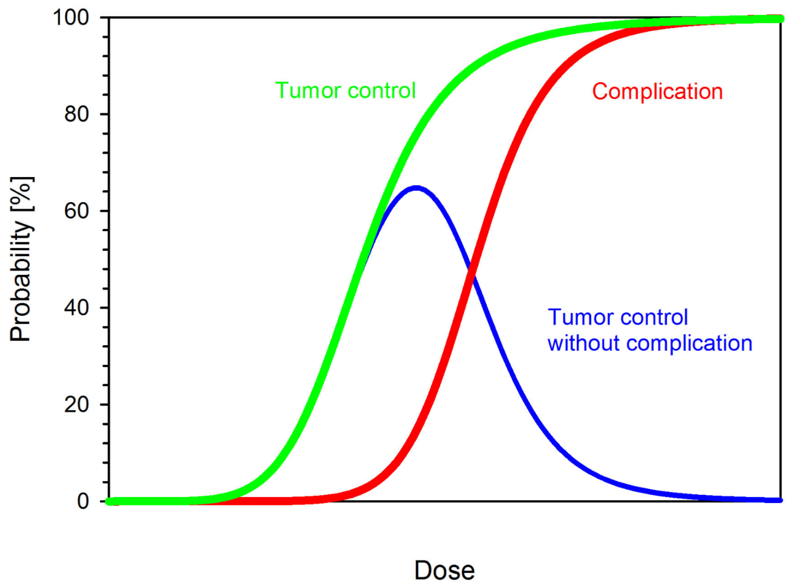

6: State of the art for Conv and Hadron therapy

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