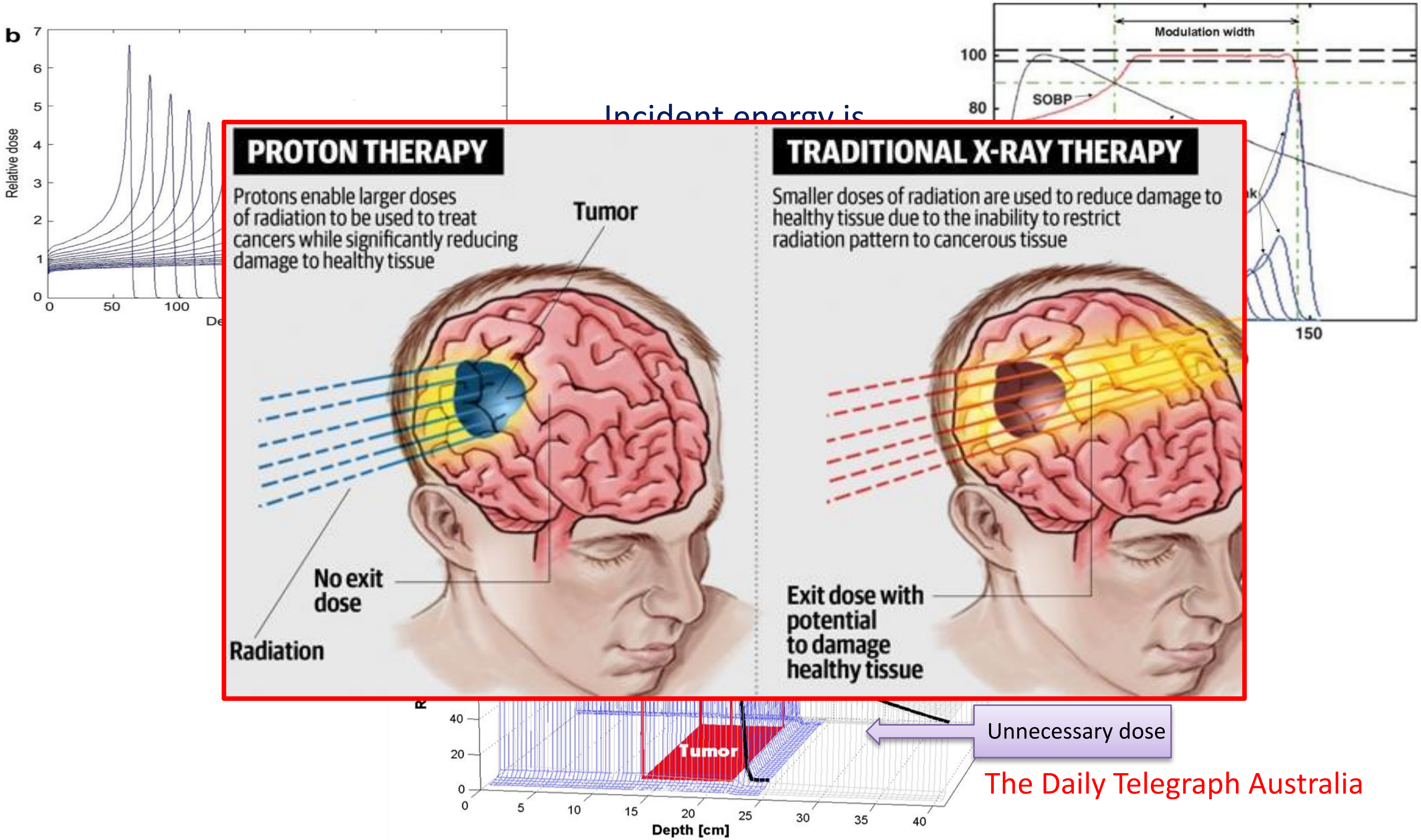




Illustrations from M. Goitein "Radiation Oncology: A Physicist's-Eye View" © Springer, 2007

