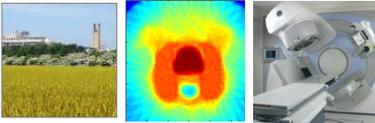


Cambridge University Hospitals **NHS**  
NHS Foundation Trust

## Radiotherapy Physics

Dr Simon Thomas.

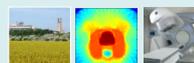


Innovation and excellence in health and care

Addenbrooke's Hospital | Rosie Hospital

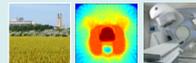
### Overview of lectures

- What is Radiotherapy?
- Example of problem to be solved – prostate cancer
- Trade-off between tumour control, and normal tissues
- External beam therapy with x-rays
  - Simple treatment plans
  - Intensity Modulated Radiotherapy (IMRT)
  - Image Guided Radiotherapy (IGRT) with x-ray imaging
- Image guided radiotherapy with MRI imaging
- Brachytherapy – treatment with radioactive sources
- Particle Therapy
  - Electrons
  - Protons



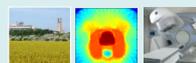
## What is Radiotherapy?

- The use of radiation to treat disease
- The vast majority of radiotherapy is for the treatment of cancer, so this is what I will talk about.
- Of those patients who are cured of cancer, surgery is the most important treatment (about 50% of cures), followed by radiotherapy (about 40% of cancer cures), with chemotherapy a poor third.
- 50% of cancer patients would benefit from having radiotherapy (either for cure or palliation) at some part of their cancer treatment.
- Often used in combination with other treatments.

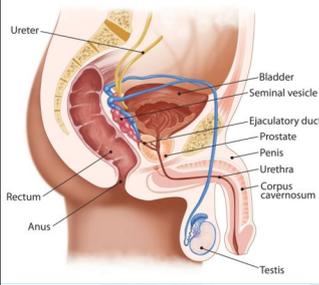
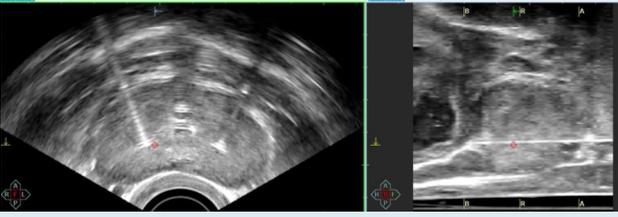
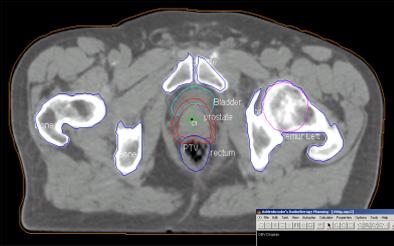


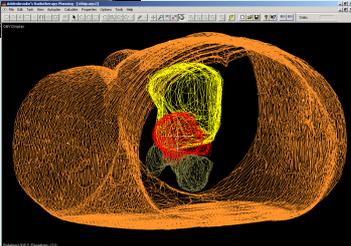
## Clinical sites

- Radiotherapy is widely used for the following tumour sites
- Breast cancer
- Prostate cancer
- Gynaecological cancer
- Head and Neck cancers
- Brain /CNS cancers
- Lung cancers
- Plus many other rarer sites
- Throughout this lecture I will illustrate things primarily with examples from prostate cancer, except for a few examples where the technique is relevant only to some other body site.



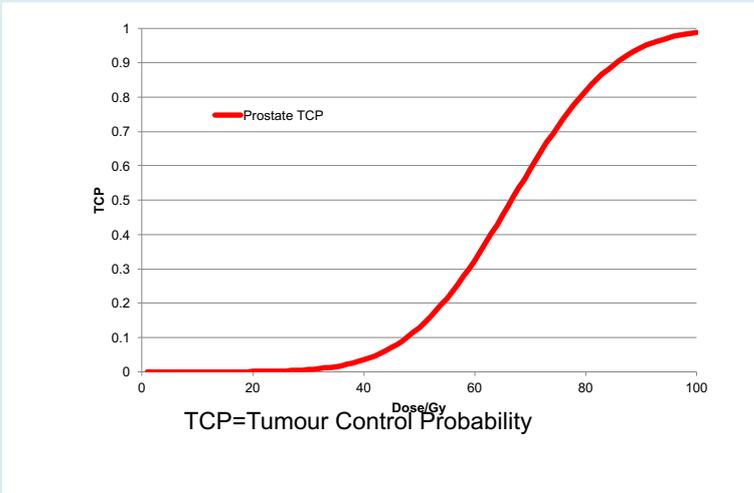
## Prostate



Very close to both bladder and rectum.  
Cancer can spread into Seminal Vesicles

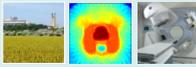
## Probability of destroying the cancer increases with dose



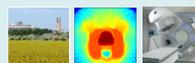
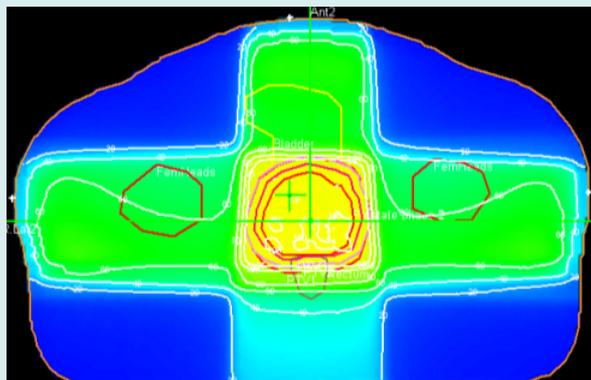
Dose (Gy)	TCP (Probability)
0	0.00
20	0.00
40	0.05
60	0.40
80	0.85
100	1.00

TCP=Tumour Control Probability

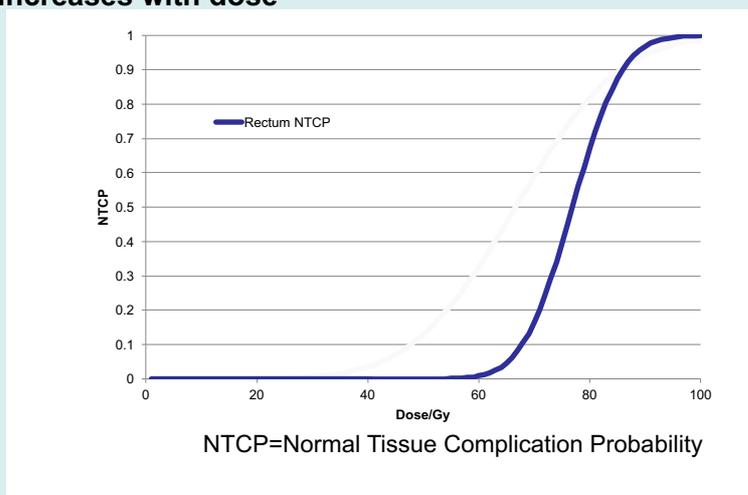
Doses are given in daily "fractions" of a lower dose, typically 2Gy. So 74Gy would be given in 37# over 7.4 weeks



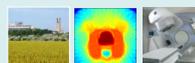
Unfortunately we can't always give the dose that would be certain to destroy the cancer, since we also end up irradiating nearby normal tissues – in this example the rectum is getting a high dose when we treat the prostate.



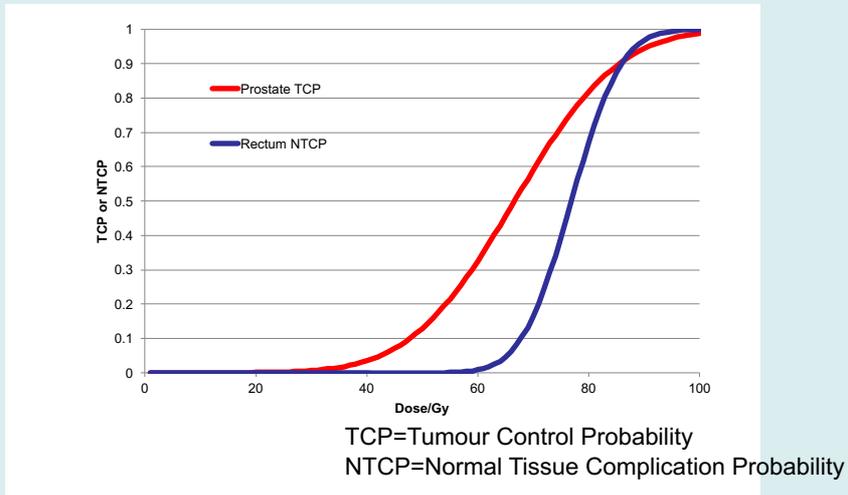
the probability of causing unacceptable side effects also increases with dose



