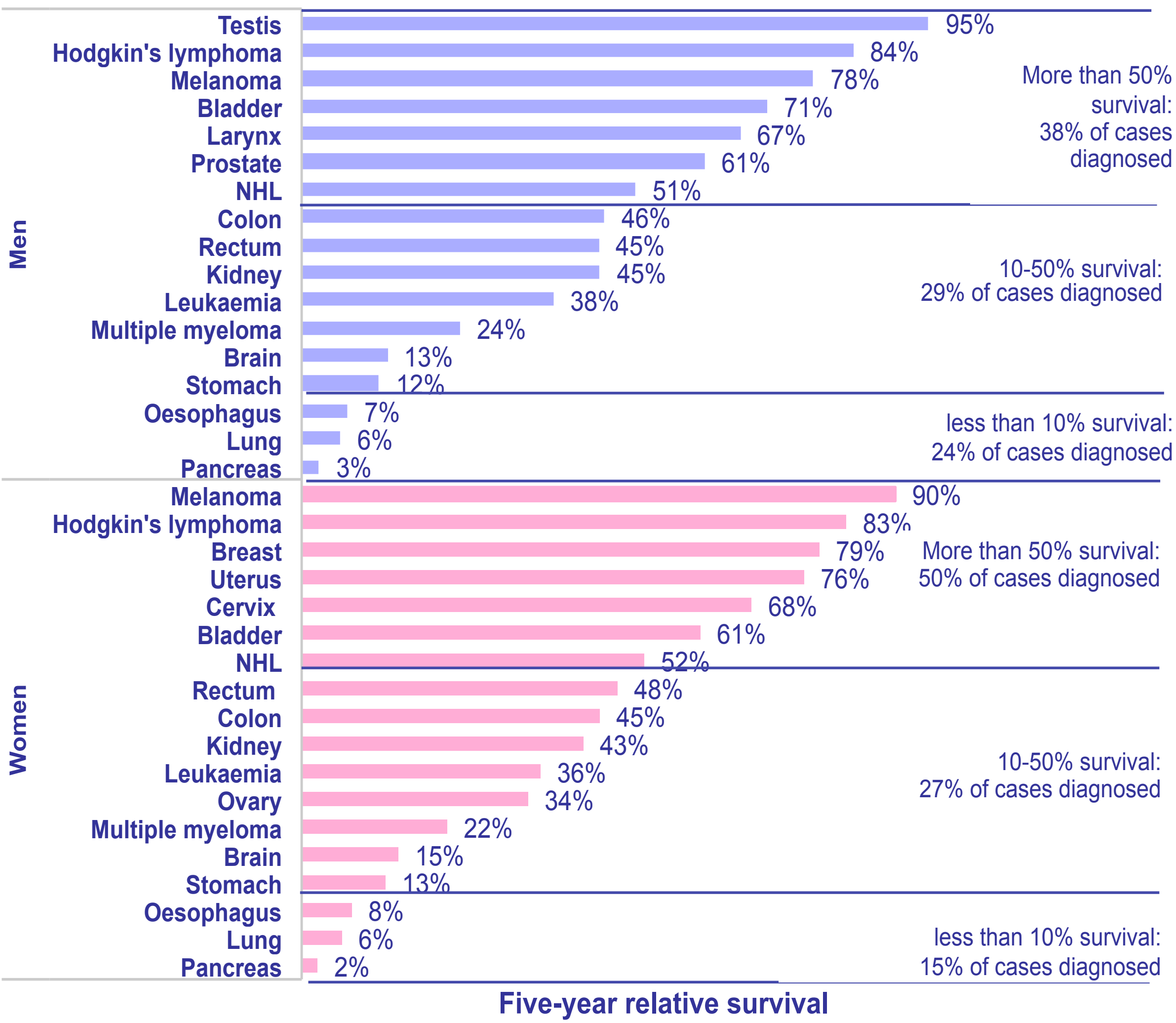
UCL
HOSPITALS

UCL

Proton Beam Therapy at UCLH

Simon Jolly
University College London

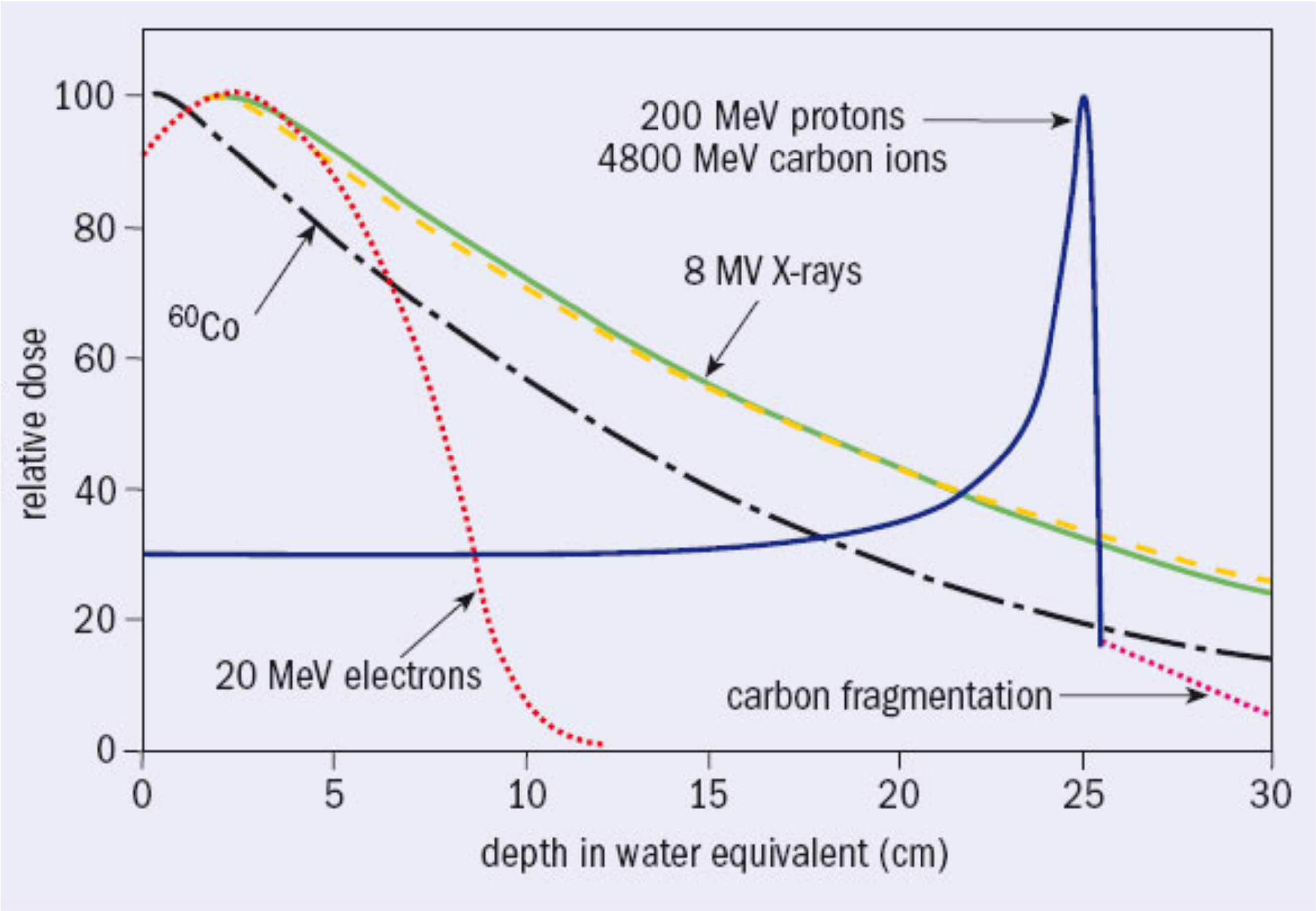
Cancer Types & Survival Rates



Women	Pancreas	2%
	Lung	6%
	Oesophagus	8%
	Stomach	13%
	Brain	15%
	Multiple myeloma	22%
	Ovary	34%
	Leukaemia	36%
	Kidney	43%
	Colon	45%
	Rectum	48%
	NHL	52%
	Bladder	61%
	Cervix	68%
	Uterus	76%
	Breast	79%
	Hodgkin's lymphoma	83%
	Melanoma	90%
Men	Pancreas	3%
	Lung	6%
	Oesophagus	7%
	Stomach	12%
	Brain	13%
	Multiple myeloma	24%
	Leukaemia	38%
	Kidney	45%
	Rectum	45%
	Colon	46%
	NHL	51%
	Prostate	61%
	Larynx	67%
	Bladder	71%
	Melanoma	78%
	Hodgkin's lymphoma	84%
	Testis	95%

The Bragg Peak

$$-\frac{dE}{dx} = \frac{4\pi}{m_e c^2} \frac{nz^2}{\beta^2} \left(\frac{e^2}{4\pi\epsilon_0}\right)^2 \left[\ln\left(\frac{2m_e c^2 \beta^2}{I\left(1-\beta^2\right)}\right) - \beta^2\right]$$