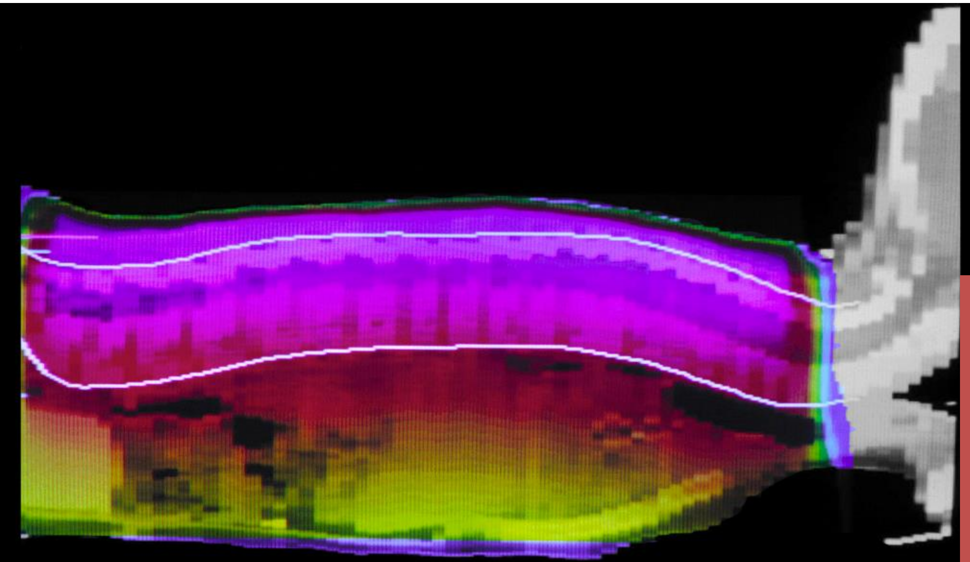


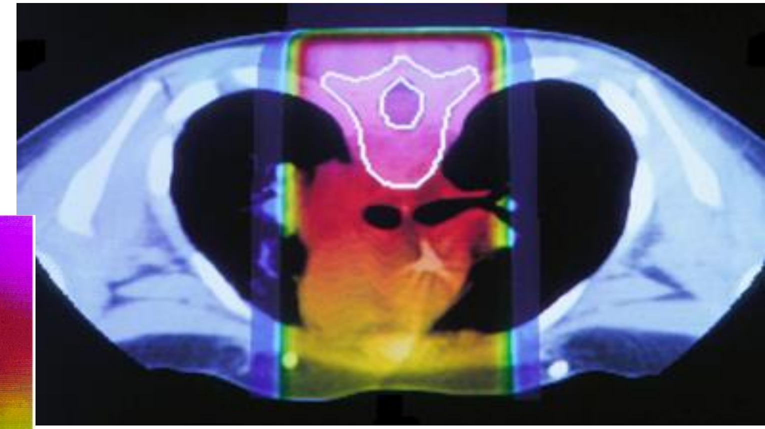
Proton dose deposition

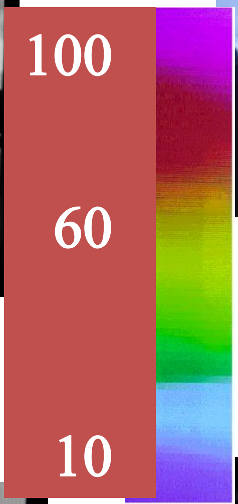


The Daily Telegraph Australia

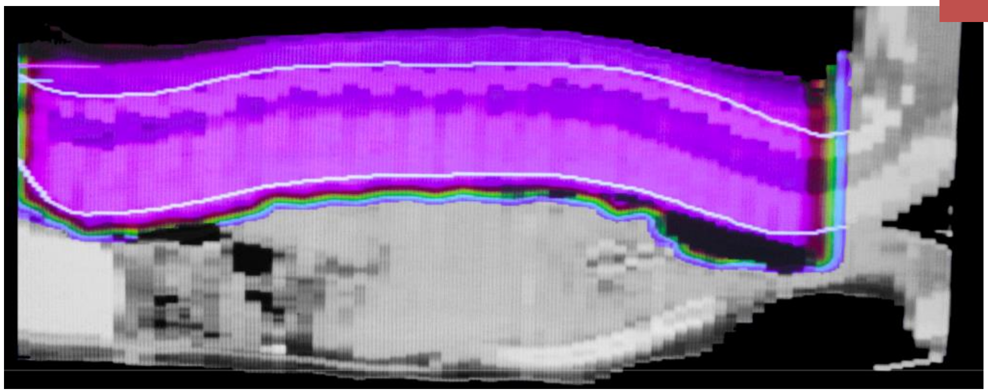
Medulloblastoma in a Child

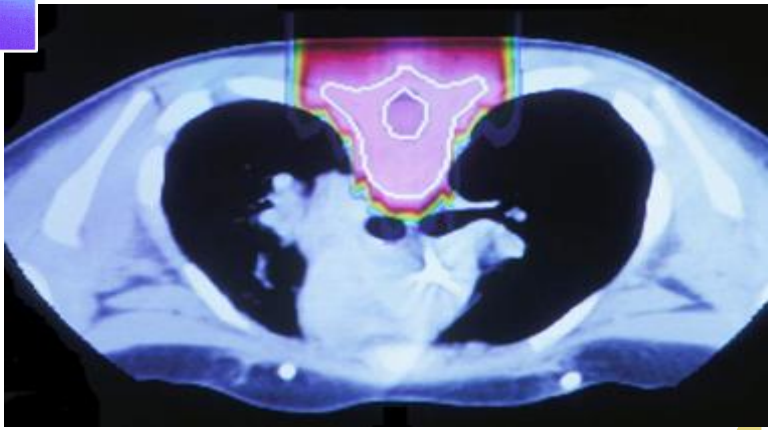






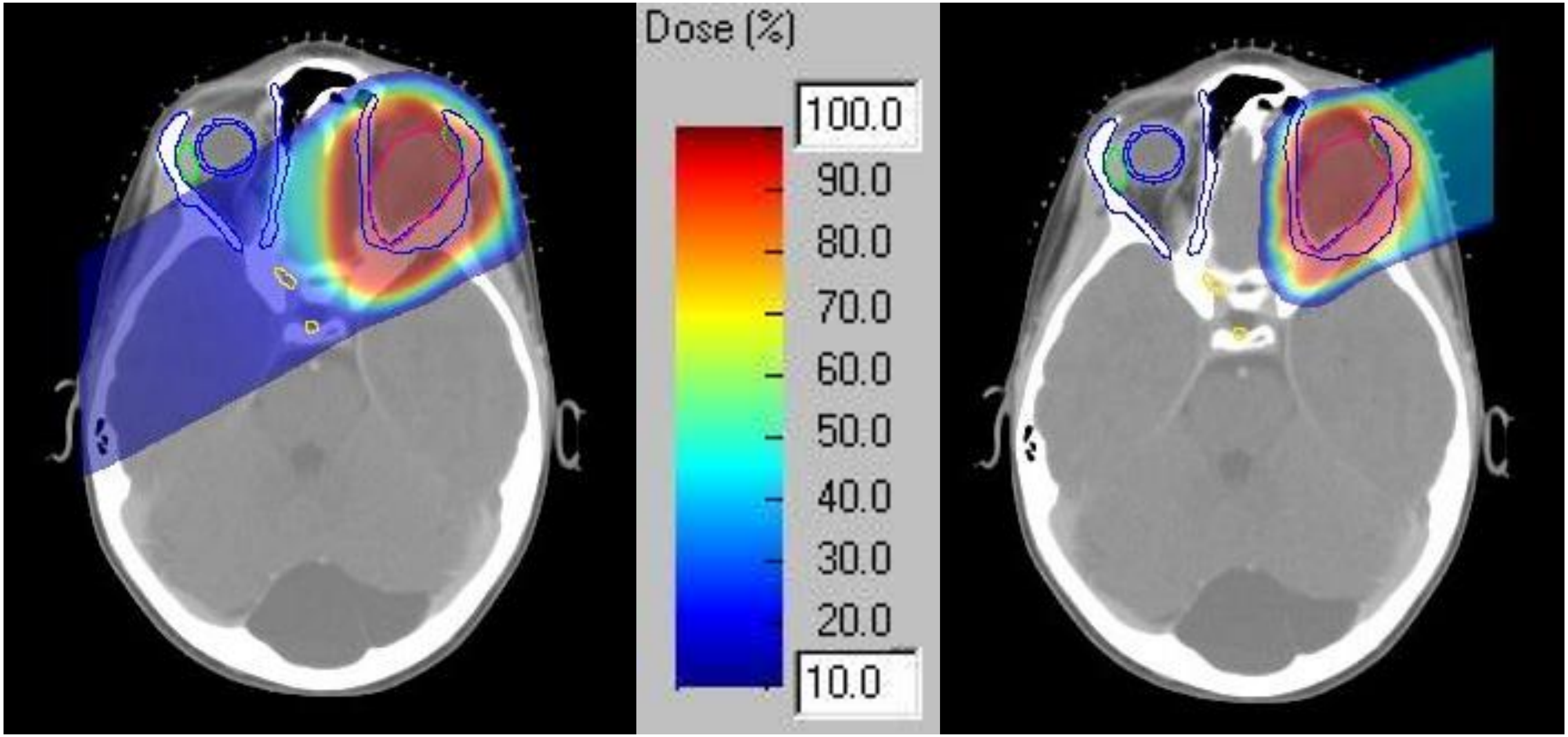
With X-rays





With Protons

Orbital Rhabdomyosarcoma



X-Rays

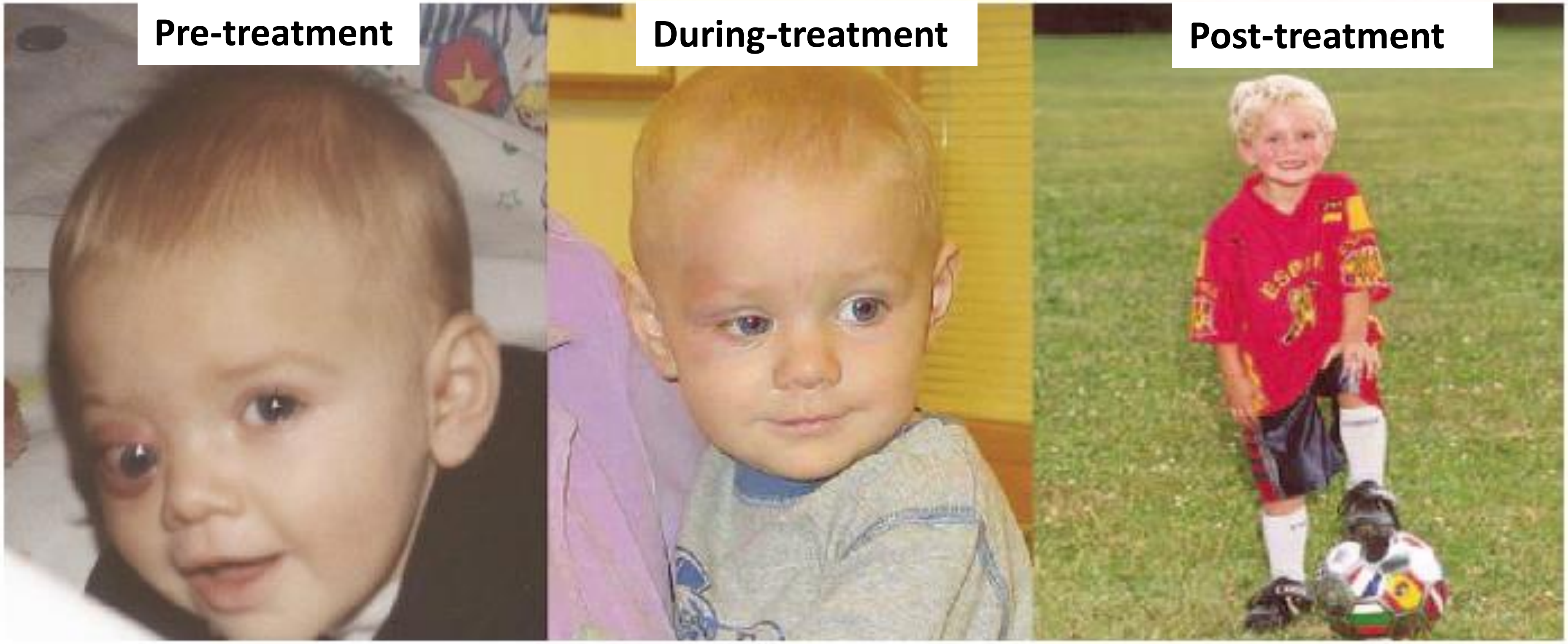
Protons/Ions

Courtesy T. Yock, N. Tarbell, J. Adams

Proton Therapy in Action

Anaplastic Ependymoma Brain Tumour

http://news.bbc.co.uk:80/1/hi/england/7784003.stm
http://news.bbc.co.uk/1/hi/england/7795909.stm
http://news.bbc.co.uk/1/hi/england/7906084.stm