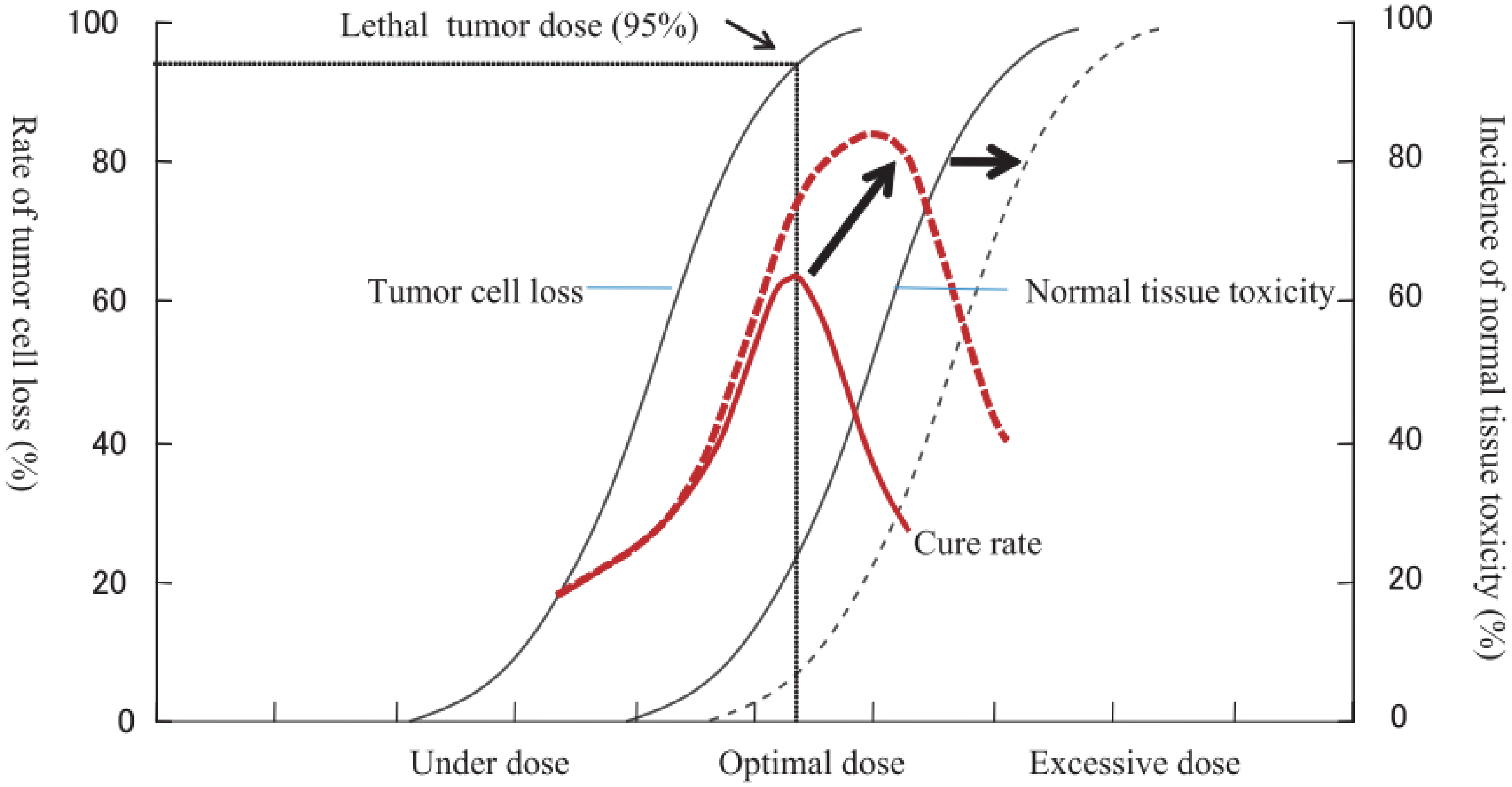
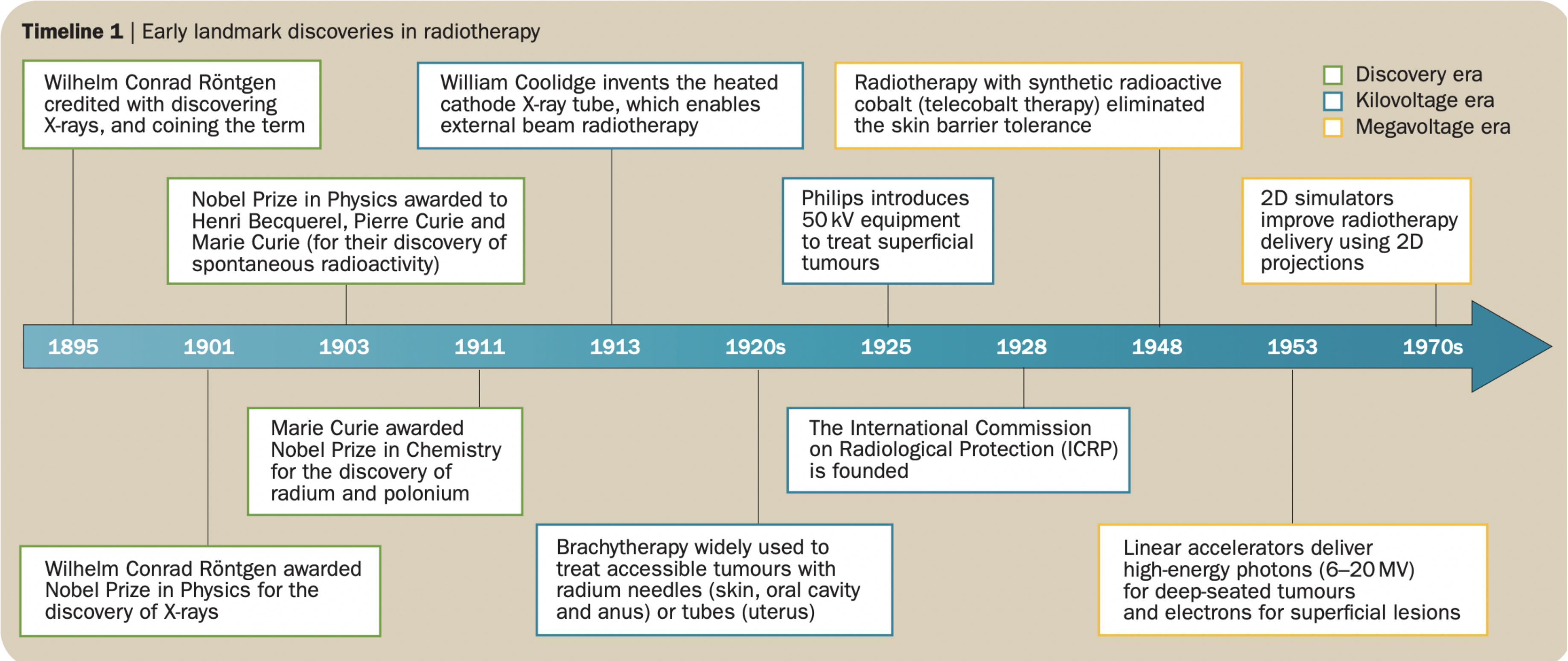
Goal of radiotherapy