<u>Bethe-Bloch:</u>

E = energy

x = distance

m_e = electron mass

n = electron density

z = particle charge

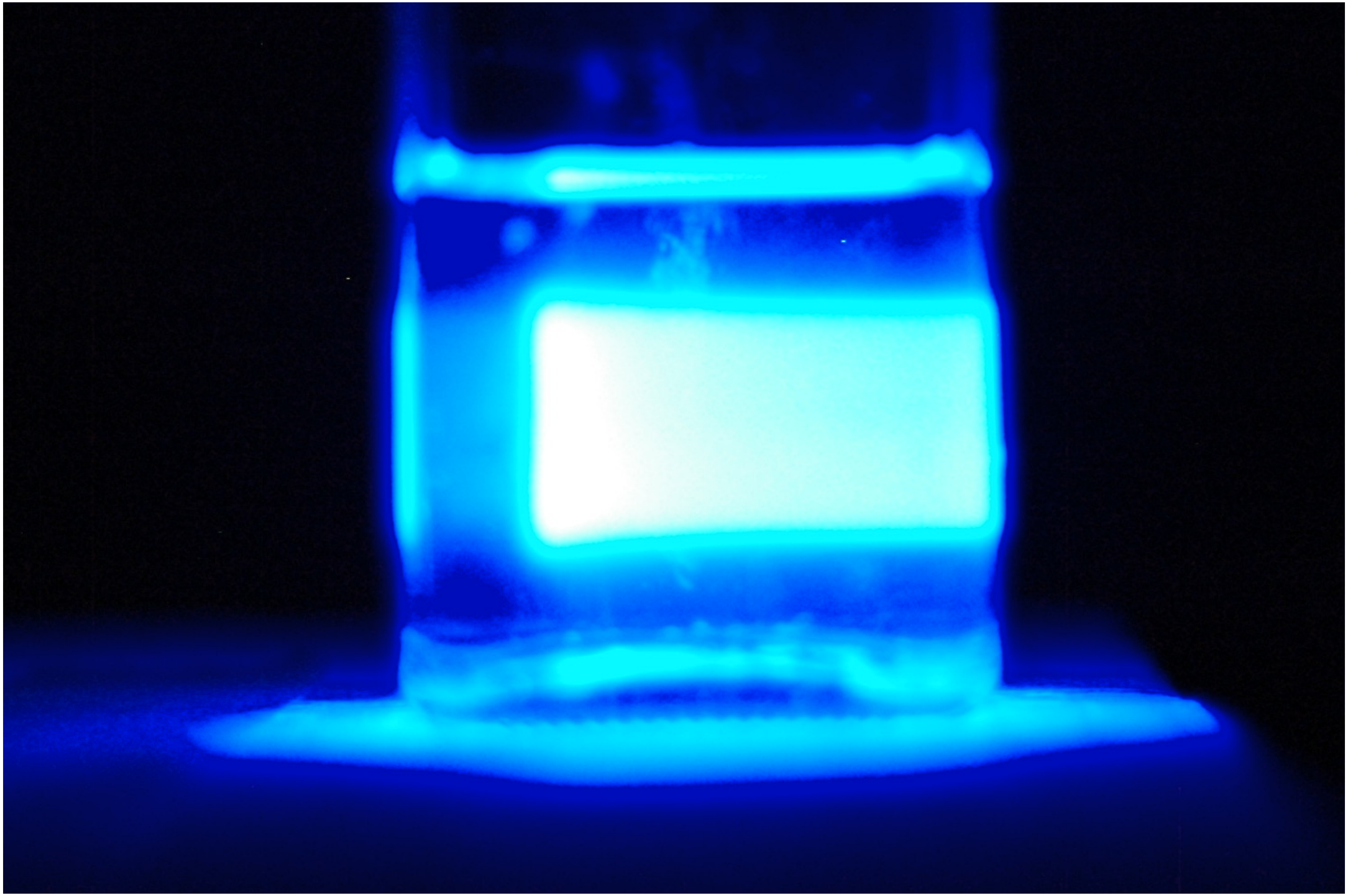
β = particle velocity

e = electron charge

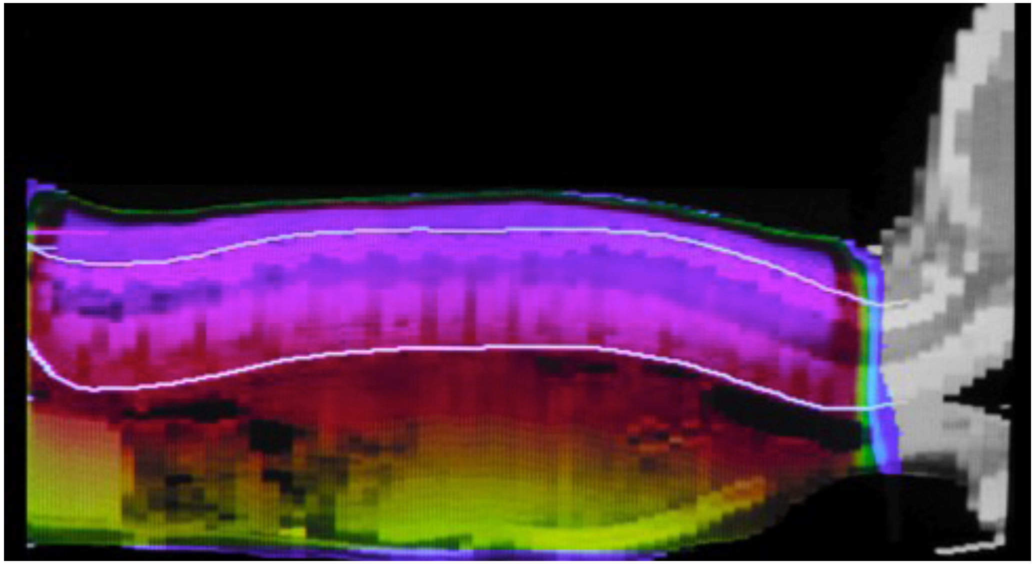
ϵ_0 = vacuum permittivity

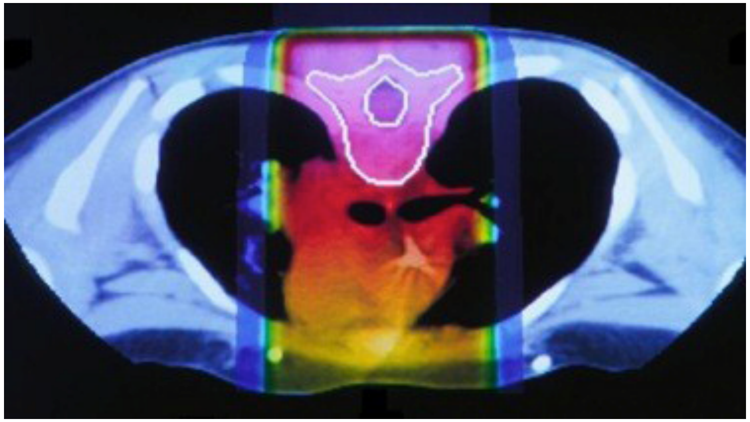
I = mean excitation potential

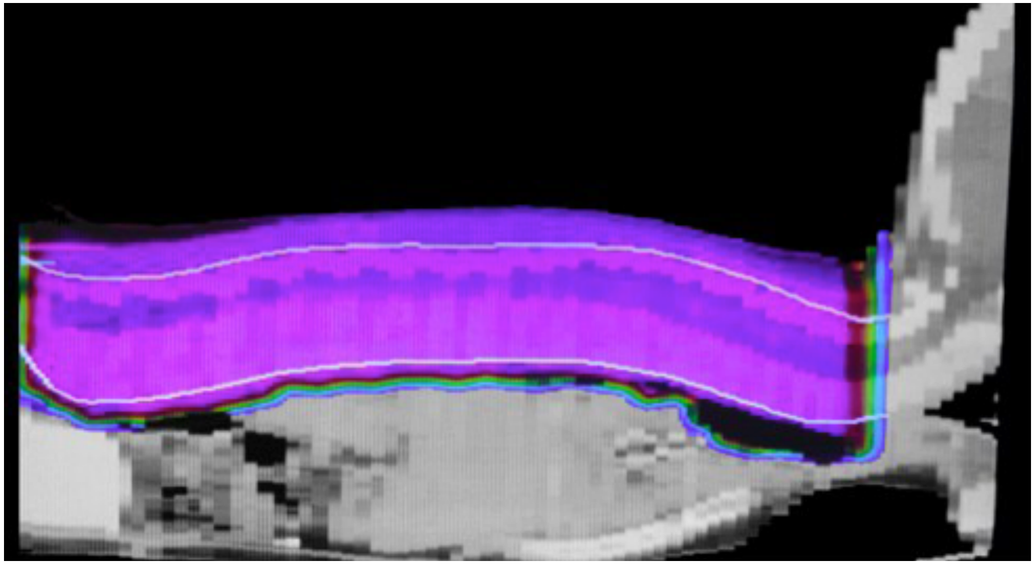
60 MeV Bragg Peak in Liquid Scintillator