CPC, Friedmann, NEJM, 350:494, 2004

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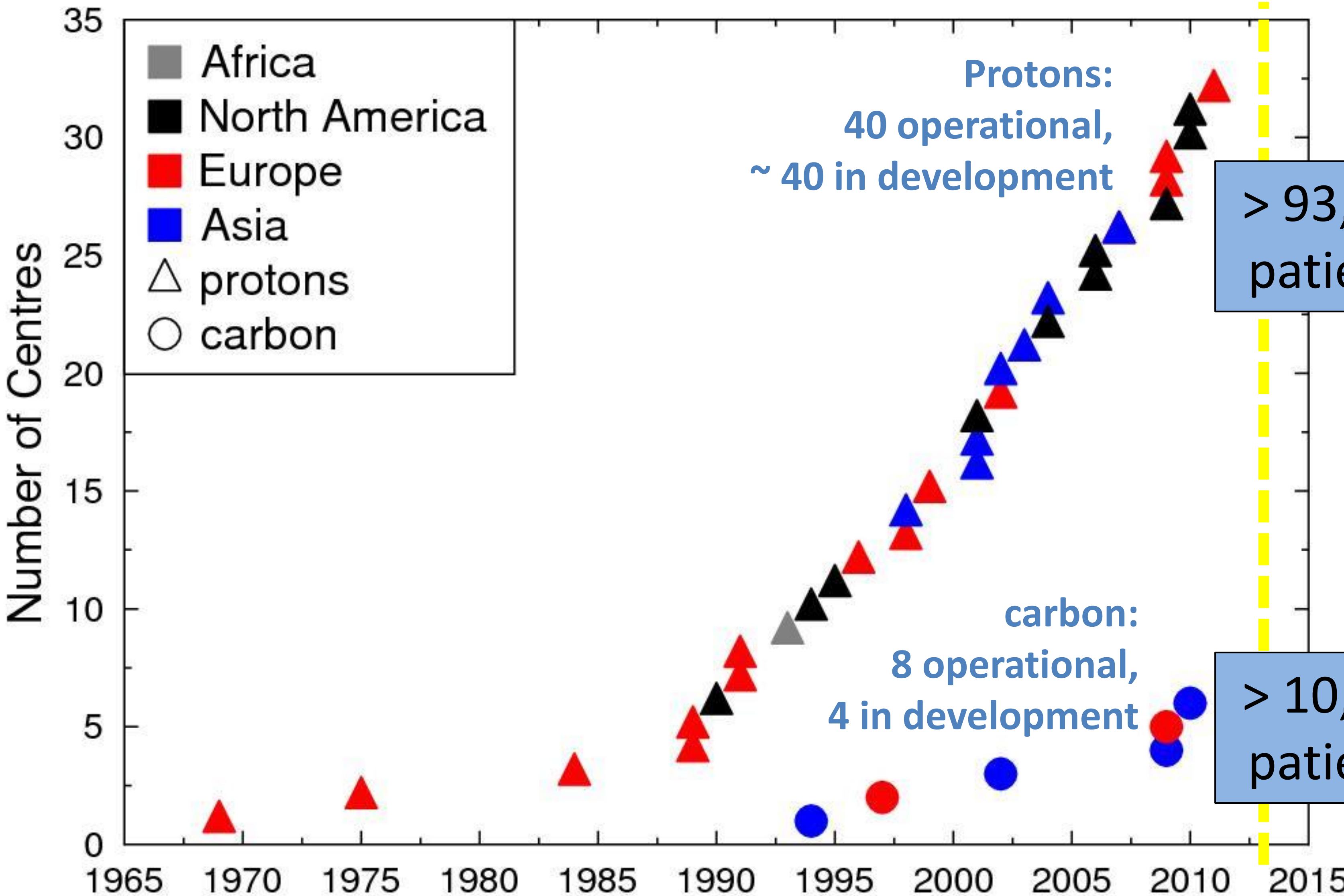
Number of treatment centres worldwide