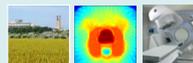
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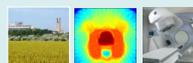
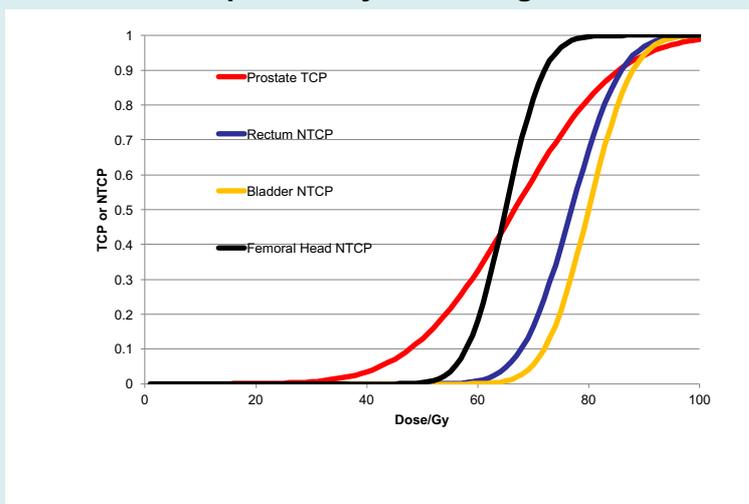
**Probability of destroying the cancer increases with dose  
But so does the probability of causing side effects**



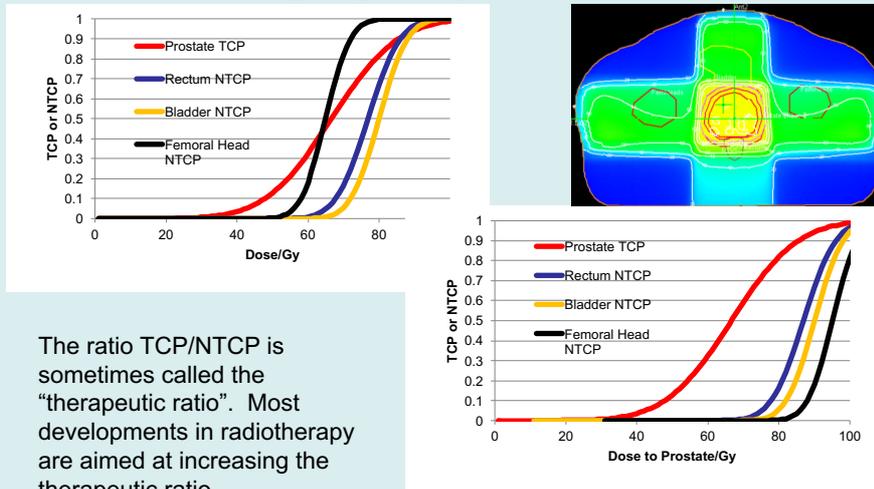
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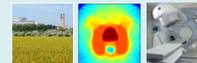
**Probability of destroying the cancer increases with dose  
But so does the probability of causing side effects**



The aim of radiotherapy is to design a treatment solution that gives the organs at risk lower doses than the target, and hence enables us to give a curative dose without getting unacceptable side effects.



The ratio TCP/NTCP is sometimes called the “therapeutic ratio”. Most developments in radiotherapy are aimed at increasing the therapeutic ratio.



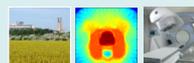
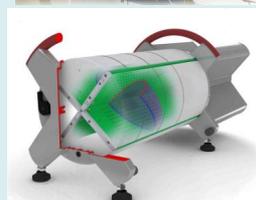
## Safety is very important

- We are giving doses of typically 60Gy to 74Gy.
- Too little dose will fail to destroy the tumour.
- Too much dose, or dose to the wrong part of the patient, will risk serious harm or death.
- (Whole body lethal dose is about 4Gy. Cancer induction about 5% per Sv)
- Diagnostic radiology is dealing in doses of mGy.
- For them a reportable incident is giving more than 250% of the intended dose.
- For us a reportable incident is giving an overdose of 10%



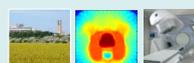
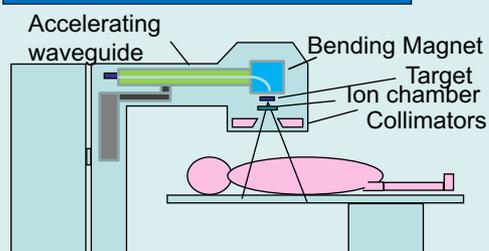
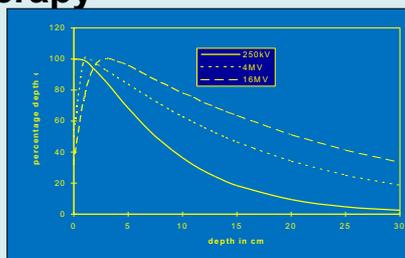
## Safety is very important.

- I've only got time in this lecture to talk about applications of radiotherapy.
- However a lot of the work of a radiotherapy physicist is concerned with
  - Radiation Dosimetry, using detectors traceable to national standards (at NPL) and development of codes of practice to ensure consistency between radiotherapy departments.
  - Regular Quality Assurance measurements on equipment to ensure that it delivers the intended doses to the right place.
  - Patient-specific QA, delivering the radiation plan to a phantom, to ensure that we do what we think we are doing.



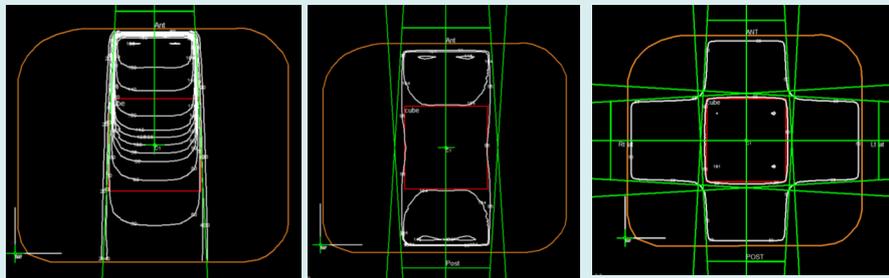
## External beam radiotherapy

- The vast majority of radiotherapy treatments are done with linear accelerators that produce beams of x-rays by accelerating electrons to between 4MeV and 16 MeV and firing them into a metal target.



The machines at Addenbrooke's use 6MV or 10MV

### Simple radiotherapy

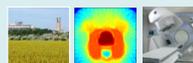


one beam

two opposed beams

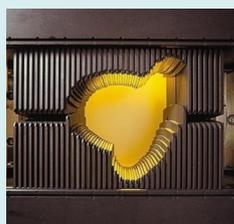
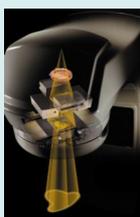
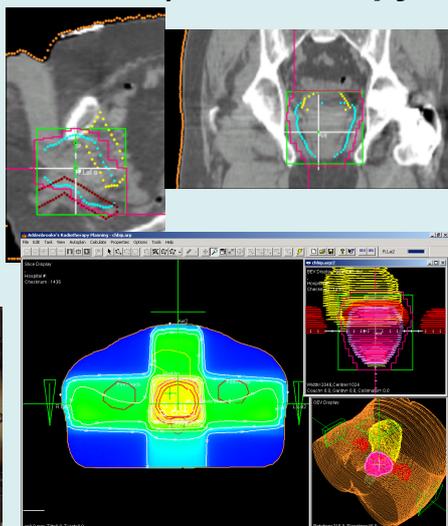
four beams

Until the late 1990s, most radiotherapy was given with square or rectangular fields, and at best looked like the distribution on the right. This enabled a uniform dose to the target, and about 50% of this to a large area outside. We tended only to be able to plan in 2D.



### Slightly less simple (“conformal”) radiotherapy.

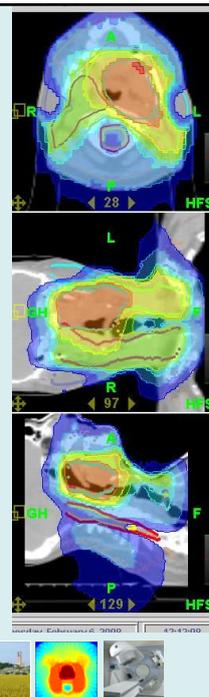
- By the late 1990s, multi-leaf collimators (MLCs) and 3D planning systems were available.



Able to shape fields to spare far more of the rectum and bladder. This enabled us to go up from 64Gy to 74Gy

## Intensity Modulated Radiotherapy (IMRT)

- As well as shaping the field, an MLC can be used to vary the intensity of radiation in the field by being in the field for only part of the treatment.
- This gives the planning system many more degrees of freedom.