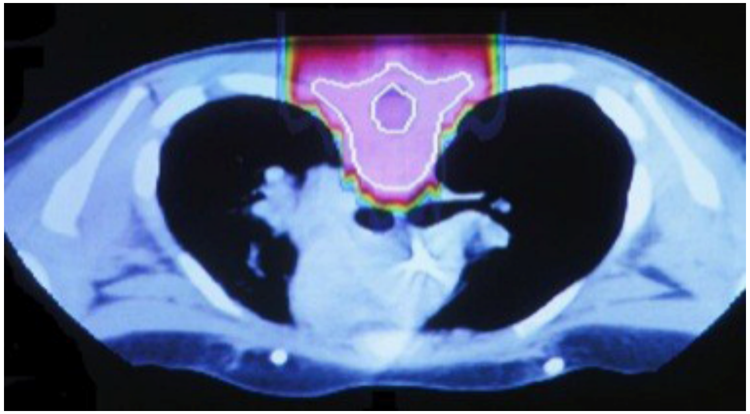


Protons Vs. Photons: Medulloblastoma

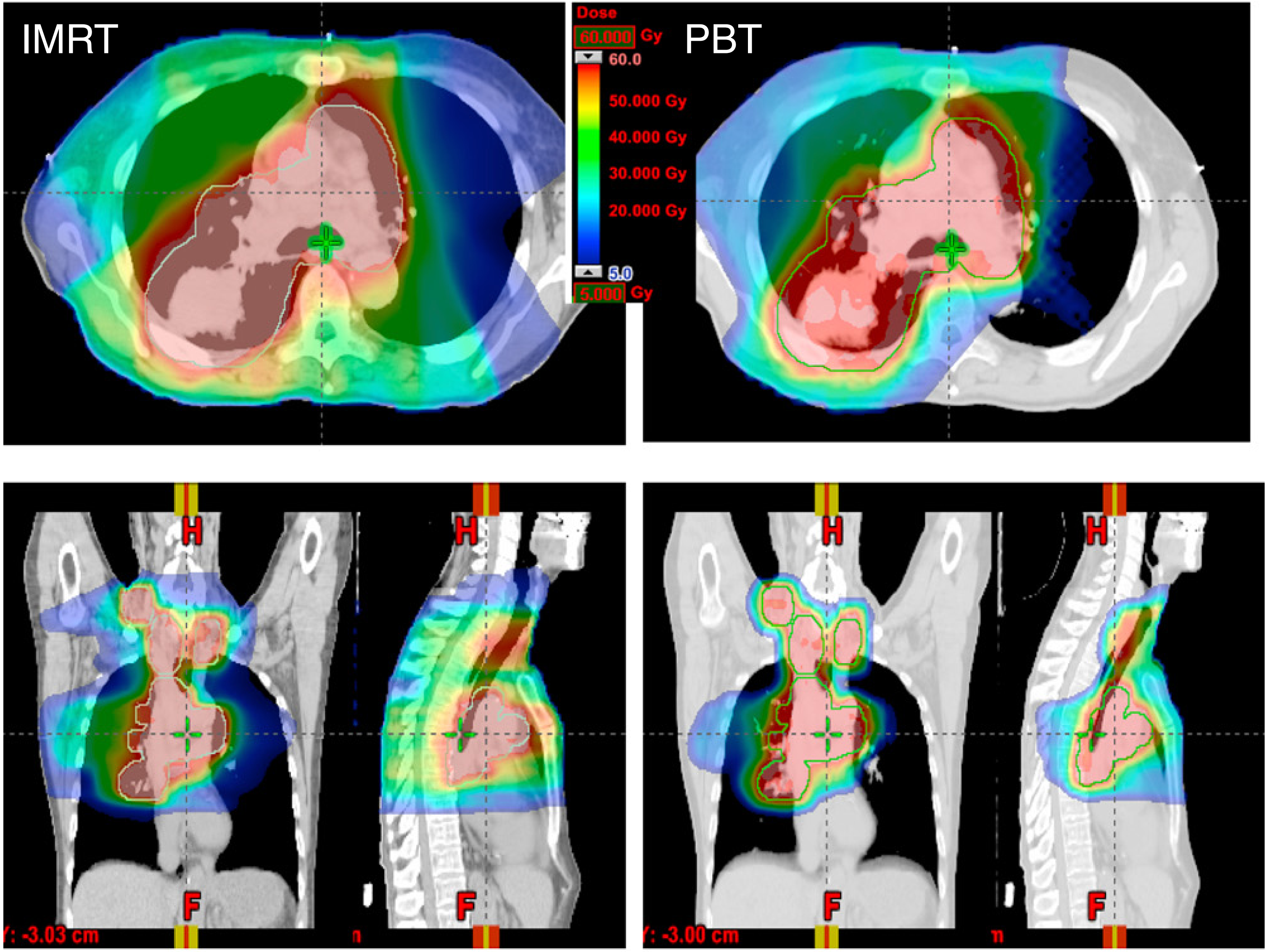






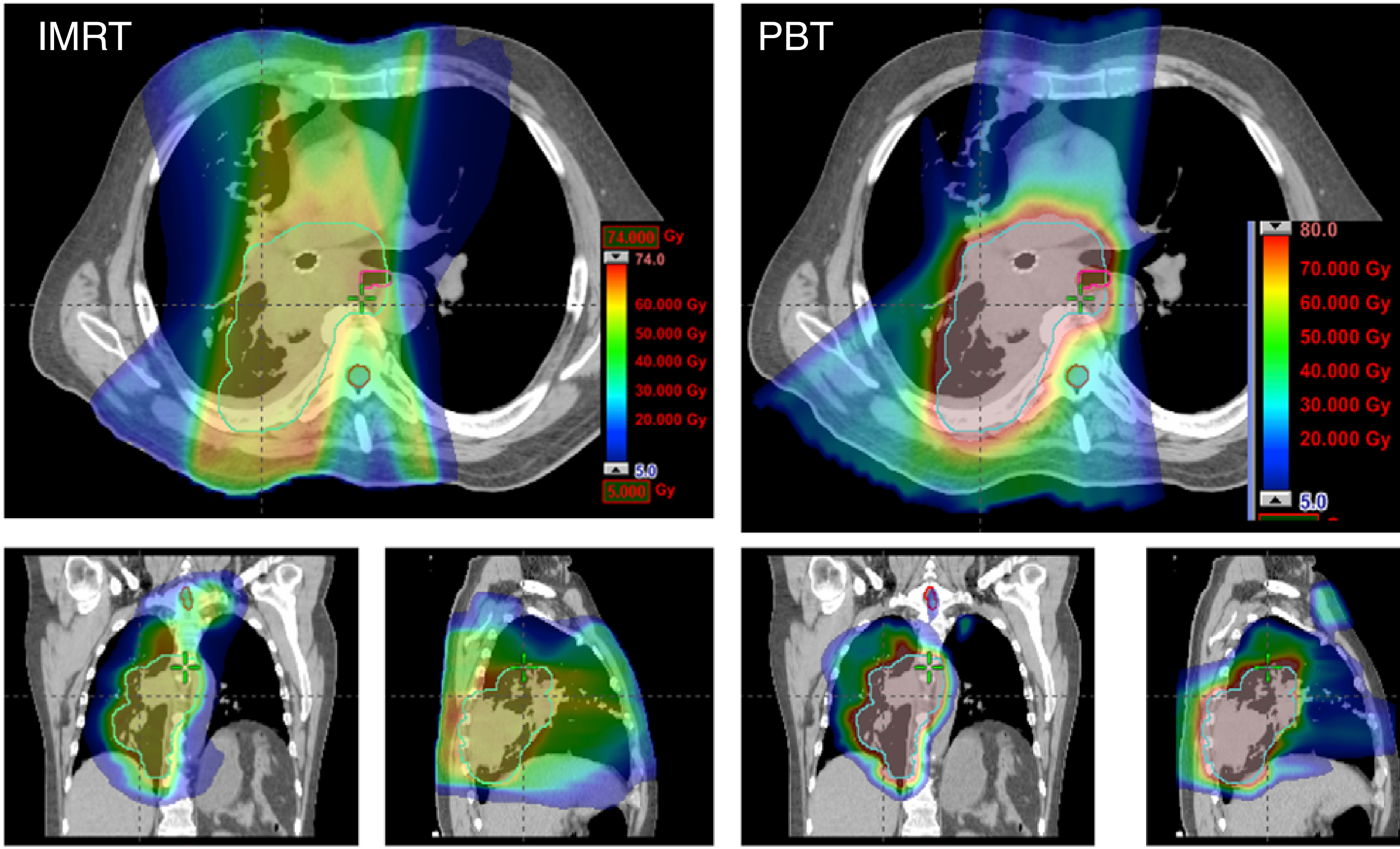


Protons Vs. Photons: NSC Lung Cancer



Zhang X, Li Y, Pan X, et al. *Int J Radiat Oncol Biol Phys.* 2009;77(2):357-366

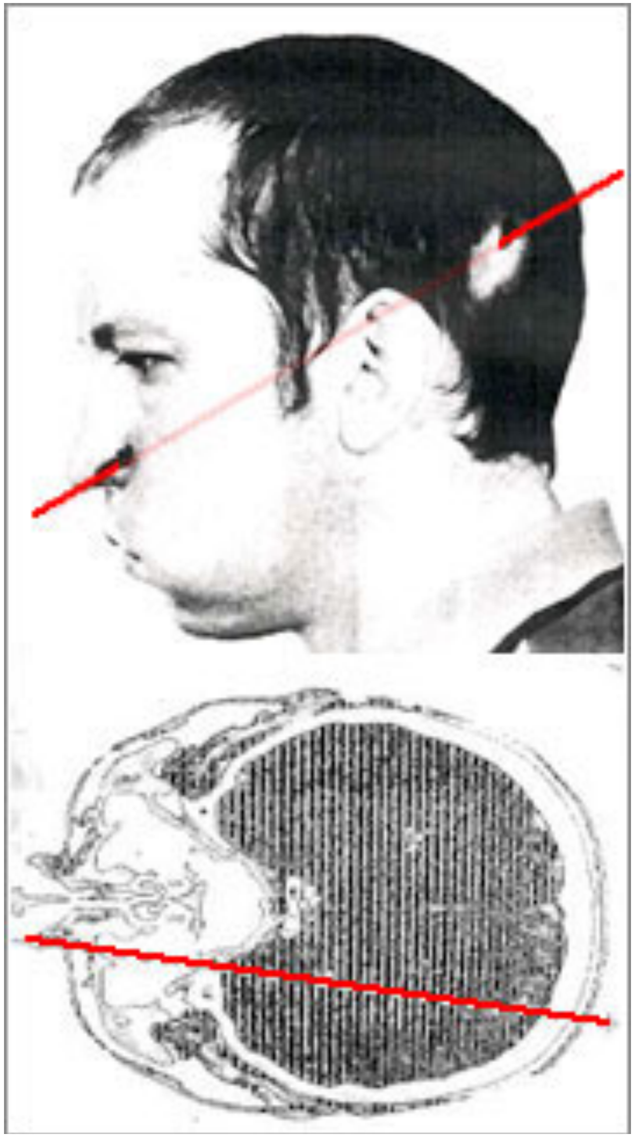
Protons Vs. Photons: NSC Lung Cancer



Zhang X, Li Y, Pan X, et al. *Int J Radiat Oncol Biol Phys*. 2009;77(2):357-366

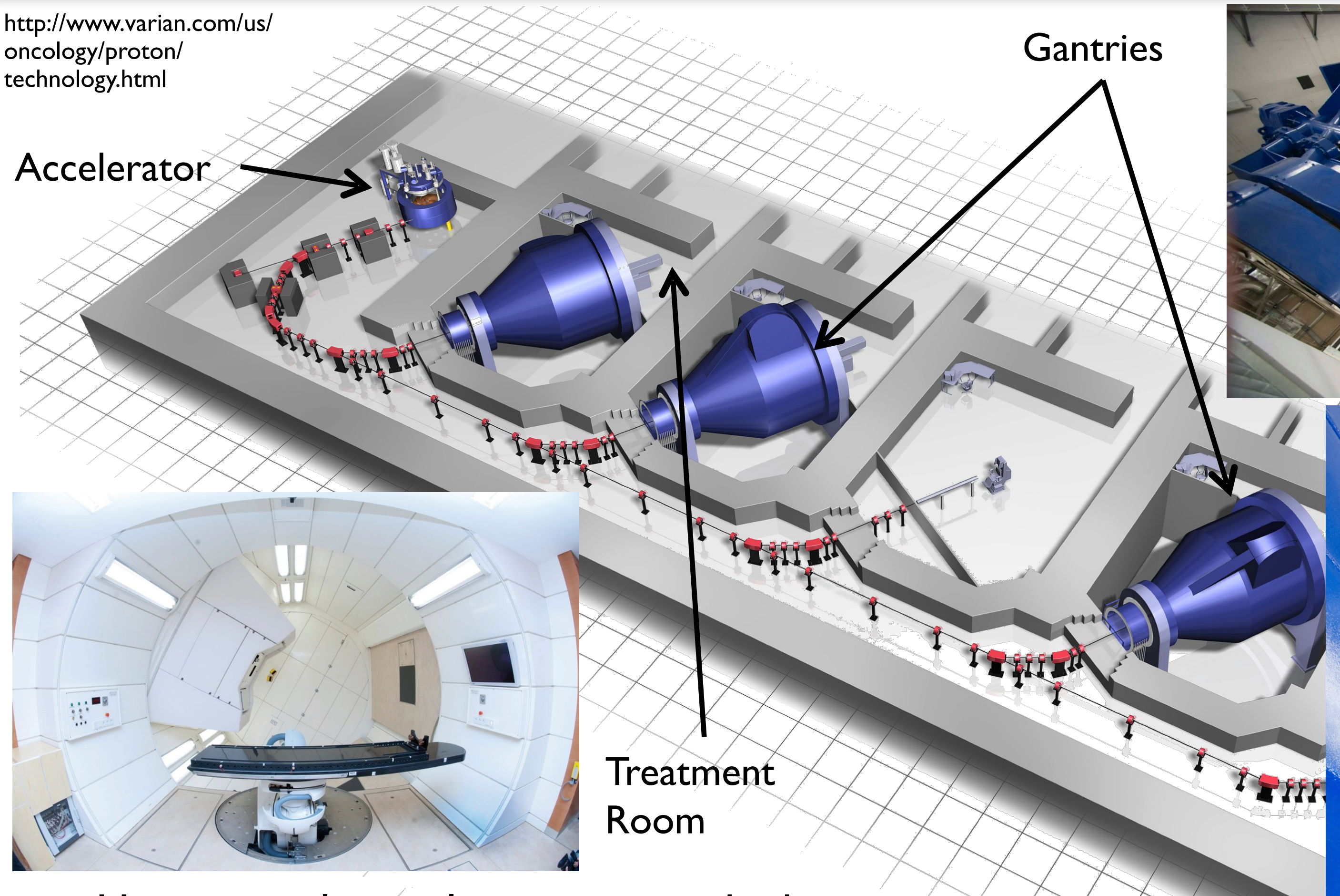
Anatoly Bugorski

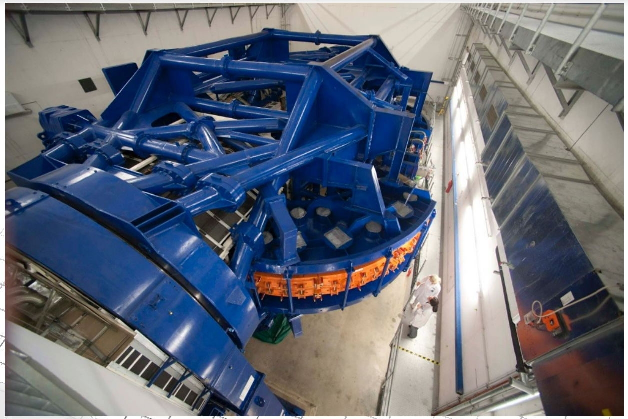
- Researcher at the Institute for High Energy Physics in Protvino, working on U-70 synchrotron.
- On 13 July 1978, safety mechanisms failed while Bugorski was checking some malfunctioning equipment when he stuck his head in the path of the proton beam.
- He saw a flash "brighter than a thousand suns," but did not feel any pain.
- The left half of Bugorski's face swelled up and started peeling off over the next several days, revealing the proton beam path.