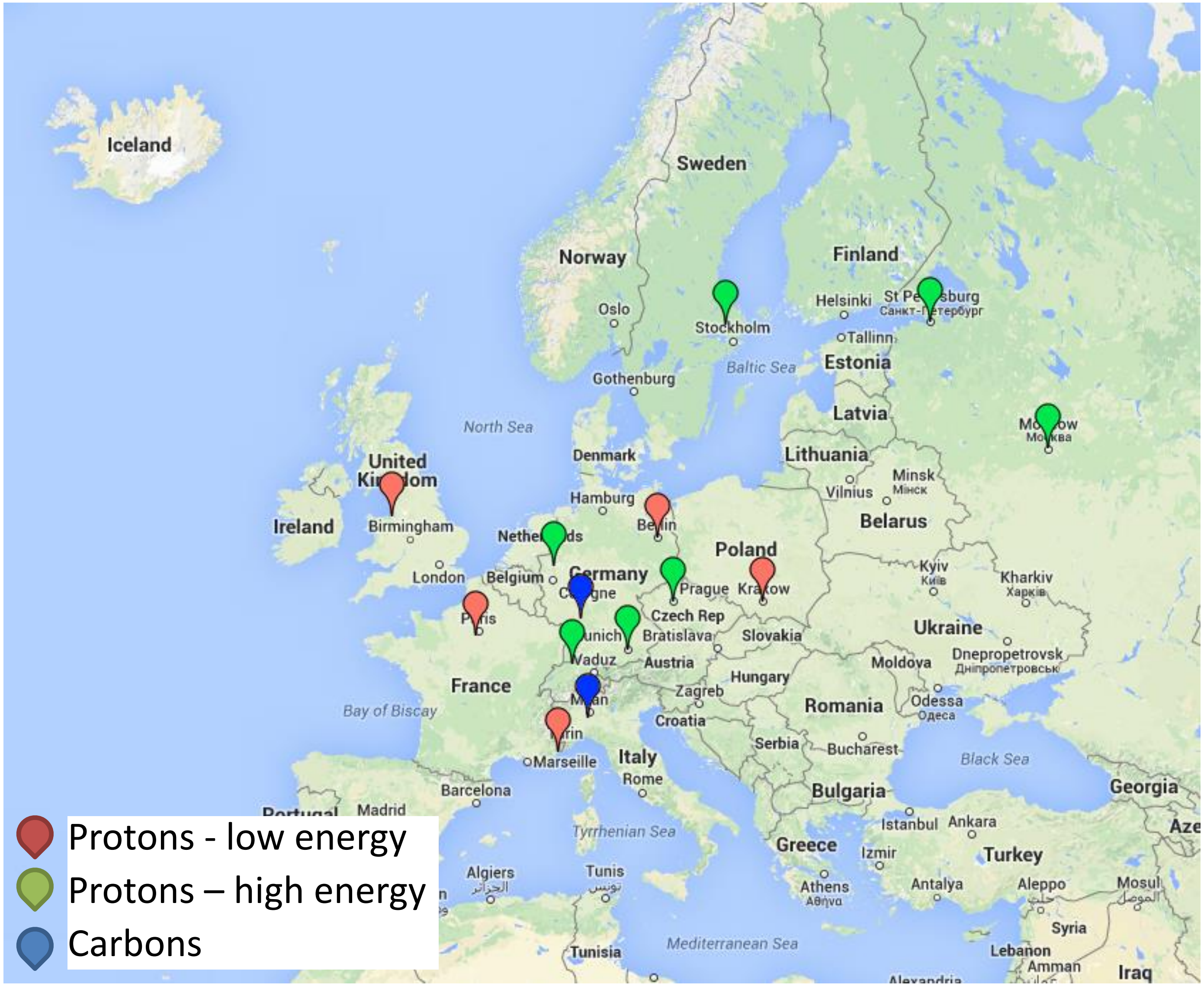
> 93,000 patients

> 10,000 patients

PTCRi

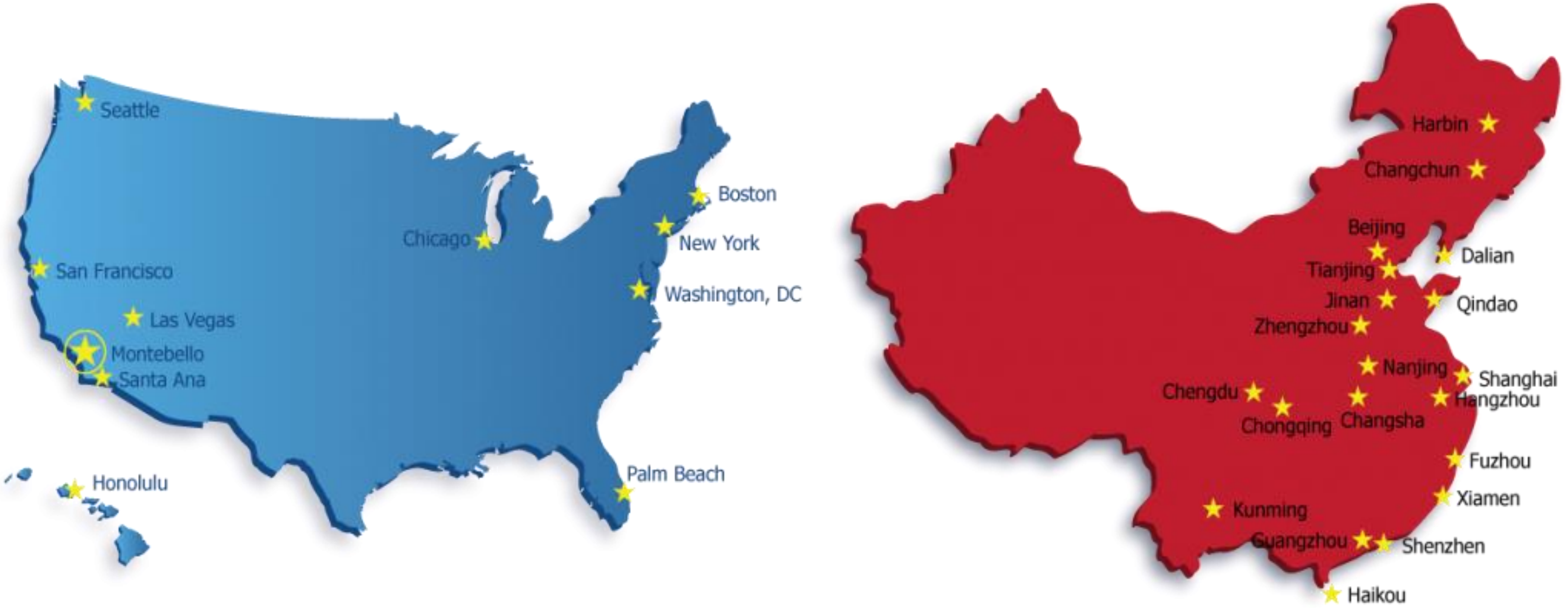
Proton Therapy Centre World Map

Proton Therapy Centre Europe Map



Many more in the planning stages….

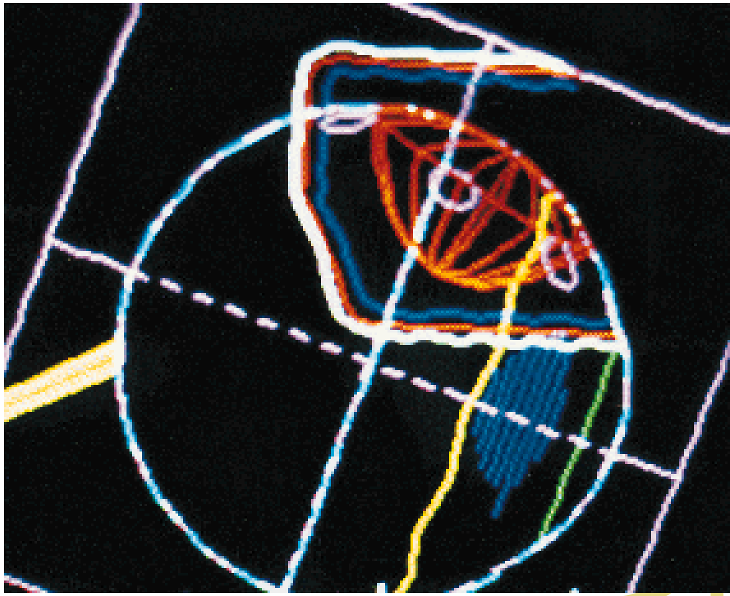
Planned Sites in US and China



Proton Therapy in UK

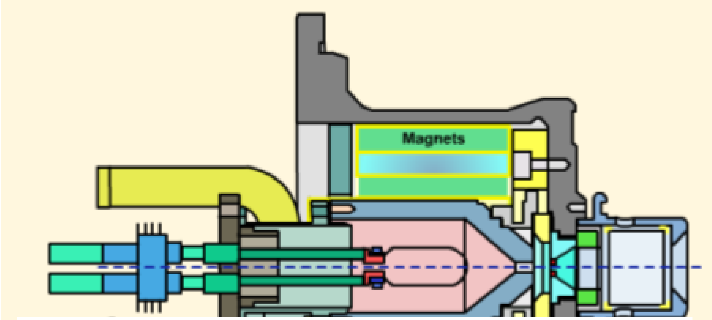
- Clatterbridge
  - 1989: First hospital based proton therapy at Clatterbridge, near Liverpool
  - ~2500 patients with ocular melanoma; local control ~97%.
  - Targets the cancer
  - Avoids key parts of eye (optic nerve, macula, lens)

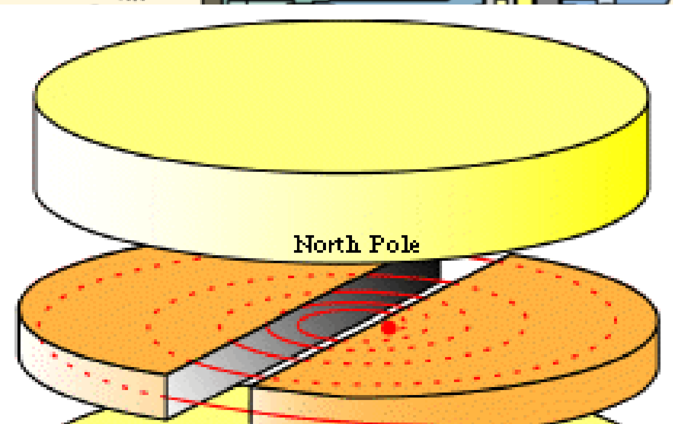
- Simon to talk about UCLH and Manchester….

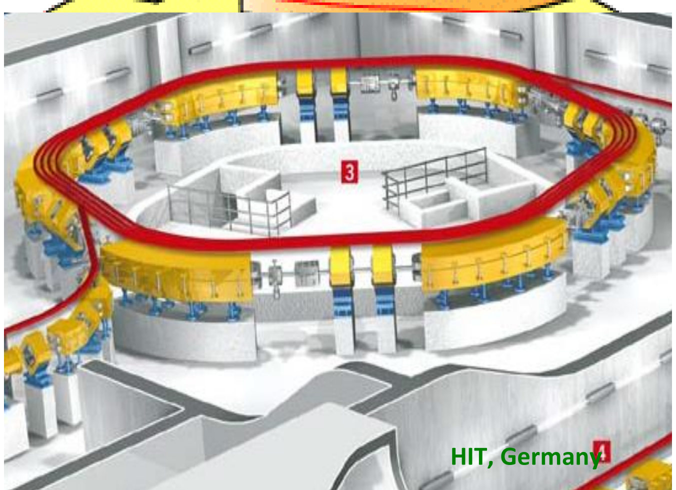


Production and Delivery of Medical Proton Beams

Beam Production and Acceleration







- Ion source
  - Plasma accelerated in electric field
- Acceleration
  - Cyclotron
    - Fixed magnetic field
    - Fixed energy
    - Constant frequency
  - Synchrotron
    - Fixed radius
    - Variable magnetic field
    - Synchronous frequency
  - Future accelerators that do the job better?