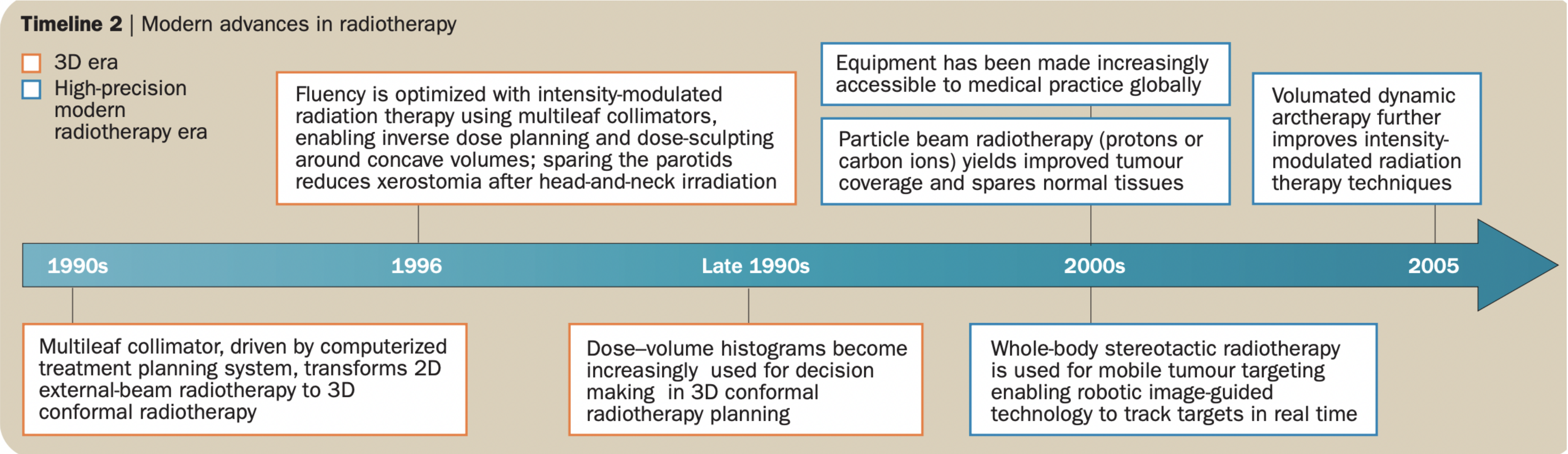
You have seen something similar in the first lesson…
This is just a "kindly reminder":

The cure probability of RT depends on the difference between tumor cell kill and the development of normal tissue toxicity due to radiation