- Despite receiving a dose believed to be far in excess of fatal, Bugorski survived and even completed his PhD.
- There was virtually no damage to his intellectual capacity, but the fatigue of mental work increased markedly.
- The left half of his face was paralysed; he completely lost hearing in his left ear.
- He was able to function well, except for the fact that he had occasional complex partial seizures and rare tonic-clonic seizures.
- http://en.wikipedia.org/wiki/Anatoli_Bugorski



Accelerators and Gantries

http://www.varian.com/us/oncology/proton/technology.html

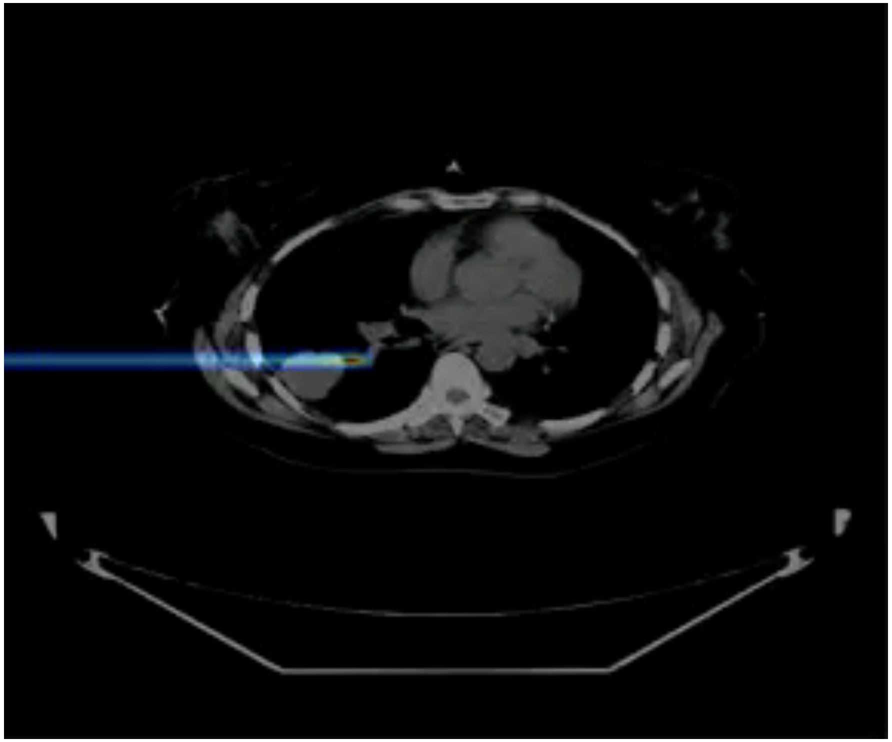


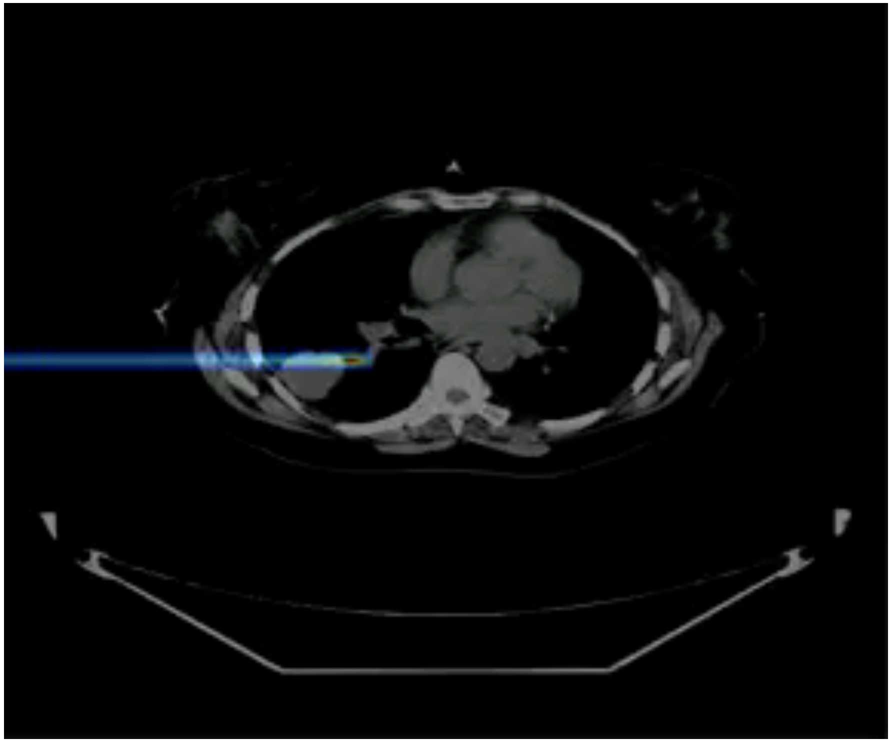


- Use a particle accelerator to get the beam up to 250 MeV.
- Delivered to patient through gantry.
- Gantry must be big enough to deliver beam from any angle: 3 stories tall!
- UCLH and The Christie will each have 3 gantries.