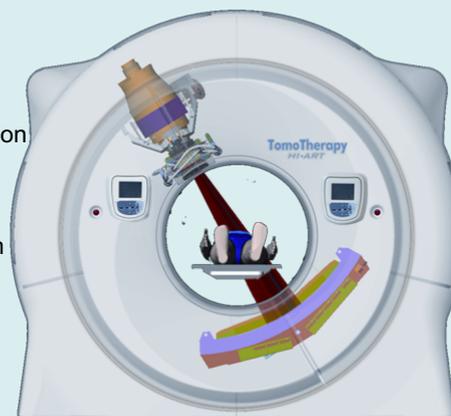
## Types of IMRT

- Multiple static fields (“step and shoot”)
- Dynamic MLC (“Sliding window”) – similar, but radiation stays on whilst MLCs move. Faster, but more to go wrong.
- Rotational IMRT – gantry rotates continuously whilst beam on and MLC varies. Known as “Rapid Arc” or “VMAT” (volumetric modulated arc therapy)
- Tomotherapy – Rotational IMRT on non-standard linac, with CT-like gantry and helical delivery.



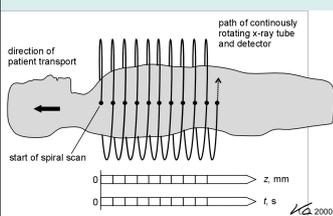
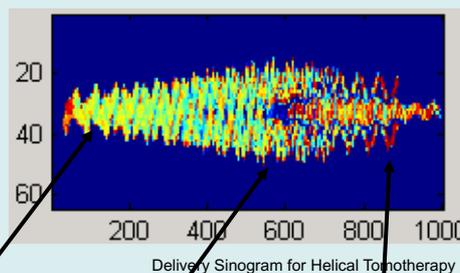
## Helical Tomotherapy

- Purpose-built, integrated device for IMRT & IGRT (of which more later)
- Helical delivery
  - Fast
  - Potential for high level of modulation
- Designed for IMRT
  - Low leakage/scatter
  - No flattening filter => simple beam modelling

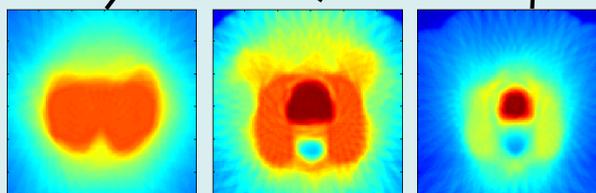


## Tomotherapy –IMRT delivery

- Based on same idea as spiral CT
- 50-300 rotations, treated as 51 projections per rotation.
- At each projection, choose how long each of the 64 binary MLCs is open for



Spiral CT

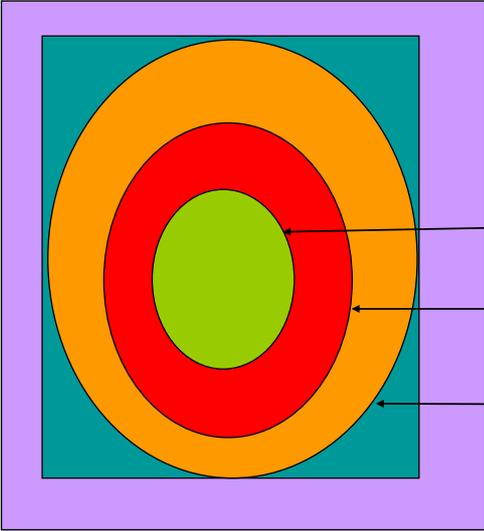


Giving high dose to prostate, medium dose to nodes, and sparing the rectum.

## Geometric uncertainty

The CTV is a tissue volume that contains a demonstrable Gross Tumour Volume (GTV) and/or subclinical malignant disease, which has to be eliminated. This volume thus has to be treated adequately in order to achieve the aim of radical therapy. (ICRU62)

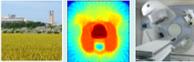
The PTV is a geometrical concept used for treatment planning, and it is defined to select appropriate beam sizes and beam arrangements, to ensure that the prescribed dose is actually delivered to the CTV



Gross Tumor Volume

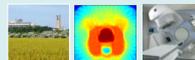
Clinical Target Vol.

Planning Target Vol.



## Types of errors

- Gross errors
  - include incorrect anatomical site or patient orientation, incorrect field size, shape or orientation or incorrect isocentre position of 3 standard deviations or more of the random error.
- Systematic errors
  - occur in the same direction and are of a similar magnitude for each fraction throughout the treatment course. They may arise due to target delineation error, a change in the target position, shape and size, phantom transfer errors or set up errors.
- Random errors
  - vary in direction and magnitude for each delivered treatment fraction. They arise from varying, unpredictable changes in the patients position, internal anatomy or equipment between each delivered fraction. (Radiotherapy usually delivered over a large number of daily fractions)



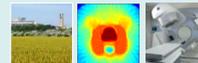
### Margin Recipe

- For a group of patients, determine the standard deviations of random errors  $\sigma$  and of systematic errors  $\Sigma$ . Also need to know how sharp the penumbra is (characterized by  $\sigma_p$ ).

$$\text{margin} = 2.5\Sigma + 1.64 \left( (\sigma^2 + \sigma_p^2)^{0.5} - \sigma_p \right)$$

$$\text{margin} \approx 2.5\Sigma + 0.7\sigma$$

- Systematic errors are worse than random errors

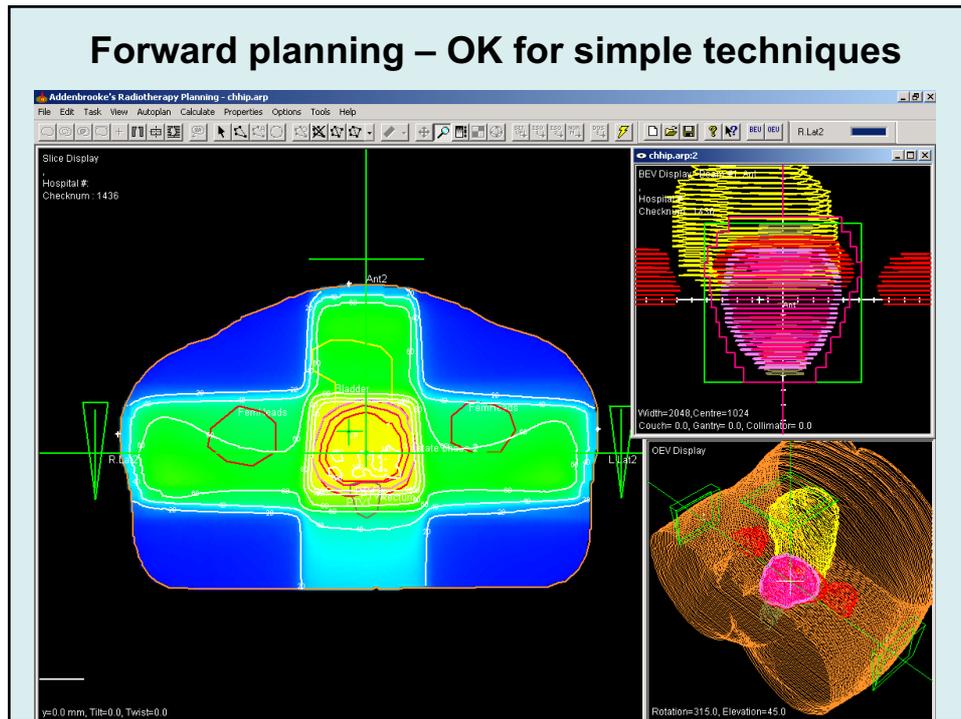


### Practical process of radiotherapy treatment planning.

- CT scan (and possibly MRI and/or PET)
- Outline on the images to delineate the target volumes and organs at risk.
- Add CTV margin for microscopic spread
- Add appropriate margins for geometrical uncertainty.
- Decide on appropriate doses
- Choose appropriate arrangement of beams
  - either: Forward Planning (choose arrangement of beams until you get what you want).
  - or: Inverse Planning (specify what you want, and get the computer choose the beams to achieve it).