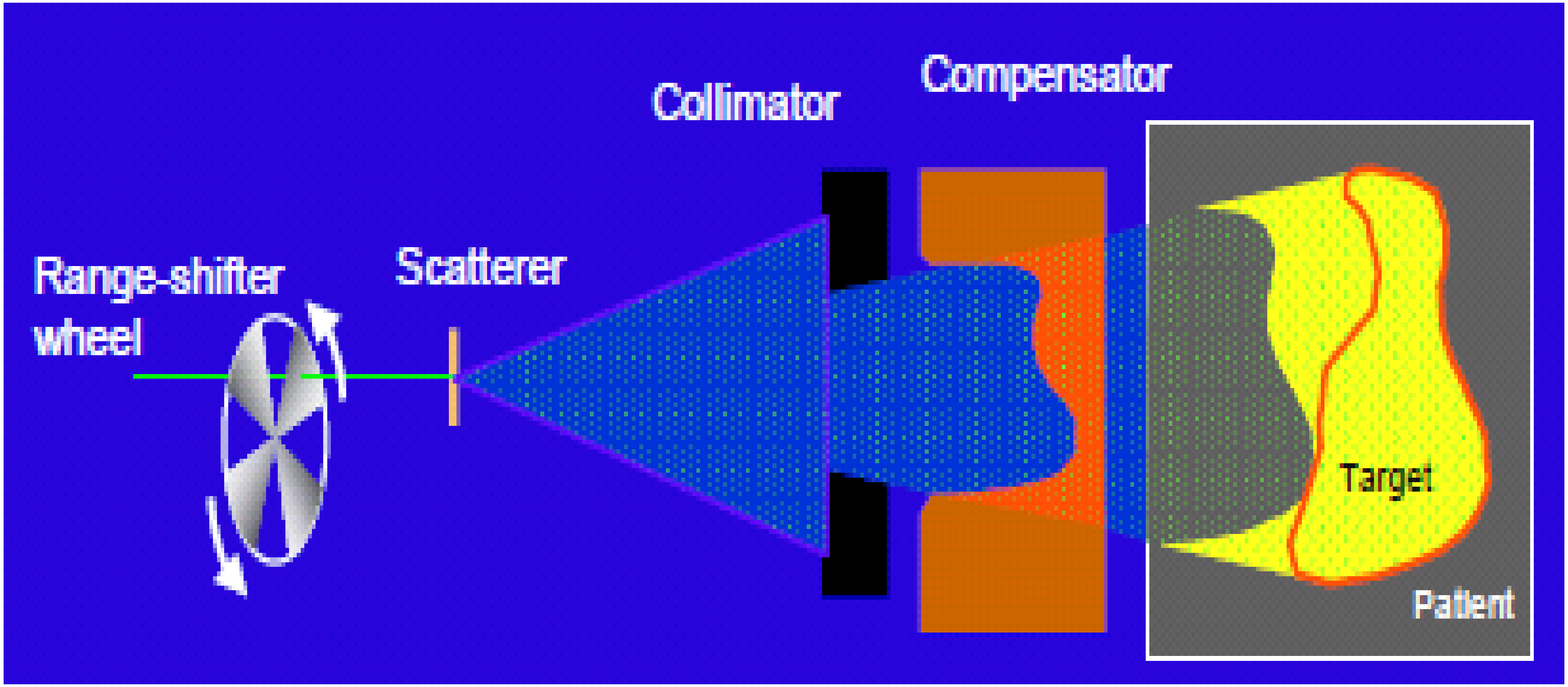
Beam Transport

- Gantries

- Fixed Beams

•Clinical Indications
•Flexibility
•Space
•Cost

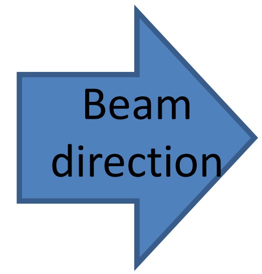
Beam Delivery - Scattering



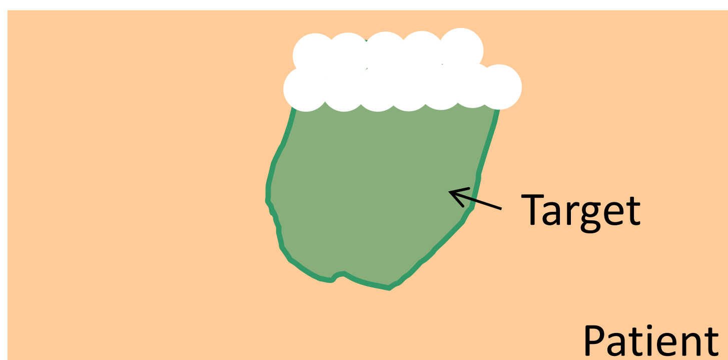
Courtesy of T. Lomax, PSI, Switzerland.

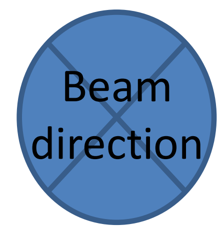
Beam Delivery - Scanning

Exploiting depth control



Exploiting charge





Some challenges in Proton Therapy

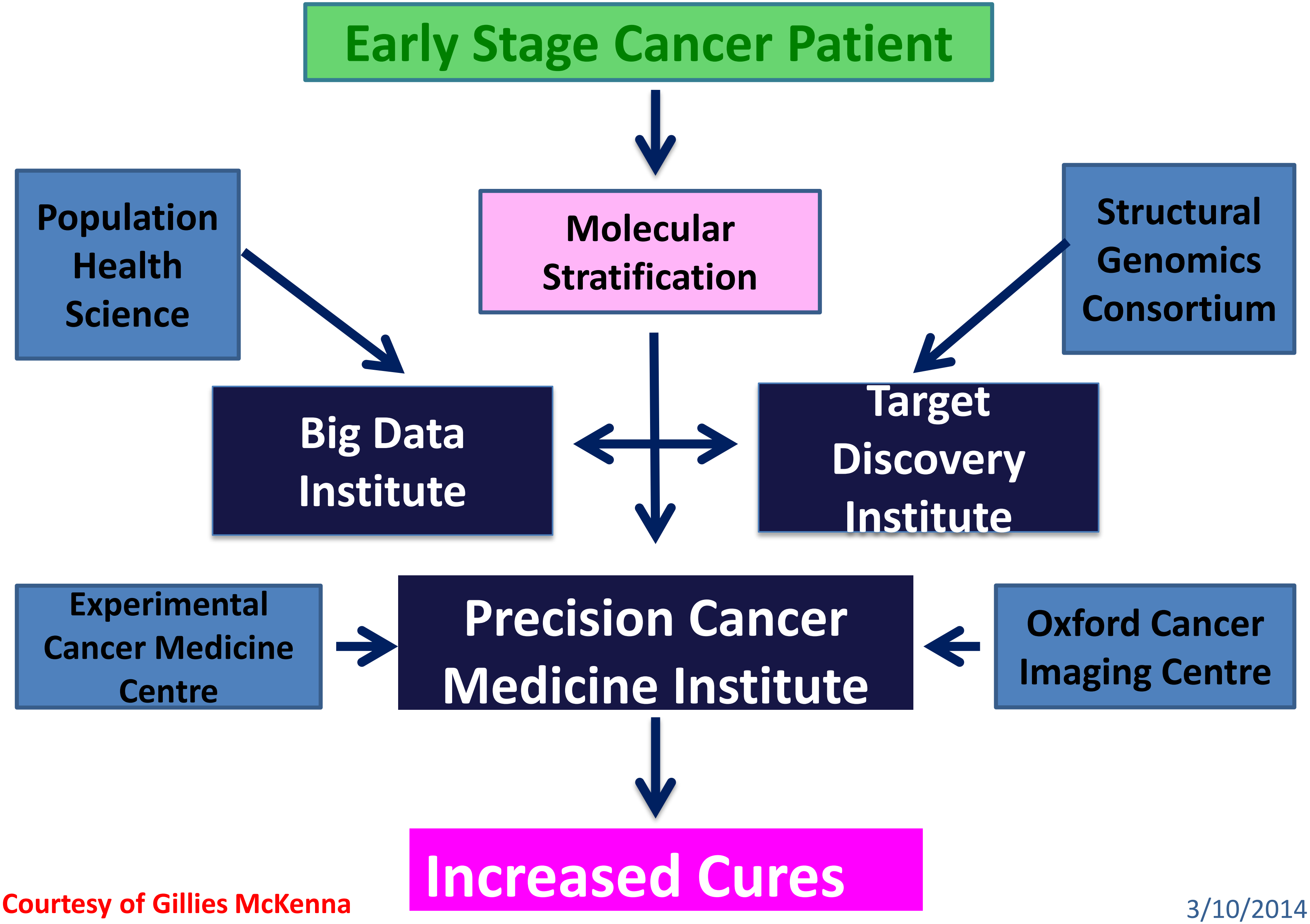
- Acceleration and Beam transport:
  - Faster spot scanning
  - More compact accelerators and gantries
  - Beam switching and splitting
- Uncertainty in planned vs. delivered dose:
  - Range uncertainties
  - Relative biological effectiveness
- Treatment delivery
  - Organ motion
  - Hypo-fractionation
- Which clinical indications?
  - Cost-effectiveness
  - Ethics
- Lack of data and models to predict late effects e.g. second cancers

Some possible solutions

- Accelerator development
- Radiobiological modelling and experiments
- Advanced treatment planning and delivery techniques
  - Novel, high resolution, minimally damaging imaging
  - Dose validation/online dosimetry
- Consistent data recording and data sharing
- Clinical studies with long-term follow-up