http://www.klinikum.uni-heidelberg.de/HIT-Bildergalerie.114799.0.html

Pencil Beam Scanning

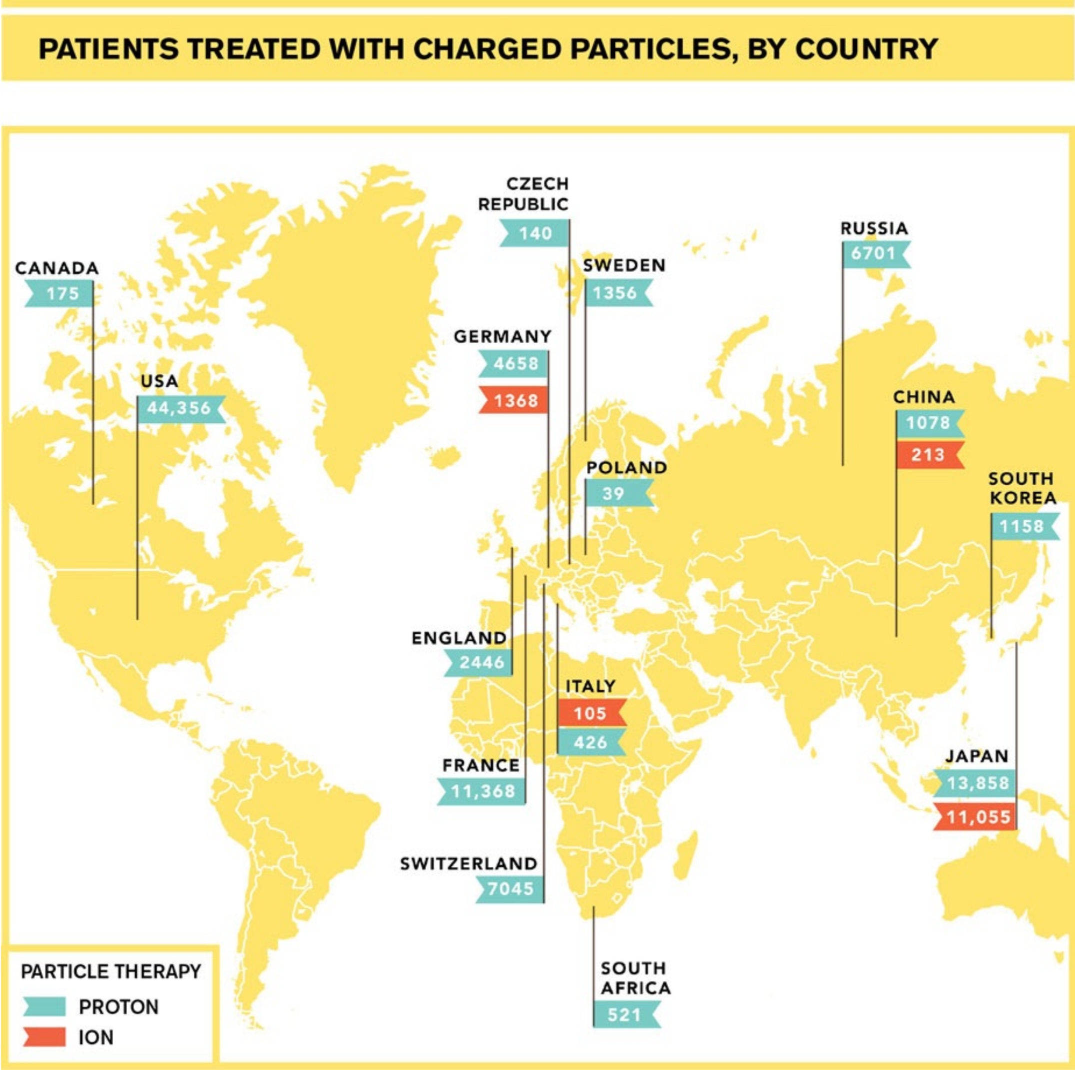




- Pencil beam scanning allows better conformal dose to be delivered to target volume.
- Beam delivered in small "pencil" beams and scanned across target.
- Energy modulated by accelerator: target subdivided into layers and "painted" by using energy variation.

UK Proton Therapy

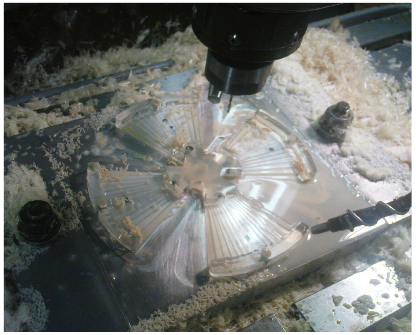
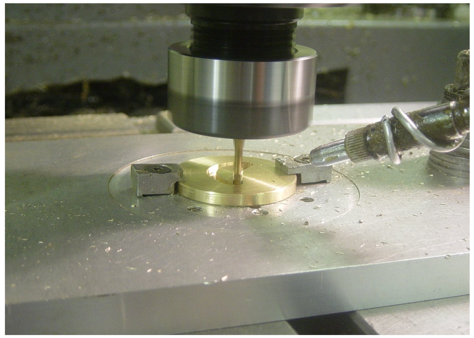
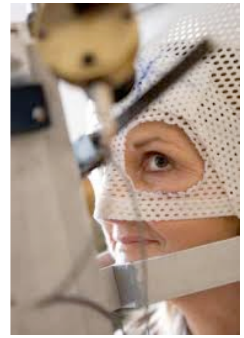
- Currently UK only has 1 proton therapy centre: Clatterbridge (Wirral) treats eyes with 60 MeV protons.
- Around 20 existing proton therapy centres worldwide with around the same number planned.
- Most countries treat private patients with simple tumours (85% prostate…).
- Some British children sent abroad for treatment in Jacksonville, FL.
- Earlier this year, government gave the go ahead for 2 new cancer treatment facilities using protons:
  - UCLH.
  - Manchester/Christie.
- Procurement began 2013, up and running in 5 years.



http://www.symmetrymagazine.org/article/september-2014/accelerating-the-fight-against-cancer

Clatterbridge Cancer Centre

UCL



UK Proton Therapy Indications

- Indications list is available on the web:
  - Strategic Outline Case: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213045/national-proton-beam-therapy-service-development-programme-value-for-money-addendum.pdf
  - Value-for-money Addendum: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213045/national-proton-beam-therapy-service-development-programme-value-for-money-addendum.pdf
- Will treat most difficult cases:
  - Brain: Chordoma, Glioma, Craniopharyngioma, Meningioma, Intracranial Germinoma.
  - Skeletal: Chondrosarcoma, Rhabdomyosarcoma, Osteosarcoma, Ewings sarcoma.
  - Central Nervous System: Ependymoma, Medulloblastoma (PNET), Spinal Sarcoma.
  - Head & Neck: Retinoblastoma, Nasopharynx, Acoustic Neuroma, Choroidal Melanoma.
  - Others: Hodgkins.

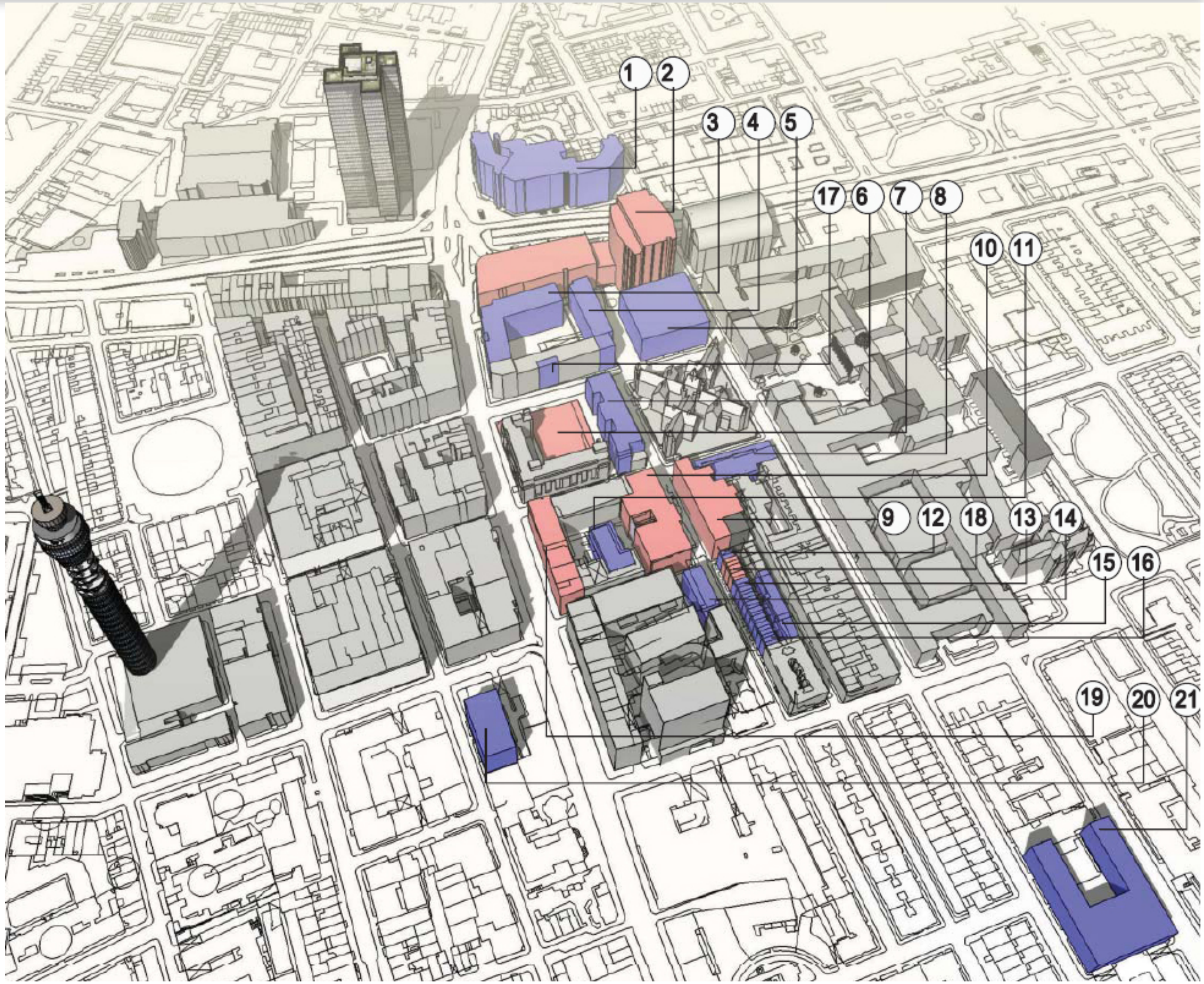
	Indication	**Number of patients**
Paediatric	Chordoma/ Chondrosacoma	15
	Rhabdomyosarcoma (Orbit)	5
	Rhabdomyosarcoma (Prameningeal and H&N)	15
	Rhabdomysarcoma(Pelvis)	10
	Osteosarcoma	3
	Ewings	9
	PPNET	5
	Ependymoma	25
	Low Grade Glioma	5
	Optic Pathway Glioma	12
	Craniphayngioma	15
	Medulloblastoma (PNET)	70
	Hodgkins	5
	Retinoblastoma	5
	Meninggioma	3
	Intracranial germinoma	10
	Nasopharynx (H&N)	15
	Difficult Cases Esthe/Neuro/Liver)	5
	Very Young Age	20
	Total	**252**
Adult	**Choroidial Melanoma**	100
	Ocular/Orbital	25
	Chordoma	60
	Chondrosarcoma	30
	Para- Spinal / Spinal Sarcoma	120
	Sacral Chordoma	60
	Meningoma	100
	Acoustic Neuroma	100
	Craniospinal NOS (Pineal)	10
	Head & Neck & Paranasal Sinuses	300
	PNET(medulloblastoma Intracranial)	30
	Difficult cases	300
	Total	**1,235**
	GRAND TOTAL	**1,487**