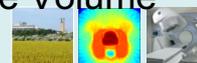


## Forward planning – OK for simple techniques



## Inverse planning

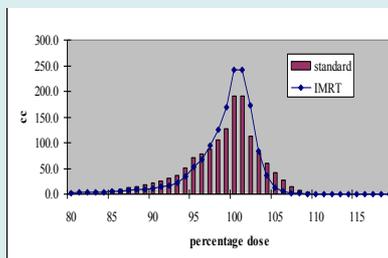
- IMRT is too complex to just choose arrangement of beams manually until the plan “looks OK”
- Instead have software that optimises the plan to produce the “best” treatment plan
- For this to work, you need to have some measure of what makes a good plan; you need some mathematical objective function that you can minimise.
- These can be based on Dose (minimum, maximum etc. to volume), or on Dose Volume Histograms



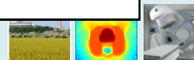
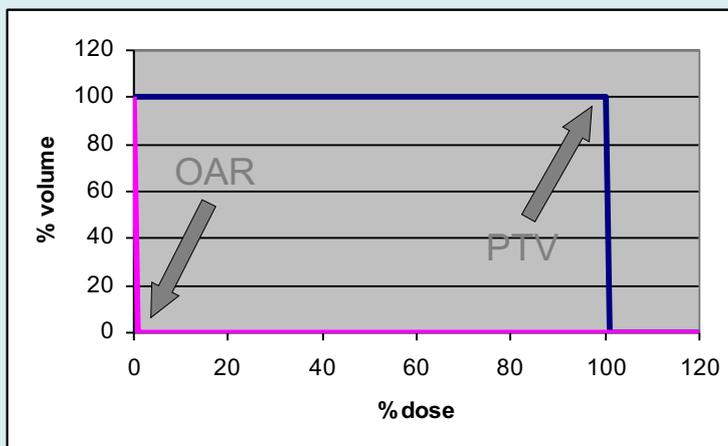
### Dose Volume Histograms

Either:

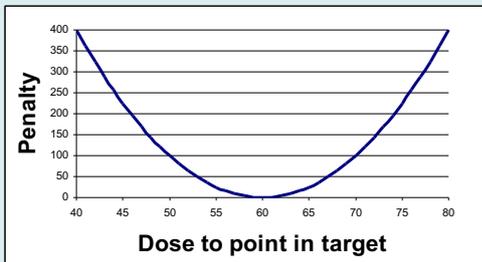
- What volume receives a particular dose (differential DVH)
- What volume receives *at least* a particular dose (cumulative DVH)



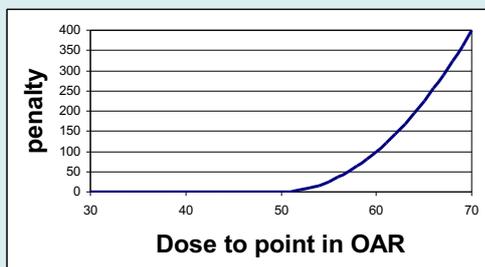
### The Ideal DVH



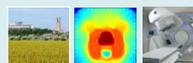
### Dose-based penalty



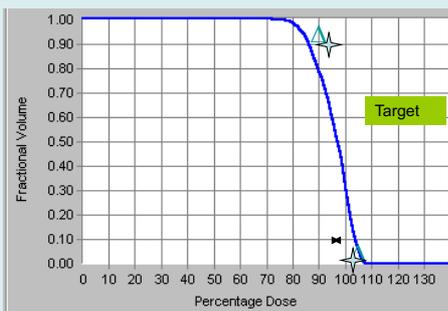
Penalty increases with square of difference.



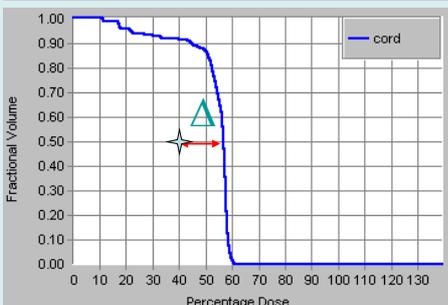
OAR has no penalty for under dosing.



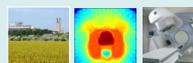
### DVH objectives and constraints



- Target
  - At least X% of the target should receive at least dose Y
- OAR (and some targets)
  - No more than X% of the volume should receive more than dose Y
- Hard Constraint
  - If it does not achieve the constraint, then do not allow the solution.
- Objective or soft constraint
  - Apply a penalty for failure, increasing the more you fail

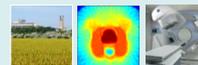


- $penalty = w \Delta^2$ 
  - The larger w the harder the constraint



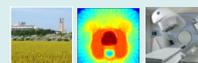
## Optimise to reduce objective function

- Gradient based – (need to be able to take derivative of objective function relative to weight of all the sub-beams). Relatively fast, but can potentially get trapped in local minima
- Stochastic (e.g. simulated annealing) – much slower, but less risk of local minima.
- In practice you need to keep modifying your objective function to produce a clinically acceptable plan – mathematically optimal is not always clinically optimal.

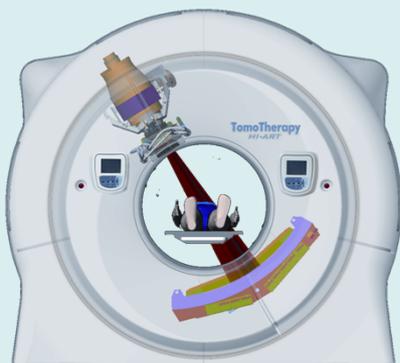


## Image-guided Radiotherapy

- If you can image the patient every day in the treatment position, you can reduce the systematic and random errors. This should enable a smaller margin to be used, and hence reduce normal tissue damage.
- Image patient from exit beam.
- Can reconstruct CT-image
  - Cone-beam using detector on conventional linac
  - Dedicated “tomotherapy unit” based on CT gantry



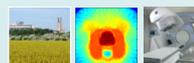
# IGRT



MV helical CT on Tomotherapy unit



kV cone-beam CT on Elekta Synergy.



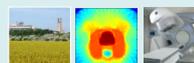
# IGRT

The screenshot displays a software interface for image registration and dose distribution. It includes several panels:

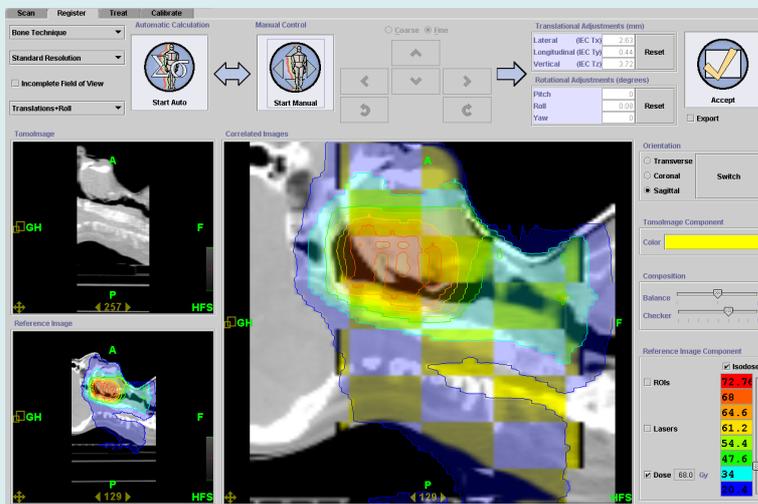
- Control Panel:** Features buttons for 'Start Auto' and 'Start Manual', and a 'Translational Adjustments (mm)' table:
 

Lateral (EC Tx)	2.53	Reset
Longitudinal (EC Tx)	0.44	Reset
Vertical (EC Tx)	3.23	Reset
- Image Views:** Shows 'Tomotherapy' and 'Reference Image' in sagittal views, with a 'Correlated Images' view showing the two images overlaid. A yellow region highlights the target area.
- Orientation:** Radio buttons for Transverse, Coronal, and Sagittal (selected).
- Reference Image Component:** A color-coded scale for 'Isodose' levels:
 

72.74
68
64.6
61.2
54.4
47.6
34
20.81

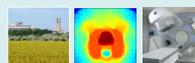


## IGRT



### Effect of IGRT on margins

- Daily imaging should reduce both the systematic and random positional uncertainties.
- However there are still a number of residual uncertainties.



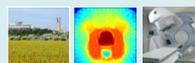
## What remains after daily IGRT?

Systematic:

- *(Doctor Delineation Error)* – will assume this is completely in the CTV.
- Intrafraction Motion
- Systematic Matching Error (Intra- and Inter Observer)
- Treatment Beam / Imaging System misalignment
- Systematic Rotational Shifts
- Couch Drive Inaccuracy

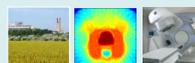
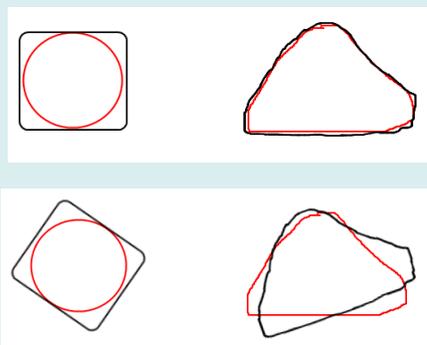
Random:

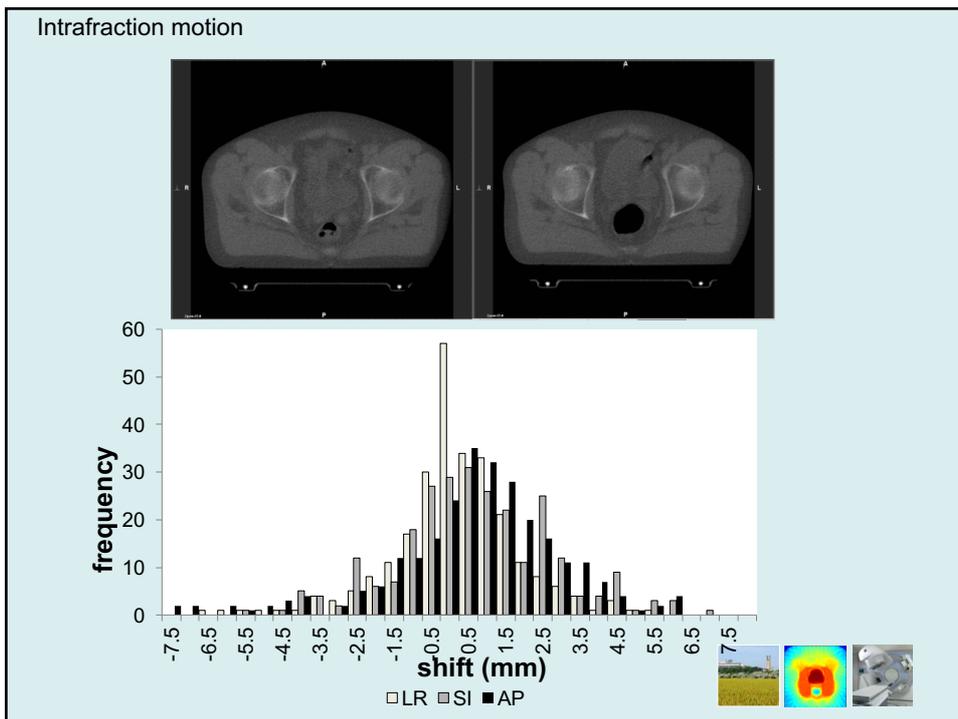
- Intrafraction Motion
- Random Matching Error (Intra / Inter)
- Random Rotational Shifts
- Couch Drive Inaccuracy



## Rotations

Residual rotations can be an important source of residual error, dependent on shape





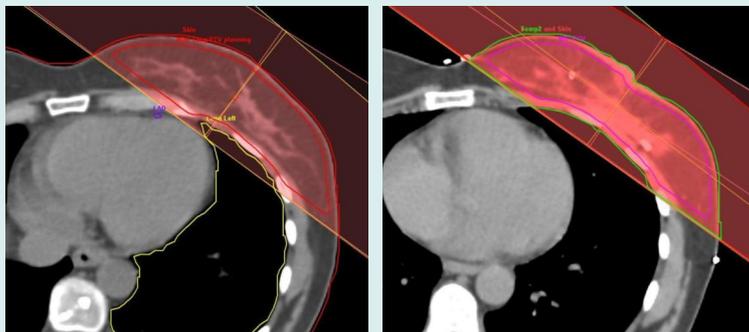
## Combined effect of residual errors

A	B	C	D	E	F	G	H	I	J	K	L	M	N
1	Error	Quantity Required	Value			Incremental Margin Contribution			Other Parameters Required				
2			Isotropic	Lateral (mm)	Craniocaudal (mm)	Anteroposterior (mm)	Lateral	Craniocaudal	Anteroposterior	Lateral Estert (mm)	Craniocaudal Estert (mm)	AP Estert (mm)	Asphericity Factor
3			X	Y	Z								
4	Treatment Beam / Imaging System	Top-Hat half-width (mm)	0.4				3%	2%	2%				
5	Systematic Matching Error	Standard Deviation of difference between two observers (equivalent to true positional error / sqrt(2) (mm))		0.5	0.5	0.5	7%	4%	4%				
6	Systematic Intrafraction Motion	Standard Deviation of difference (mm)		1.1	0.6	0.8	38%	10%	10%				
7	Systematic Rotational Shifts	Standard Deviation (degrees)		6.6	0.6	2.4	5%	30%	23%	50.0	50.0	50.0	0.3
8	MLC Positional Variation	95% confidence (mm)	0.0				0%	0%	0%				
9	Motion relative to surrogate	Standard Deviation (mm)		0.0	0.0	0.0	0%	0%	0%				
10	Couch Dive Inaccuracy	Top-Hat half-width (mm)	0.3				2%	1%	1%				
11	Intrafraction Motion (no Inter-Observer Matching Error)	Standard Deviation of difference (mm)		1.3	2.0	2.2	7%	7%	13%				
12	Inter-Observer Random Matching Error	95% confidence with respect to "true" target position (mm)		4.6	0.3	1.5	0%	0%	0%				
13	Random Rotational Shifts	Standard Deviation (degrees)		4.6	0.3	1.5	0%	1%	2%				
14	MLC Positional Variation	95% confidence (mm)	0.0				0%	0%	0%				
15	Motion relative to surrogate	Standard Deviation (mm)		0.0	0.0	0.0	0%	0%	0%				
16	Couch Dive Inaccuracy	Top-Hat half-width (mm)	0.3				0%	0%	0%				
17	Mean	Mean Intrafraction Motion	Population Mean (mm)	0.0	0.5	0.5	0%	13%	13%				
18	$\sigma_p$	Penumbra Width	"1-sd" (mm)	3.7	6.3	3.7							
19			Margin (mm):	2.6	3.7	3.9							
20													
21		More Data Required											
22		Reasonably Robust Data											
23		All interobserver error usually allocated to systematic error to ensure conservative estimate											
24													

Site: Prostate Gland  
Unit: Tomo  
IGRT: Daily, online MVCT

Even with IGRT, margins of up to 5mm may be needed.

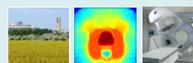
## Breathing motion (example from breast cancer)



Free breathing

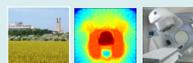
Deep inspiration breath hold

In normal breathing, the left breast is very close to the heart. By getting the patient to control her breathing, so that imaging and treatment is given only at deep inspiration, it is possible to spare the heart.

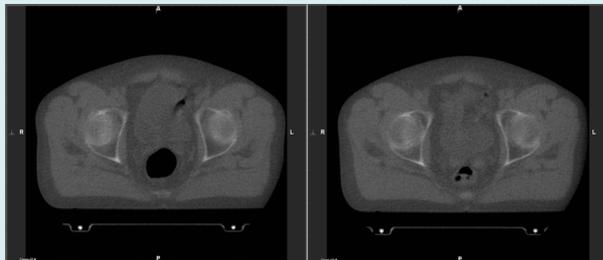


## Relationship between delivered dose and toxicity

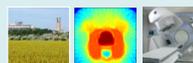
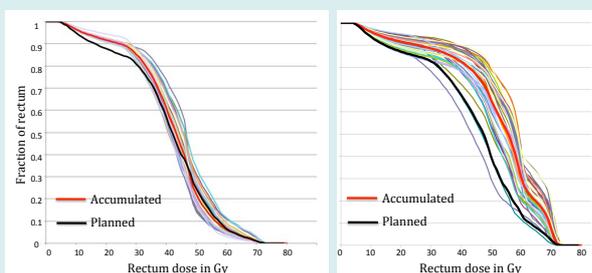
- The DVH constraints on the rectum are based on studies that link the doses in the treatment plan with clinical data on side effects.
- But for organs like the rectum the shape changes from day to day. So the doses actually received by the rectum may differ considerably from the dose in the treatment plan.
- The VoxTox project is collecting data on a few thousand patients, using the daily IGRT data to determine the dose to organs at risk, and collecting detailed toxicity data.



## Accumulated DVH can be different from Planned DVH



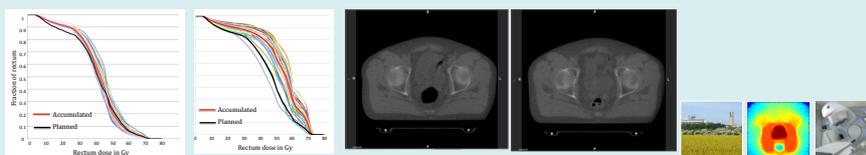
- Some patients have a fairly consistent rectal shape over the 7 weeks of treatment
- Some patients have more of the rectum in the high dose region than at planning
- Some have the opposite.



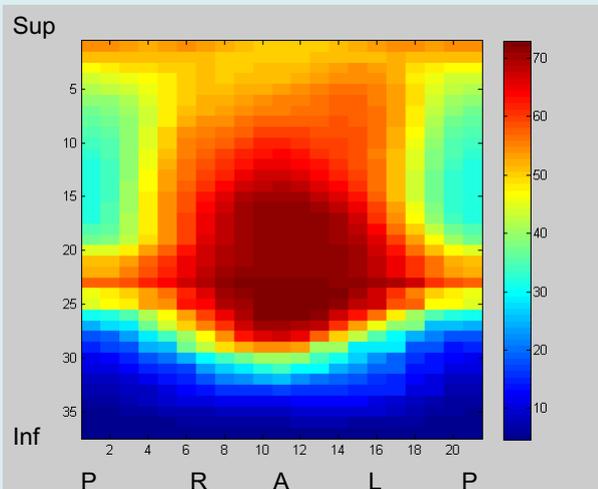
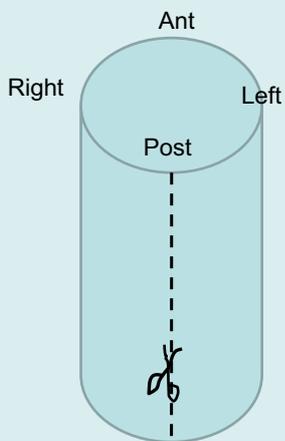
## Problems with the use of DVH

- Combining DVHs from different fractions by adding them up is not correct
- The part of the rectum receiving the high dose in one fraction may not be the same as in another fraction
- However the MV CT is not good enough to enable us to identify which voxel in one CT set maps to which voxel in another CT set
- The Dose **Volume** Histogram suffers from the problem that much of the volume included is rectal contents (gas and faeces). The dose to these is not clinically relevant, only to the rectal wall.
- However the MV CT images are not good enough to distinguish the inside and outside of the rectal wall separately.