University of Oxford's hope for Protons

Targeted cancer treatment pathway



 Courtesy of Gillies McKenna

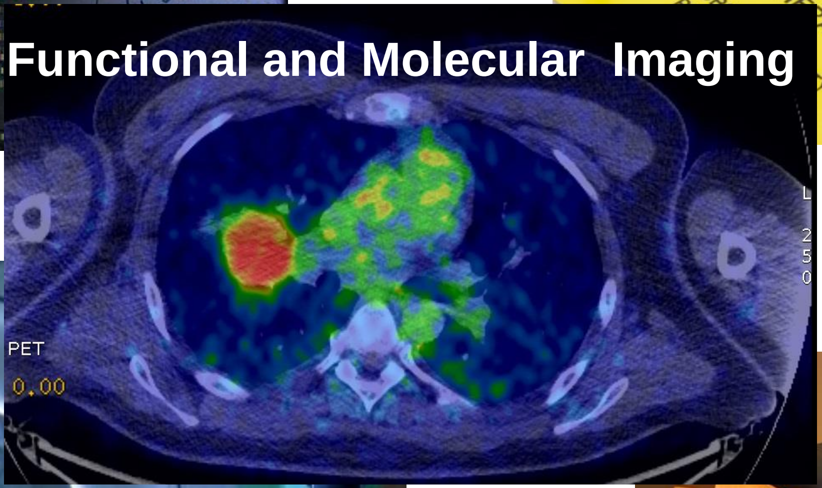
Precision Cancer Medicine

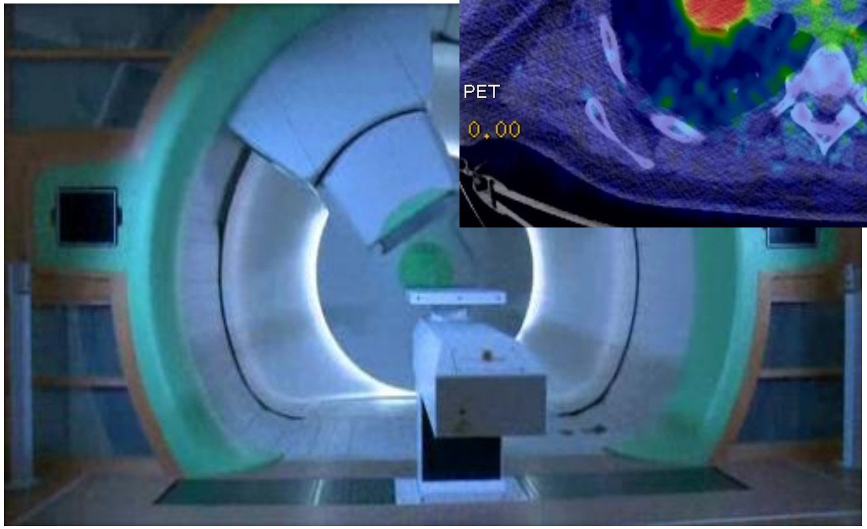
- Physically Targeted
  - Robotic Surgery
  - Proton Therapy
  - HIFU
- Physiologically Targeted
  - Molecular Imaging
- Molecularly Targeted
  - Deep Genomic Sequencing
  - Biomarker Driven
  - Biologically targeted

 Courtesy of Gillies McKenna

Genomics

Targeted Agents





Particle Therapy

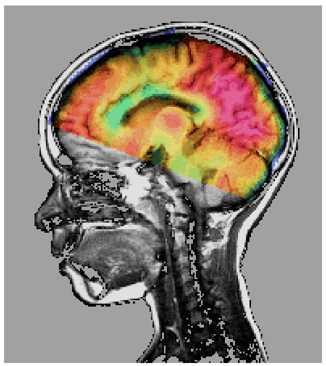
Robotic Surgery

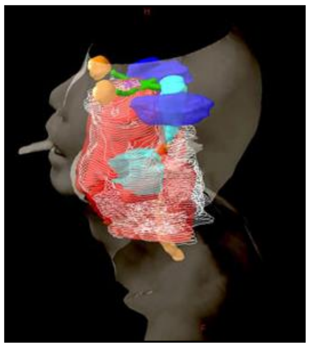
 Courtesy of Gillies McKenna

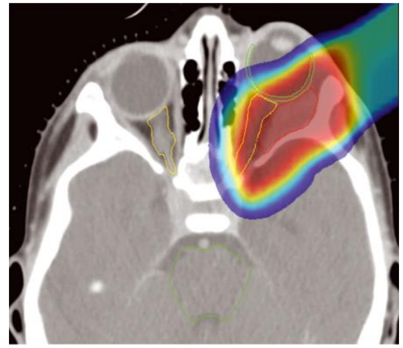
The Evolution of Cancer Therapy

Increased Effectiveness, Reduced Toxicity

CT, MRI, PET

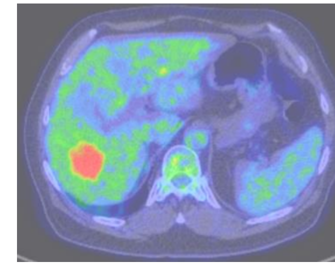


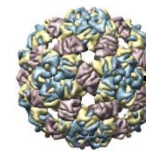




Proton Therapy

Molecular Imaging



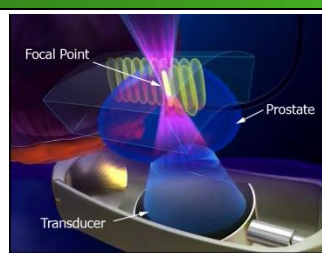


— $(CF_3)_{180}$

Nanotechnology

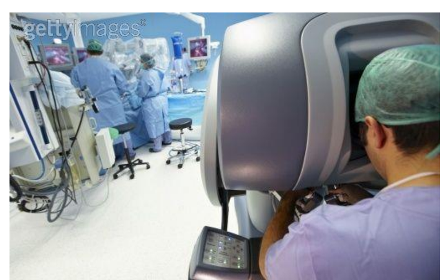
1980 1990 2000 2010 2020

Targeted Agents



HIFU

Robotics



Genomics

Courtesy of Gillies McKenna

- Thank you….

……….any questions?

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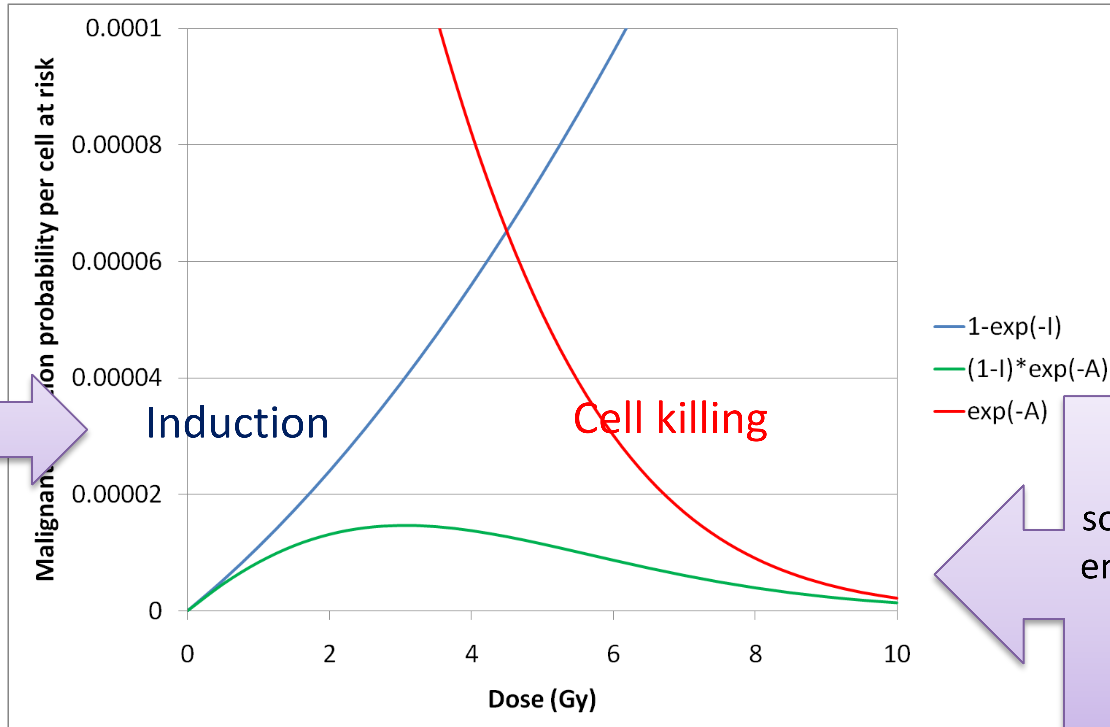
Extra Slides

Induction and cell kill

What is the form of the induction function? Linear, quadratic?