UCLH Cancer Campus

UCL

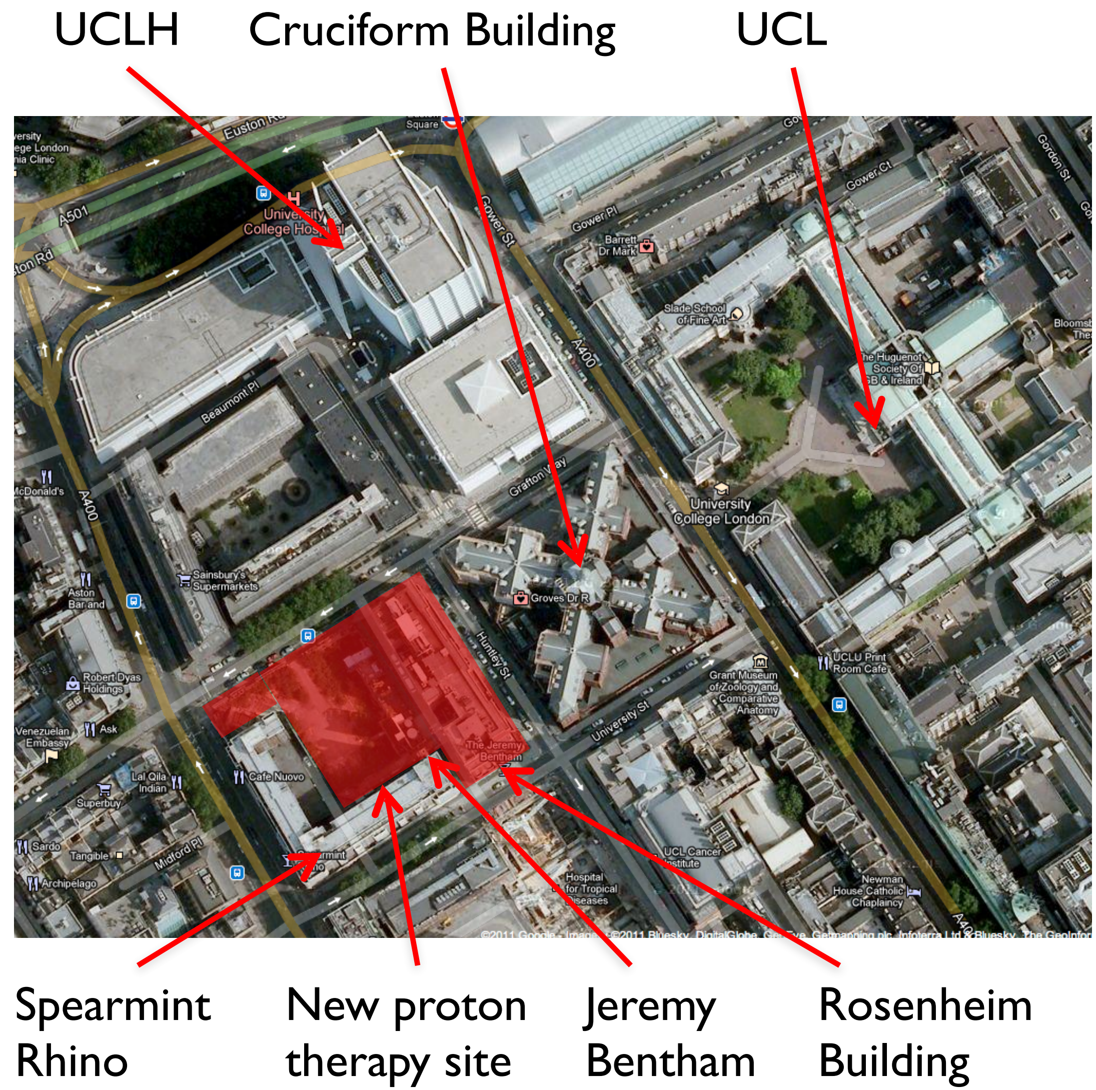
UCH CAMPUS
CANCER RELATED IN 2015

1. 250 EUSTON ROAD
2. UCHL MAIN WING
3. MAPLE HOUSE
4. MAPLE HOUSE LABORATORIES
5. UCHL EGA WING
6. ROSENHEIM BUILDING
7. ODEON SITE
8. ROCKEFELLER BUILDING
9. PAUL O'GORMAN BUILDING
10. CANCER CENTRE
11. HOSPITAL FOR TROPICAL DISEASES
12. 70 HUNTLEY STREET
13. 62 HUNTLEY STREET
14. ROYAL EAR HOSPITAL
15. CHENIES MEWS
16. 46-60 HUNTLEY STREET
17. MAPLE HOUSE FLATS
18. PAUL'S HOUSE (CLIC SARGENT)
19. PROPOSED PATIENTS' HOTEL 170 TOTTENHAM COURT ROAD
20. WHITFIELD STREET LABORATORIES
21. BONHAM CARTER HOUSE / WARWICKSHIRE HOUSE

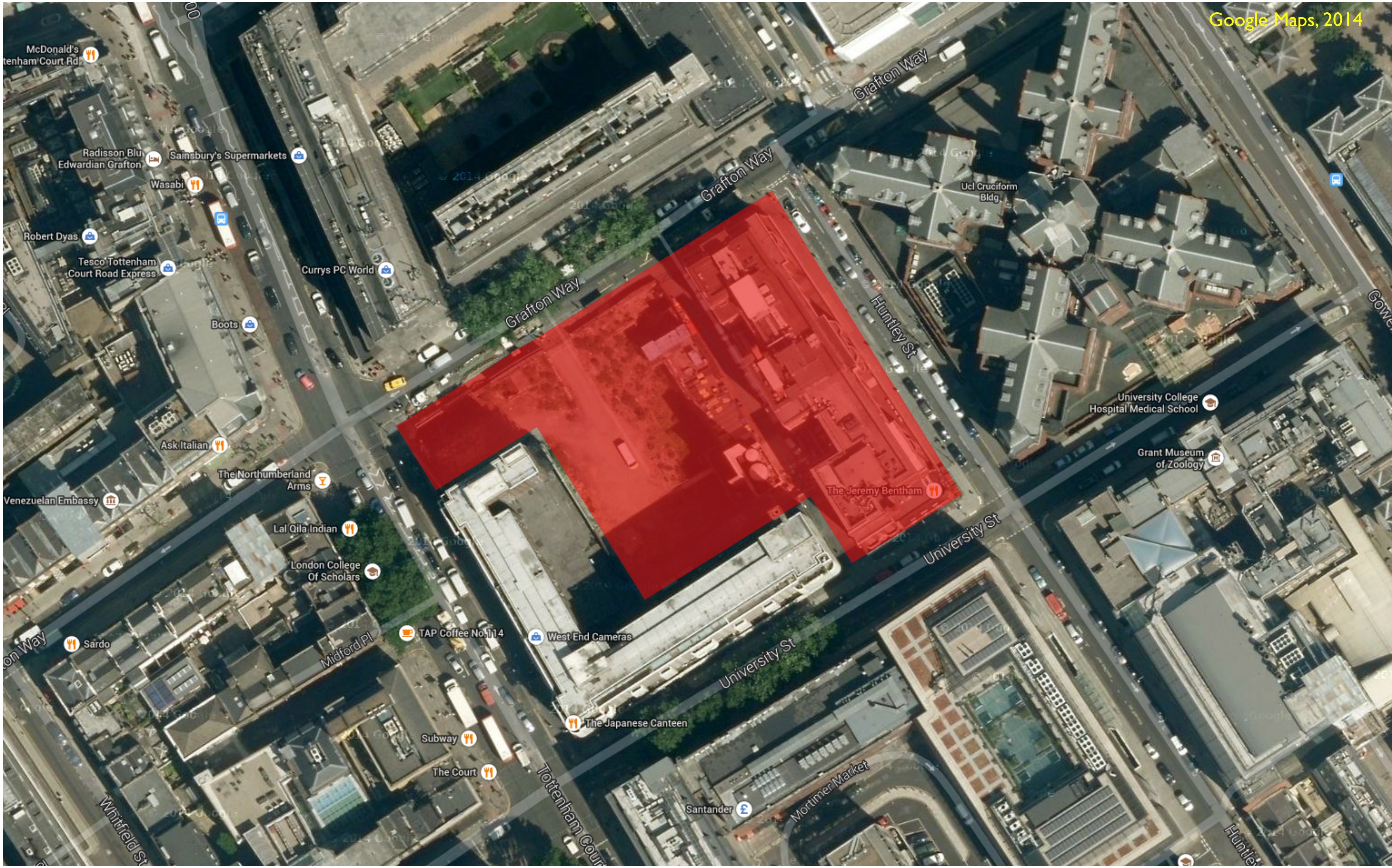


UCLH Proton Therapy Site

- New facility will be on existing UCLH site, next to Tottenham Court Road.
- Linked to UCLH via walkways to allow easy patient transfer.
- Planning to treat ~750 patients a year.
- 1 proton accelerator feeding 3/4 gantries (plus research room).
- Total cost: £150 million.