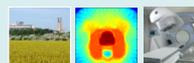
- One potential solution to these problems is the use of the normalised dose surface map (DSM)



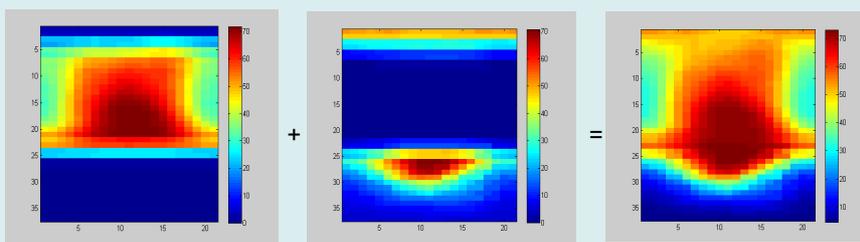
## Dose Surface Maps



Plot the dose on the surface that would be achieved by cutting along the posterior side of the rectum, and stretching to normalise



## Dose Surface Maps over 37 fractions

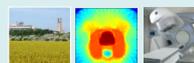


Summed MV DSM

kV DSM where MV not available

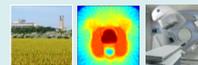
final summed DSM

•We are working to correlate the measured toxicities with whatever parameters in the summed DSM give the best predictive measure. The ultimate aim is to identify part way through a treatment whether it is safe to give extra dose.



## Fractionation in radiotherapy

- If radiation given as a course of small “fractions” of radiation, recovery occurs between fractions
- If normal tissue can recover more quickly than tumour, this improves the therapeutic ratio
- Most fractionation schemes are empirical, based on clinical experience



## Linear Quadratic theory

$$\ln(\text{target cell survival}) = -(\alpha d + \beta d^2)$$

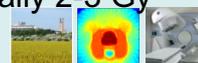
- If dose  $D_x$  is given in fractions of  $d_x$ , this gives equivalent cell killing to a dose of  $D_2$  in 2 Gy fractions, where

$$D_2 = D_x \frac{(\alpha/\beta + d_x)}{(\alpha/\beta + 2\text{Gy})}$$

- can also define a Biologically Equivalent Dose equal to dose in notional tiny fractions

$$BED = D \left( 1 + \frac{d}{\alpha/\beta} \right)$$

- $\alpha/\beta$  is typically 10-20Gy for tumours, typically 2-3 Gy for later-responding side effects



## Linear Quadratic theory

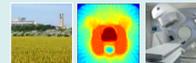
$$BED = D \left( 1 + \frac{d}{\alpha/\beta} \right)$$

$\alpha/\beta$  is typically 10-20Gy for tumours,  
typically 2-3 Gy for later-responding side  
effects

e.g. D=60Gy d=2Gy per #  
BED = 72 Gy if  $\alpha/\beta$  =10Gy  
BED = 99.96 Gy if  $\alpha/\beta$  =3Gy

e.g. D=36Gy d=6Gy per #  
BED = 72 Gy if  $\alpha/\beta$  =10Gy  
BED = 108 Gy if  $\alpha/\beta$  =3Gy

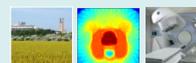
Giving a higher dose in smaller fractions  
can help to reduce the side effects



## $\alpha/\beta$ = approx 2-3Gy for prostate (and for normal tissues)

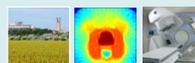
$$BED = D \left( 1 + \frac{d}{\alpha/\beta} \right)$$

- Using a value of 2.5
- 74 Gy in 37# (2Gy per #)
- BED= 133Gy
- 60Gy in 20# (3Gy per #)
- BED= 132Gy
- A recent large-scale clinical trial on prostate cancer showed that 74Gy/37# and 60Gy/20# has indistinguishable clinical outcomes.



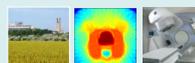
## MRI linacs

- Current area of interest is putting a linear accelerator and an MRI scanner together, to enable MRI-guided radiotherapy.



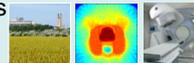
## Reasons for doing IGRT with MRI - guidance

- No worries about the imaging dose
- Can therefore image during irradiation
- Many structures more visible on MRI than on CBCT
  - Soft tissue contrast generally better with MRI than CT
- Potentially able to image moving targets in real time
- Functional imaging may allow for adaptive focal boosting



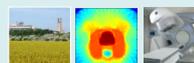
## Reasons for not having MRI-guided IMRT

- Linac technology is badly affected by magnetic fields
  - Need to design special magnets to keep field low in vicinity of linac components, whilst still giving uniform field for imaging in the area you are irradiating
- Charged particle interactions are affected by magnetic fields
  - All the dose deposition models used in treatment planning have to be changed. Monte-Carlo models are the only ones that can currently model this.
- Measurement of radiation dose is affected by magnetic fields
  - All the assumptions made in the standard dosimetry chain using ionisation chambers calibrated by NPL cease to be valid in the presence of high magnetic fields.
- MRI images cannot be directly used for radiotherapy dose calculation
  - Radiotherapy dose calculation requires information on relative electron density, which is easy to obtain from CT, but not from MRI.
  - Geometric distortion more of an issue in MRI than in CT
- Vastly more expensive than conventional x-ray guided linacs

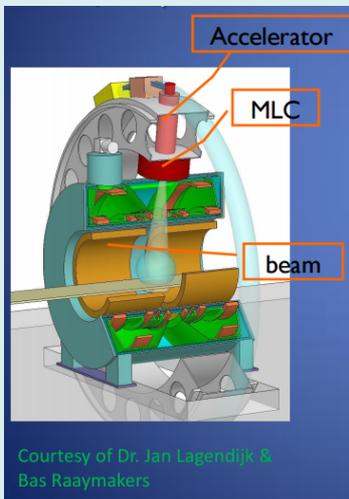


## 4 groups working on developing MRI linac

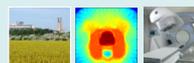
- Elekta/Philips consortium. Collaboration between major linac manufacturer and major MRI manufacturer. Using 1.5T magnet. Research systems installed in several hospitals (Utrecht, Amsterdam, Manchester, Royal Marsden, MD Anderson Texas, Wisconsin, Sunnybrooke). Not yet licensed for non-research clinical use.
- ViewRay. New company – initially clinical with a Co-60 gamma unit, now a linac, combined with a 0.35T magnet. Has FDA clearance for clinical use. Installed in a few US centres.
- Australian Group. Prototype only. 1.5T magnet in an inline configuration – radiation axis along same axis as magnetic field (first two are perpendicular)
- “Aurora” – Being developed by Canadian company, 0.5 T inline.



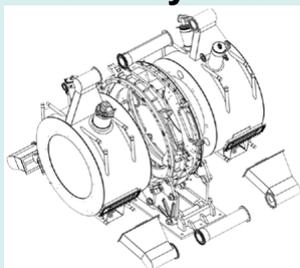
## Elekta/Philips MRI-linac at 1.5T



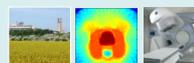
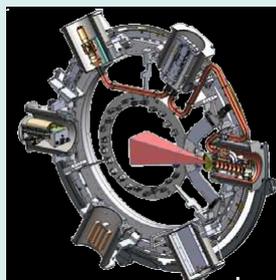
- Active magnetic shielding to avoid any magnetic field at the electron gun, and to minimise field along accelerator tube.
- Split gradient-coil design to allow beam to go through.
- Linac mounted on rotatable gantry outside the MRI magnet.
- Many compromises to design of linac and MRI to enable each to work with the other.



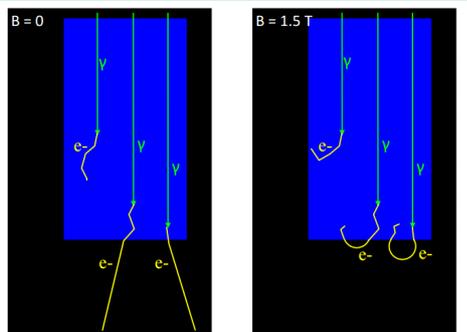
## View-Ray 0.35T system



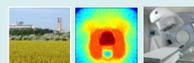
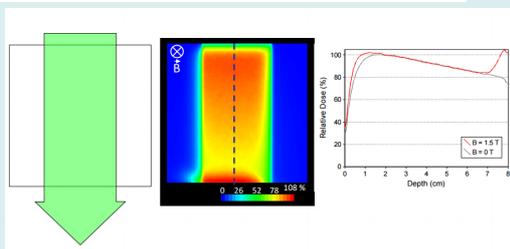
- Split superconducting magnet – less obstruction to beam path
- Lower field – avoids some of the dosimetric problems with high field systems, at a price of worse image quality



### Electron return effect



- Dose in x-ray therapy is nearly all from photons liberated by Compton scattering or Photoelectric effect
- In a magnetic field the path of these electrons is curved by the Lorentz force
- This can lead to unexpectedly high doses at exits of beam.
- This effect is less at lower field strength
- Inline magnets avoid this, but for multiple field directions you need to rotate the entire magnet system (or rotate the patient).