Form of cell killing function known with some certainty at clinical energies, the parameters are tissue dependent and can have large uncertainties.

Probability of transforming a cell

Probability the cell survives

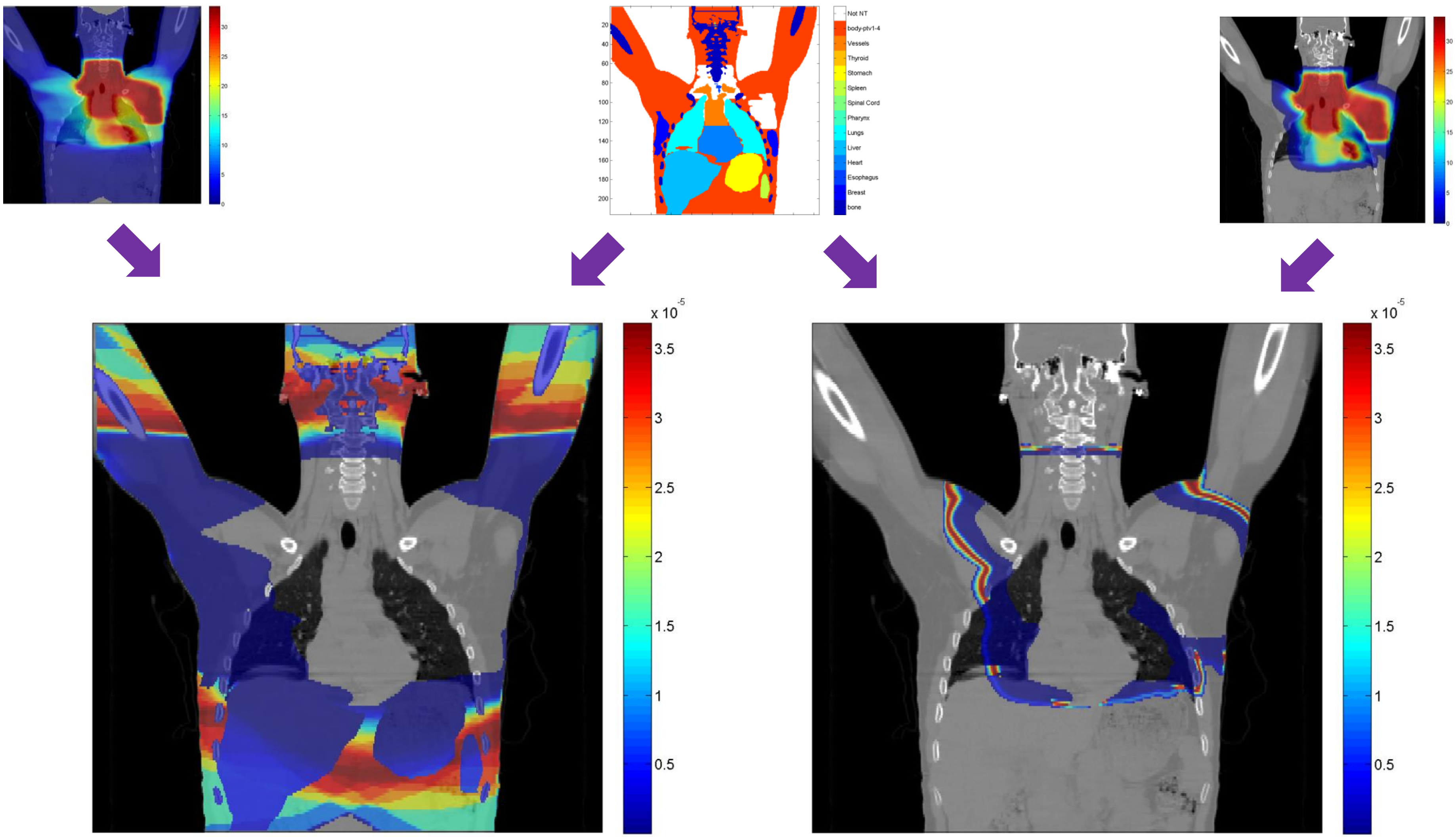
$$P_{tr} = P_I P_S$$

Probability of inducing a potentially malignant mutation

Risk needs to be

- accurately modelled
- confirmed experimentally
- taken into account when deciding on the optimal treatment plan