UCLH PBT Site



Down Comes The Rosenheim…

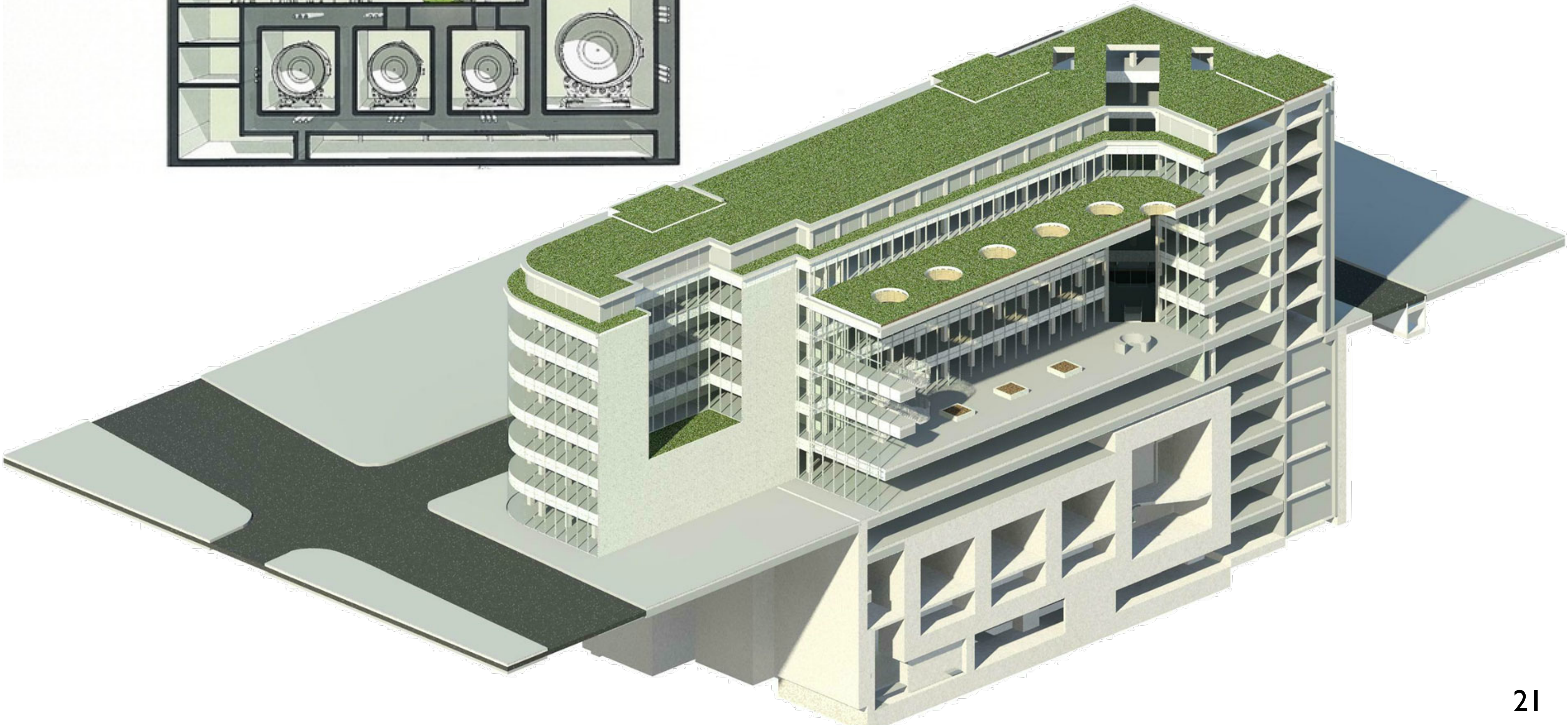
Down Comes The Rosenheim…

Down Comes The Rosenheim…

Down Comes The Rosenheim…

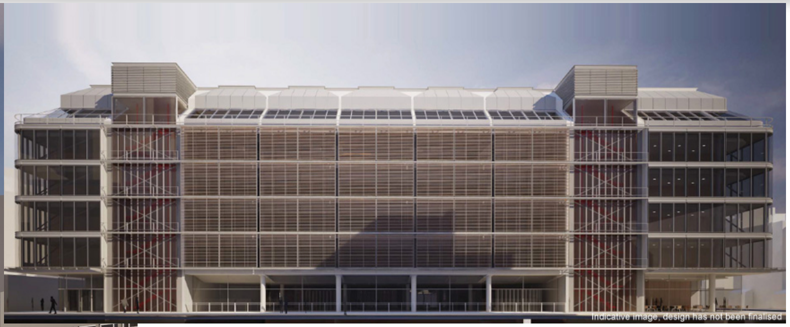
UCLH PBT Cut-through (Old)

UCL



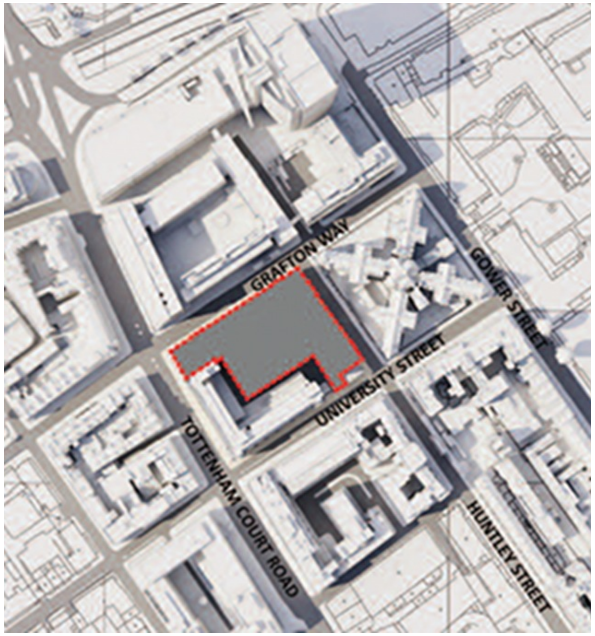
UCLH PBT Building

UCLH PBT External



17/02/15

UCLH PBT (TCR/Grafton Way)



UCLH PBT (Grafton Way)

Technology (Ran Mackay)

Censored

Build (Ran Mackay)

Censored

Plan For The UK (Ran Mackay)

Censored

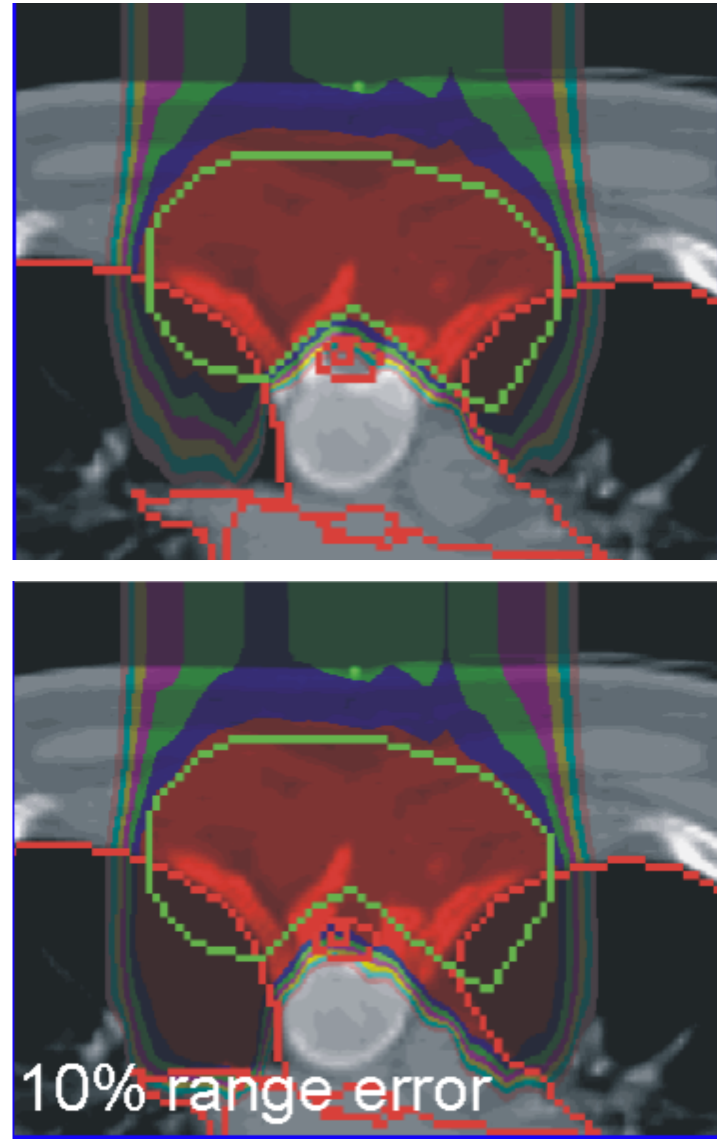
The View From UCLH (Richard Amos)

Key Areas for Research

- Imaging.
- Adaptive Therapy.
- Imaging.
- Patient Throughput.
- Imaging.
- Pathways (Data Management).
- Imaging.
- Dose Verification.
- Imaging.
- Charged Particle Dosimetry.
- Imaging.
- Neutron Dosimetry.
- Imaging.
- Variable Spot Size.
- Imaging.
- Compact Gantries.
- Imaging.
- Radiobiology

Range Uncertainty

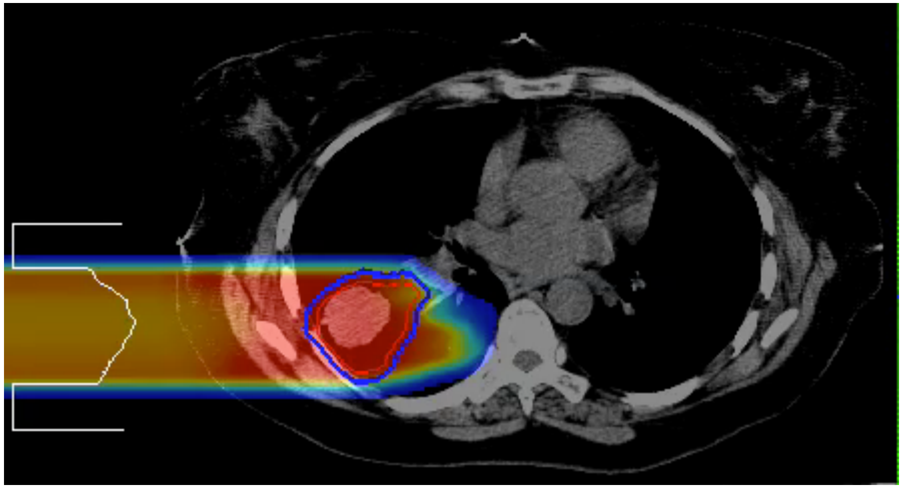
- The advantage of protons is that they stop.
- The disadvantage is that we don't always know where…
- Range verification:
  - in vivo, direct (e.g. PET, prompt), indirect (e.g. calibrated CT, other decoupled method).
  - Calibrate with phantom.
- Proton radiography/ tomography:
  - e.g. PRaVDA: Si detector range telescope with tracker at entrance and exit.
  - becoming a big area internationally; underdeveloped but not complex.
  - Working on better calorimetry for proton CT at UCL.