### Effect of magnetic field on radiation detectors

- Dose response of ionisation chambers is changed by presence of magnetic field.
- Most of the assumptions made in the theory of ionisation chambers are not valid in the presence of magnetic fields.
- The response of a chamber varies with orientation and with field strength, by over 10%

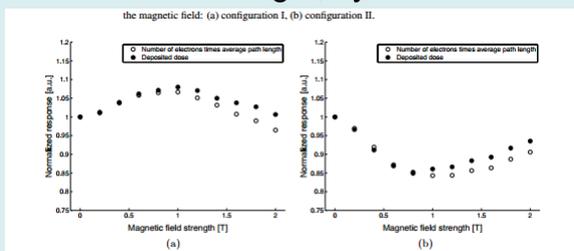
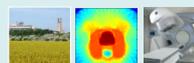
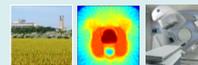


Figure 6. Relative response determined by the product of the number of electrons and the average trajectory length in the chamber as a function of the magnetic field together with the scored dose deposition in the chamber: (a) configuration I, (b) configuration II.

This is one of the many challenges that make MRI linacs an interesting research area, but not yet necessarily the best option for clinical treatment.



## Brachytherapy

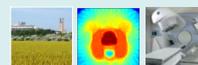


### What is Brachytherapy?

The placement of radiation sources in or near the patient.

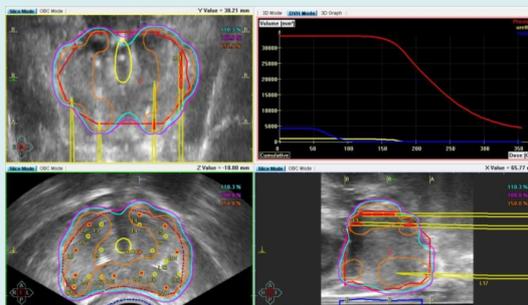
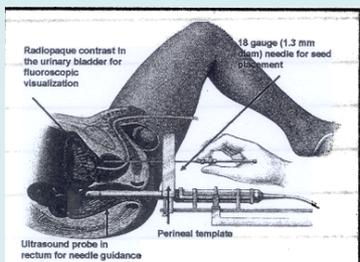
Three categories :-

- 1) Interstitial - sources surgically implanted in and around tumour. e.g. iridium in breasts. iodine seeds in prostate
- 2) Intra-cavity - sources placed inside natural body cavity. e.g. Ca cervix treated with uterine / vaginal sources.
- 3) Mould - the use of surface applicators to hold sources next to patients skin. e.g. skin tumours

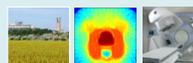


## Interstitial Brachytherapy

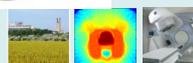
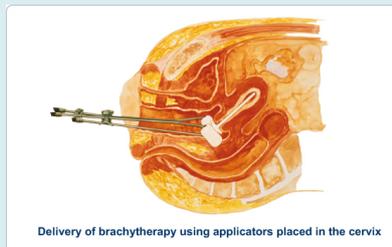
- Radiotherapy delivered by radioactive seeds implanted into the patient



- For early stage prostate cancer which has not spread into the seminal vesicles, brachytherapy (with I-125 seeds, gamma energy 30keV half life 59 days) can give a high dose to the prostate whilst sparing the rectum and bladder.

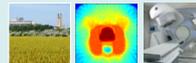


## Intracavity brachytherapy



### Ideal Source for Brachytherapy

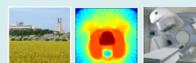
- 1)  $\gamma$ -ray emitter. High enough energy to minimise scatter and avoid increased energy deposition in bone by PE. Low enough energy to minimise protection requirements. This gives the range 200 - 400 keV.
- 2) Half life. Long enough to minimise decay corrections during treatment. Too avoid frequently buying new sources, a very long half-life is desirable. For permanent implants, shorter half-lives are needed.
- 3) Charged particle emissions absent or easily screened.
- 4) No gaseous disintegration products.
- 5) High specific activity
- 6) Insoluble and non-toxic chemical form.
- 7) Does not powder/ disperse if casing damaged.
- 8) Can be made into different sizes and shapes (tubes, needles, spheres, flexible wires). If in wire form must be able to be cut without causing contamination.
- 9) Not damaged during sterilisation.
- 10) Cheap/ easily available.



### Sources - what is available:

Isotopes :-

- naturally occurring.
- reactor produced :- fission products.
- neutron activation (n, $\gamma$ ) products.
  
- Radium and Radon no longer used.
- Most commonly used isotopes are Ir-192 and I-125
- Cs-137, Co-60 and Pd-103 used in some applications



## Commonly used gamma-emitting Nuclides

Nuclide	Co-60	Cs-137	Ir-192	Pd-103	I-125
Transmission through 2cm Pb (%)	19	12	<b>1.9</b>	(<0.1%)	<b>(&lt;0.1%)</b> HVL=1.3cm tissue
Gamma-ray energy (MeV)	1.17 and 1.33	0.66	<b>0.3-0.6 (mean=0.36)</b>	0.02	<b>0.03</b>
Half life	5.3 years	30 years	<b>74 days</b>	17 days	<b>59 days</b>

## Particle Therapy

- Proton Therapy
- Electron Therapy

### Particle Therapy

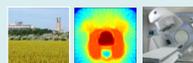
- X-ray interactions (PE, Compton, PP) lead to exponential attenuation over distance.
- Heavy charged particles (e.g. protons), each interaction leads to loss of energy from the charged particle, giving it a finite range in tissue.
- The rate of energy loss from heavy charged particles can be approximated using the Bethe-Bloch formula

$$-\frac{dT}{dx} = \left(\frac{1}{4\pi\epsilon_0}\right)^2 \left(\frac{4\pi z^2 e^4 N Z}{m_e v^2}\right) \left[ \ln\left[\frac{2m_e v^2}{I(1-\beta^2)}\right] - \beta^2 - \frac{C}{Z}\right]$$

*N* = no. of atoms per unit volume  
*Z* = no. of electrons per atom  
 $\beta = v/c$   
*I* = average excitation energy  
*C* = shell correction

- term in square brackets varies slowly with *v*

$$-\frac{dT}{dx} \approx \frac{\text{constant}}{\beta^2}$$



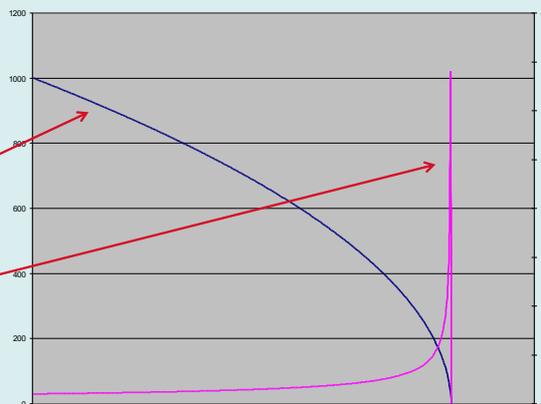
### Bragg Curve

- Very high stopping power at end of track

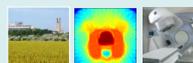
$$\frac{dT}{dx} = \frac{-k}{T}$$

$$T = \sqrt{T_0^2 - 2kx}$$

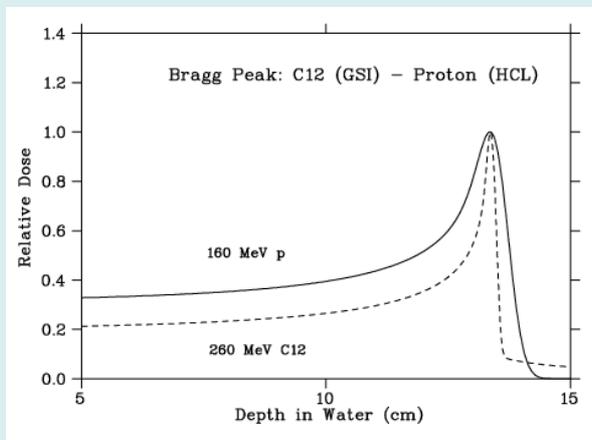
$$\frac{dT}{dx} = \frac{-k}{\sqrt{T_0^2 - 2kx}}$$