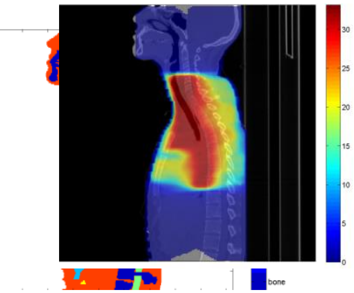
Second cancer risk

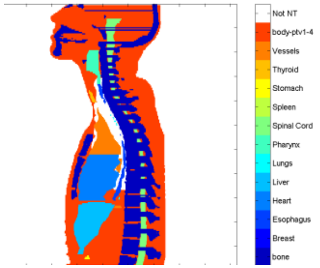


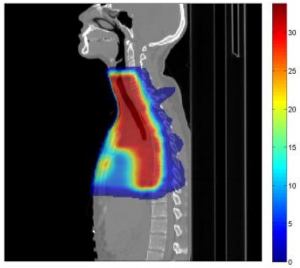
IMRT

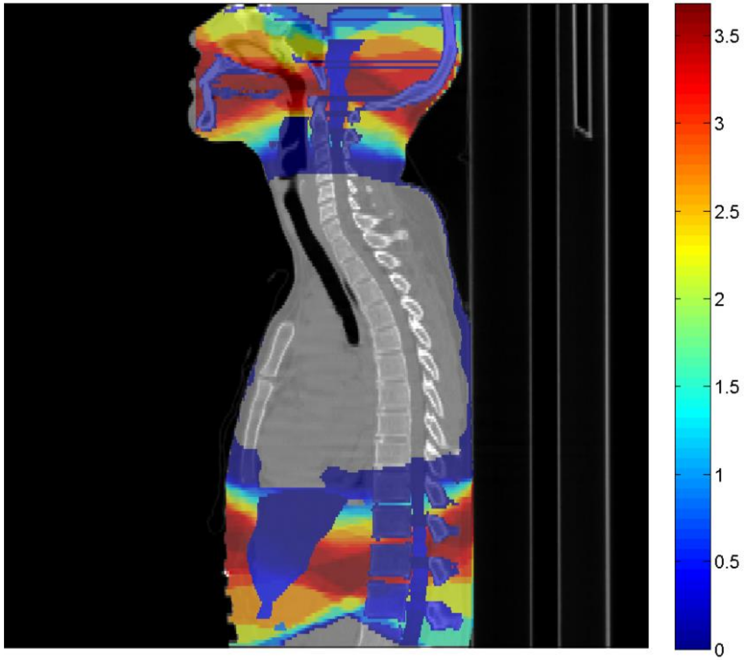
IMPT

Second cancer risk

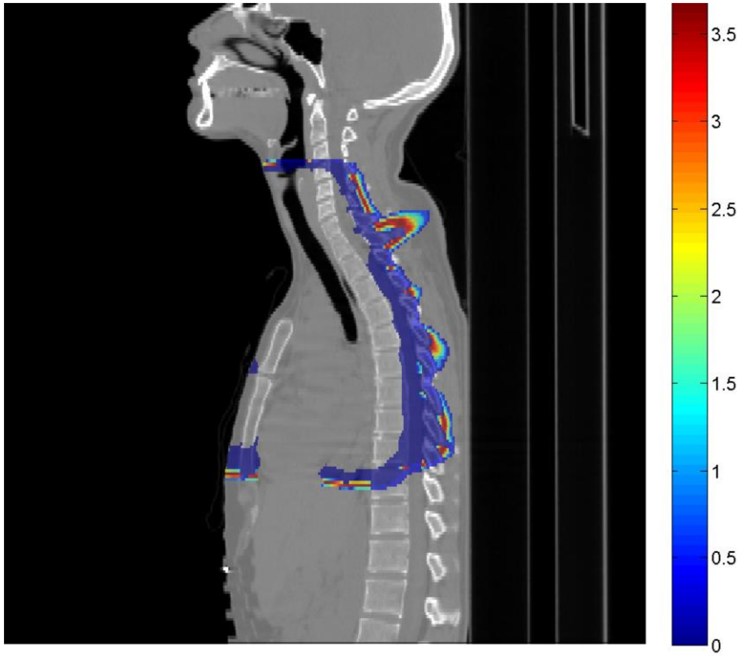






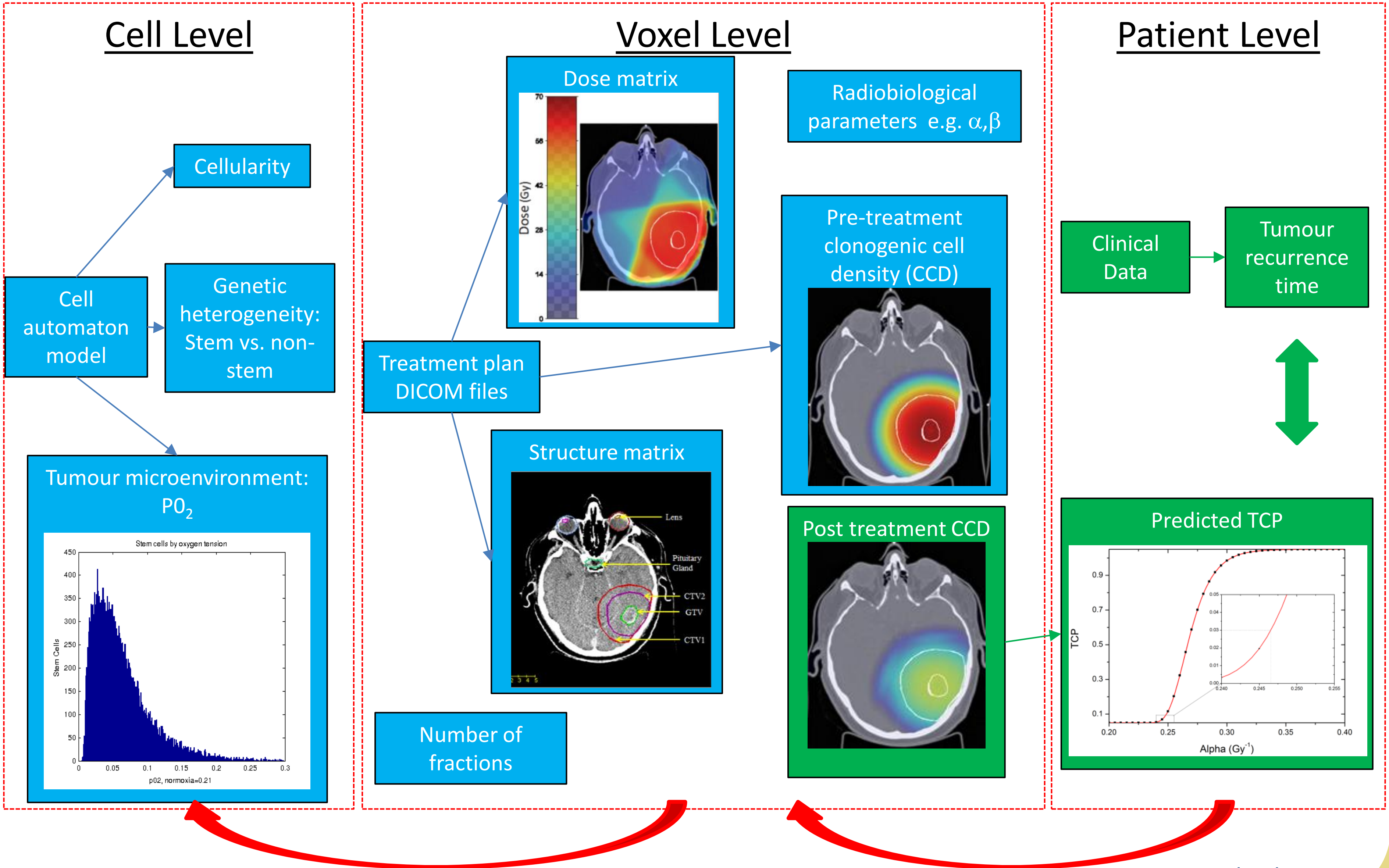


IMRT



IMPT

Multiscale, voxelised TCP calculation for GBM



Relative Biological Effectiveness

- Photons and protons (at clinical energies) have similar biological effects
  - Clinically a modifier (RBE) of 1.1 is applied to physical dose for protons

- For heavier ions (e.g. C) RBE has large uncertainties

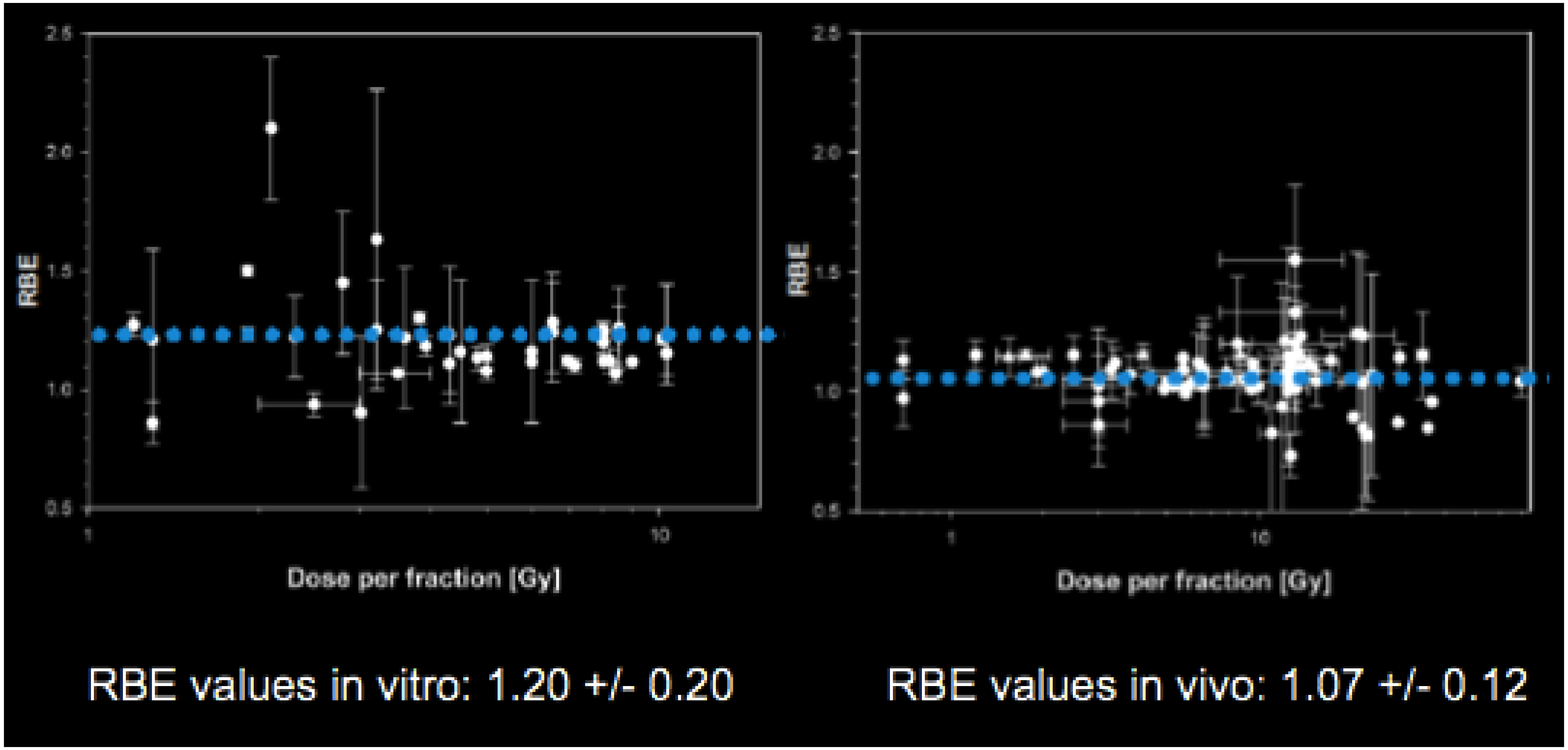
- RBE needed* to calculate physical dose to administer to achieve prescribed biological dose

*maybe there is a better way?

New treatment regimes requiring new methods of optimisation?

RBE vs. Dose for Protons

Where does the 1.1 come from?



Paganetti et al.: Int. J. Radiat. Oncol. Biol. Phys. 2002; 53, 407