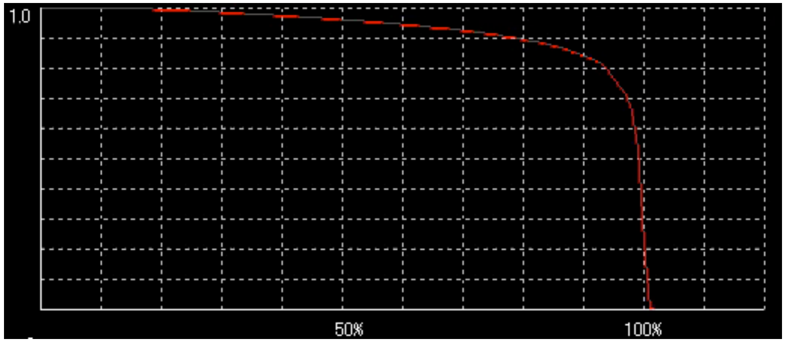


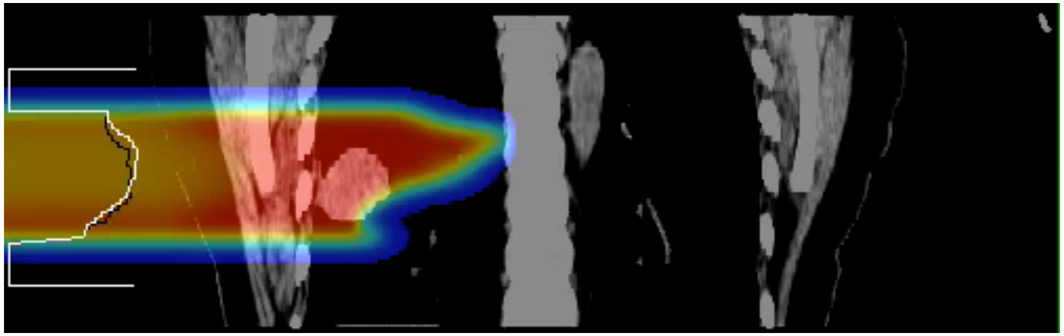
Tony Lomax, PSI

Proton Dose with Tumour Motion

Heng Li, PhD
Department of Radiation Physics
UT MD Anderson Cancer Center
(Yoshikazu Tsunashima)

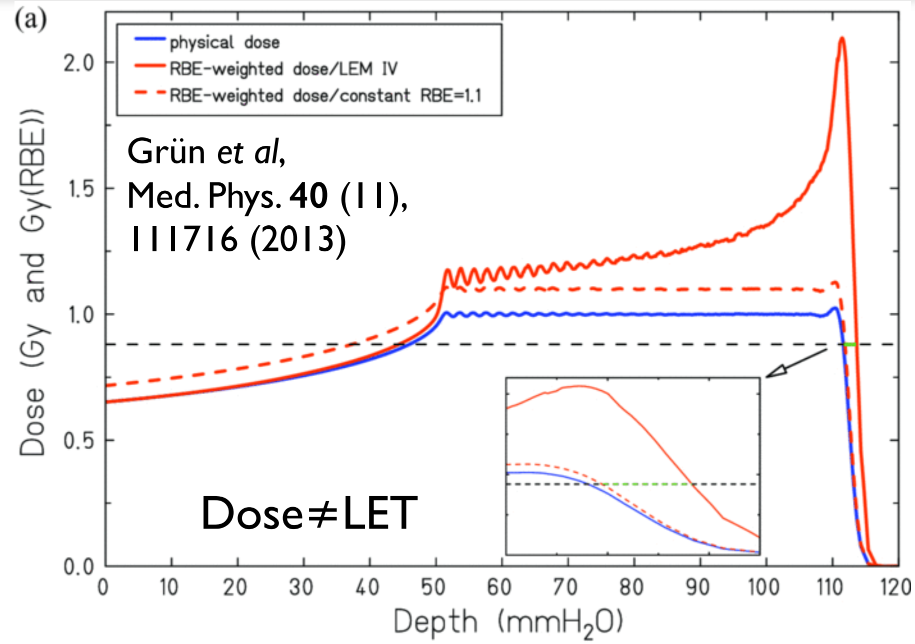




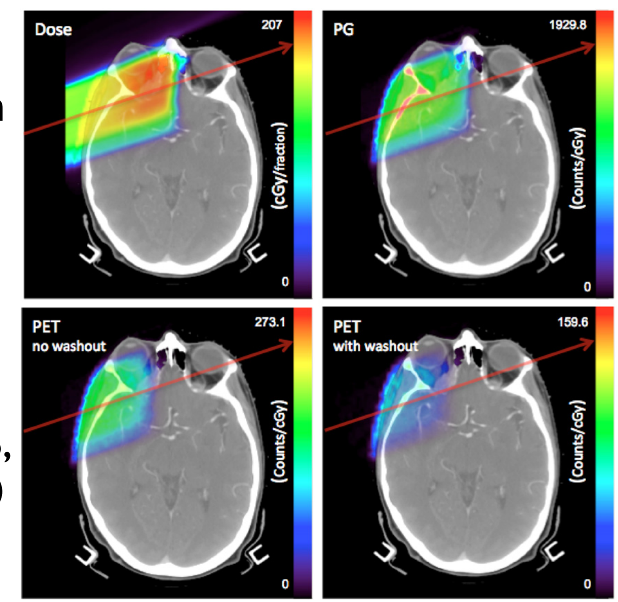


Imaging

- Imaging is **WITHOUT QUESTION** the most important challenge for proton therapy.
- High resolution imaging required for treatment planning.
- Imaging required between fractions to monitor changes in patient anatomy/tumour volume.
- In an ideal world:
  - Real-time imaging DURING TREATMENT to EXACTLY where internal anatomy is relative to nozzle.
  - Coupled to instantaneous measurement of radiobiological damage (not just dose!) during beam delivery.
  - This gives you information on precisely where dose is being delivered and whether it's being delivered in the right place…
- Clinicians will ask you for this many times over before even thinking about the accelerator…
- Proton CT goes some way towards this (better resolution than X-ray CT) but will need multi-modality imaging.
- Adaptive Therapy seeks to modify treatment on-the-fly: lots of work already under way.

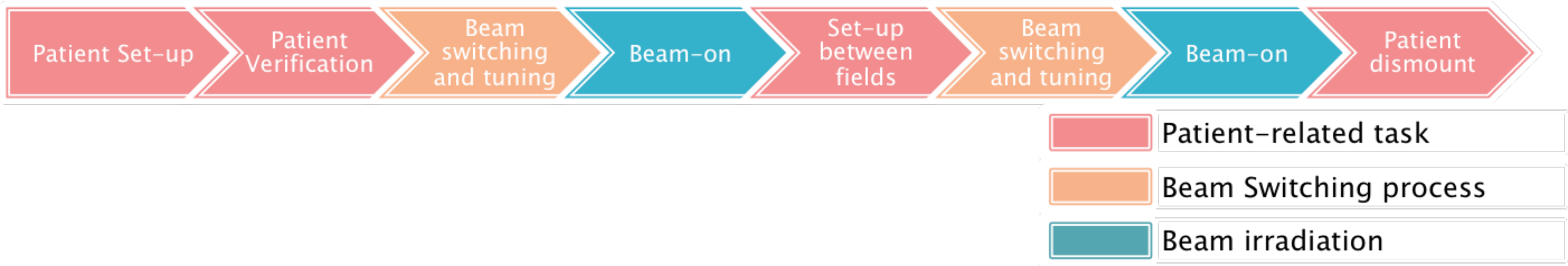


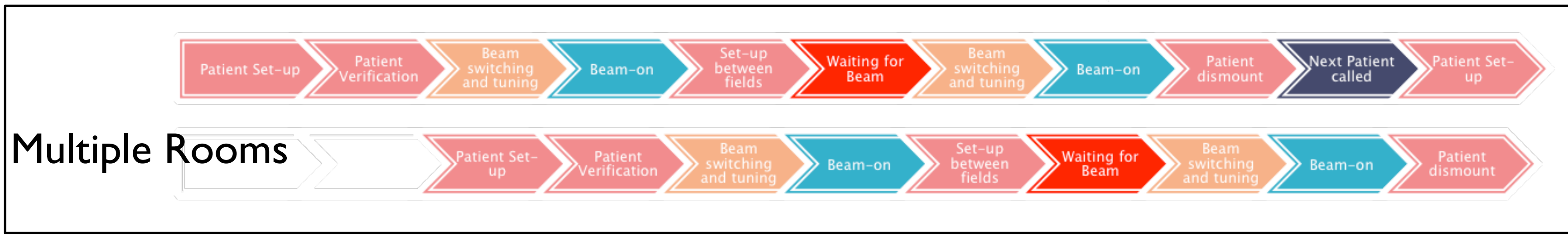
Dose Verification



Moteabbed *et al*, Phys. Med. Biol. **56**, 1063–1082 (2011)

Patient Throughput





- Need to optimise "patient scheduling" and "beam scheduling" to maximise throughput:
  - Patient treatment timetable planned a week or so in advance: how do you arrange treatments to treat as many patients each day?
  - Beam scheduling based on patient scheduling, but must be highly reactive:
    - Redirect beam if patient not ready, needs to be realigned, problems with GA etc.
    - Need to optimise beam availability, minimise switching and tuning time.
- Could be the difference between 3 rooms and 4…

Other Requirements

- Data Management:
  - Patients will be referred to UCLH/Christie from across UK.
  - Large range of referring centres, each with their own patient database: patient notes, imaging etc.
  - Will need:
    - Streamlined and transparent patient referral system (particular issue for personalised treatments)
    - Engagement of referring centres: boundary of responsibility/planning between referring hospital and treatment centres.
  - Massive amounts of data needs to be centralised:
    - Information collated at PBT centres to inform treatment.
    - Post treatment planning information passed back to original referring centre.
- Dosimetry:
  - Any particle that is not a proton at the correct energy needs to be monitored and minimised.
  - Need measurements in-room of prompt emissions during treatment.
  - Need species and energy spectra of charged particles, photons and neutrons.
- Dose Verification:
  - Relative dose verification already established: verify dose distribution from given treatment plan.
  - Need ABSOLUTE dose as well: how many protons per spot?
  - Work being led by NPL.
- Variable Spot Size:
  - Larger beam spots have more overlap than small spots.
  - Good for making dose more uniform in centre of tumour, bad for reducing hard edge of treatment volume.
  - Variable spot size would allow dynamic change in all 3 dimensions to get best possible compromise of overlap and conformality.
- Compact Gantries: smaller = cheaper = better…

Taking Technology to Market

- At the moment, virtually all innovation in proton therapy is coming from the research sector (just not in the UK…).
- Commercial manufacturers will ALWAYS follow the money (for sound financial reasons):
  - No commercial carbon solutions.
  - No proton CT systems.
  - No fast beam switching.
  - No "novel" accelerator solutions.
  - Lots of work integrating existing solutions: in-room X-ray CT, multi-leaf collimators, robotic couches etc.
- So if you want to develop new technology, it needs to be reasonably mature before you can interest any of the commercial partners!
- Building it yourself is another option: anybody have a spare £250m…?
- Also need to address the question of clinical approval: this never comes as quickly as you'd hope (see Mevion, ProTom).
- Innovation sorely lacking in the UK in this area: will need significant public investment before we can get to a stage of commercial viability.
- STFC, it's over to you…

Acknowledgements

- My thanks to the following people for providing me with information (most of it without their knowledge…):

- Department of Health:
  - Adrian Crellin
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- UCLH:
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  - Yen-Ch'ing Chang
  - Ivan Rosenberg
  - Derek D'Souza
- UCL:
  - Gary Royle
  - Robert Speller
  - Chamkaur Ghag
  - Ruben Saakyan
  - David Waters
  - Mark Lancaster
- Christie:
  - Ran Mackay
- Manchester:
  - Hywel Owen

Thank You