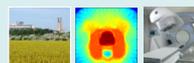
First discovered experimentally by William H Bragg  
 (published December 1904)



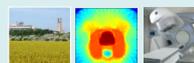
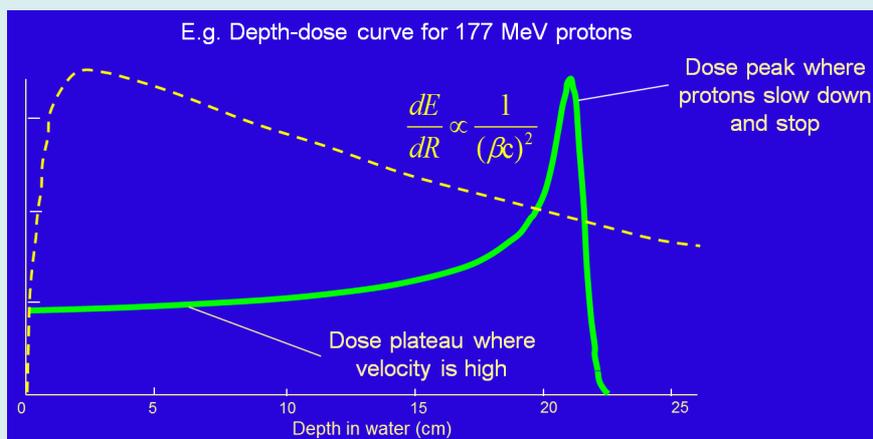
### Bragg curve in practice



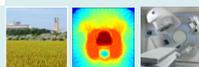
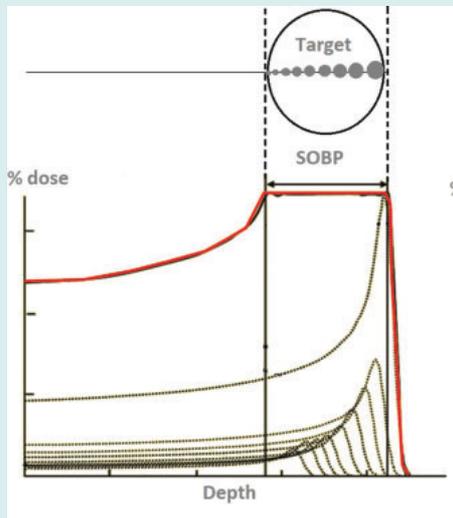
Depth dose curves for protons and carbons-ions: The broad Bragg peak of 160 MeV protons (solid line) exhibits no exit dose. The narrow Bragg peak of 260 MeV carbons ions (dashed line) - shows the distal dose tail caused by light beam fragments



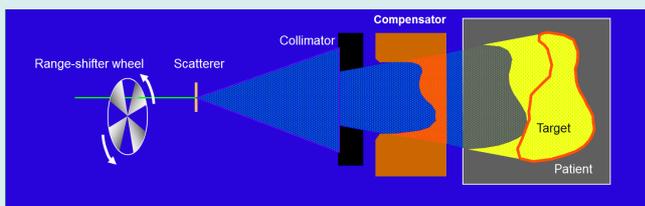
### Protons v photons – depth dose curve



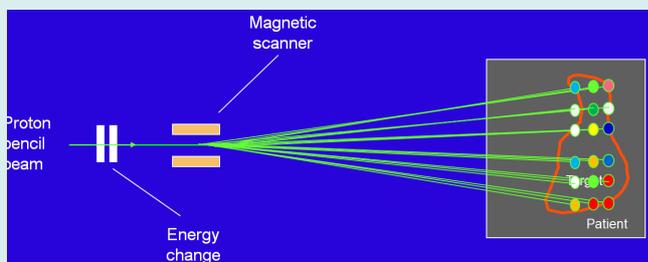
### Extending the peak over a greater range of depths



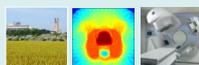
### Passive scattering v pencil beam scanning



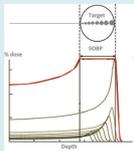
Passive scattering is used in the majority of clinical centres in the world.



Most new centres being build today (including the Manchester and UCL ones) will use pencil beam scanning

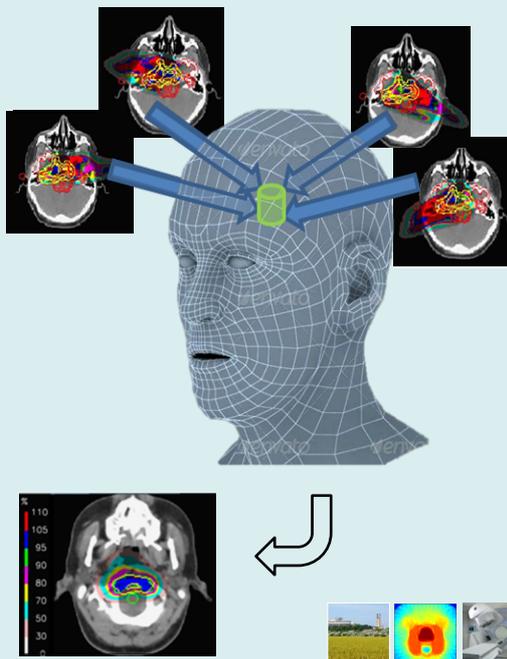


### Proton delivery



A beam from one direction can conform to the target, but will deliver dose upstream of the SOBP

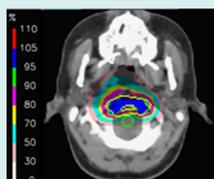
Multiple beams can give very conformal treatments.



### Pros and Cons of Proton Therapy

- Sharp fall-off at end of track gives excellent sparing of organs at risk beyond tumour.
- Some tumours (especially spinal tumours in children) have much lower side effects than with photon therapy

- Much more expensive (capital costs £120million for proton unit £2million for linac. )
- The Radiobiological effectiveness is not well known, and varies with energy. Roughly, 1Gy of protons has the same biological consequences as 1.1 Gy of x-rays
- Variations in density change range, and can cause geographical miss (OK for brains and spines, but large issue if using for prostates).
- The PTV concept needs modifying when used with protons.



Cyclotron (Italy)

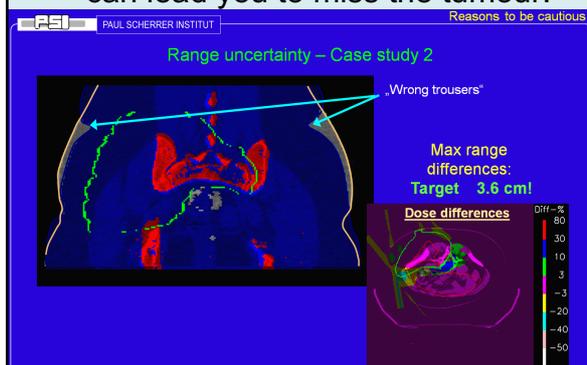


Synchrotron (France)

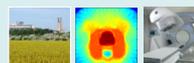


## Range uncertainty

- The fact that protons have a sharp fall-off at the end of their range is great for avoiding normal tissues.
- But a small uncertainty in range (caused by variations in tissue thickness or density) can lead you to miss the tumour.

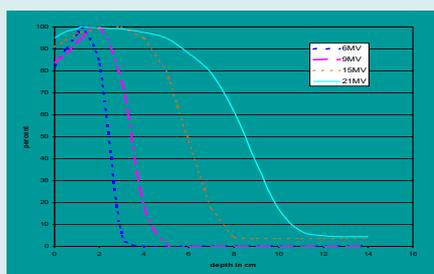


This example (courtesy of Tony Lomax, PSI) shows the difference of dose caused by the patient wearing tighter clothes for the CT scan than for treatment.



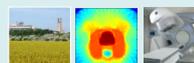
## Electrons.

- Much lighter than protons
  - (e 0.511 MeV p 938 MeV)
- Each interaction causes a change in direction
- Electron tracks are very tortuous
- No Bragg peak is observed for electrons.
- Easy to produce with medical linac (just replace the target with a scattering foil)
- RBE = 1.00



• Fewer clinical applications now than 10-20 years ago, as most cases where electrons were used are now better treated with IMRT.

- Some superficial tumours where electrons are still the best solution
- Some places use them in inter-operative radiotherapy. Some places use them for total skin electron therapy.



## Summary

- Radiotherapy involves the use of ionising radiation to destroy cancer cells without causing unacceptable damage to normal tissue.
- The aim of all advances in radiotherapy are to maximise the therapeutic ratio between control and complication.
- Most Radiotherapy worldwide is given with linear accelerators producing x-rays in the 4MV-25MV range.
- Image Guided Radiotherapy (IGRT) generally uses x-ray CT imaging, but some groups are developing MRI-guided linacs
- Other forms of radiotherapy include
  - Brachytherapy (with radioactive  $\gamma$ -ray sources)
  - Electron therapy (4MeV-25MeV range)
  - Proton therapy (Typical KE of 150-300 MeV)
- Safety is crucial