Radiotherapy timeline



Radiotherapy timeline



Radiotherapy timeline

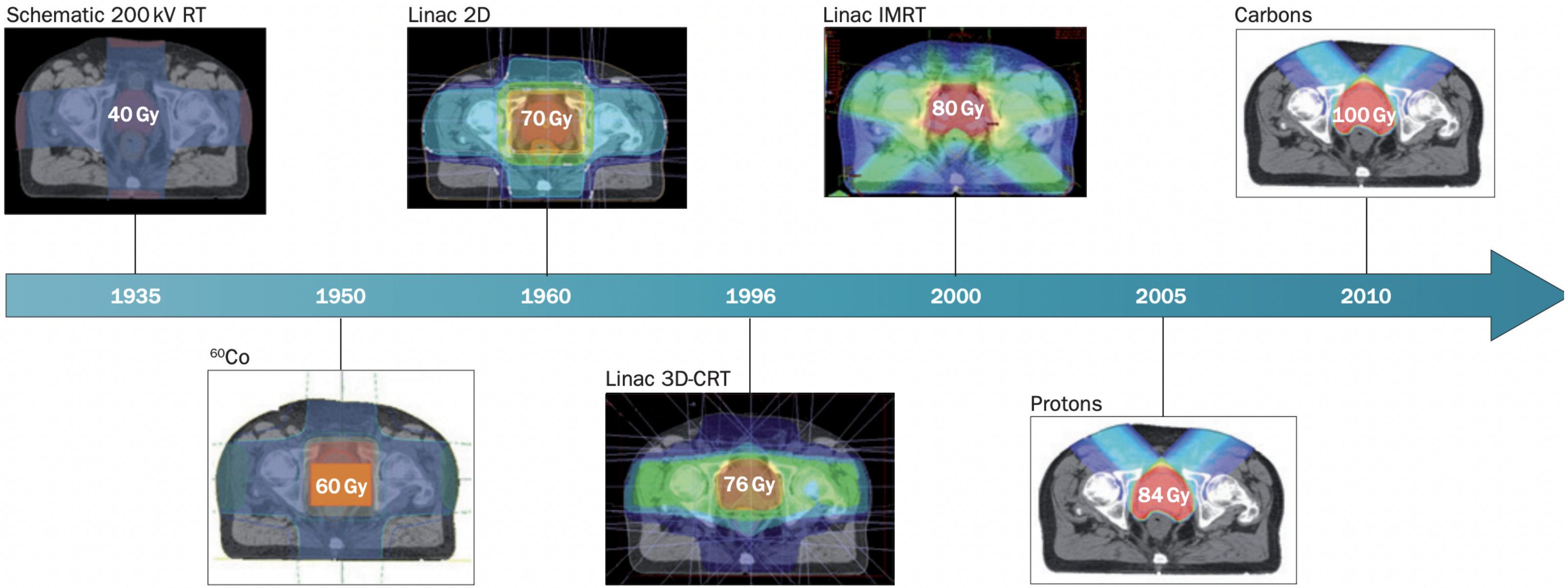


Figure 1 | Prostate cancer radiotherapy 1935–2010. Prostate cancer irradiation is a good example of the improvement of radiotherapy technology over the past decades. By increasing the beam energy and the precision of the targeting, it was possible to escalate the dose to the prostate without exceeding the tolerance dose of healthy tissues; allowing the move from palliative irradiation to curative treatment. Abbreviations: 3D-CRT, 3D conformal radiotherapy; IMRT, intensity modulated radiotherapy; RT, radiotherapy.

https://doi.org/10.1038/nrclinonc.2012.203

Image guided radiation therapy

Image guided radiation therapy (IGRT):

- One of the central pillars in the advance of radio therapy has been in the adoption and integration of imaging information in designing treatments
- IGRT integrates the imaging with the treatment machines themselves
- The purpose of IGRT is to make the PTV-margin as small as possible by improving the accuracy of positioning
- IGRT workflow:
  -collect target position with X-ray or CT scanner set up in the treatment room with the patient “in position” just before the irradiation
  -The difference from the anatomical position derived from the TPS is calculated simultaneously so that the patient position can be adjusted

Image guided radiation therapy

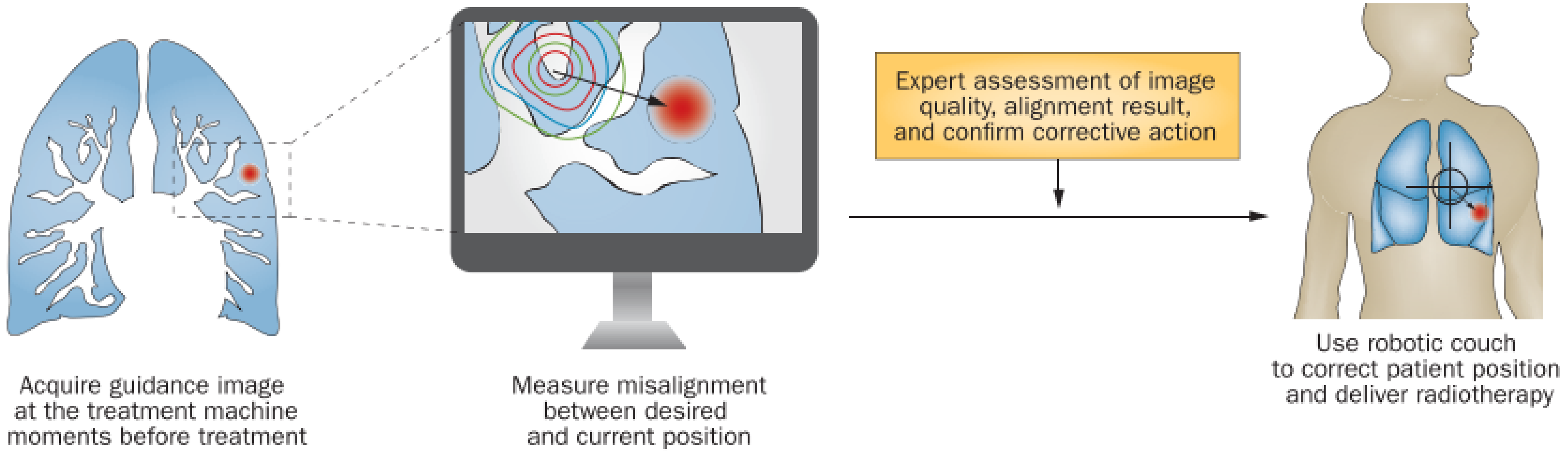
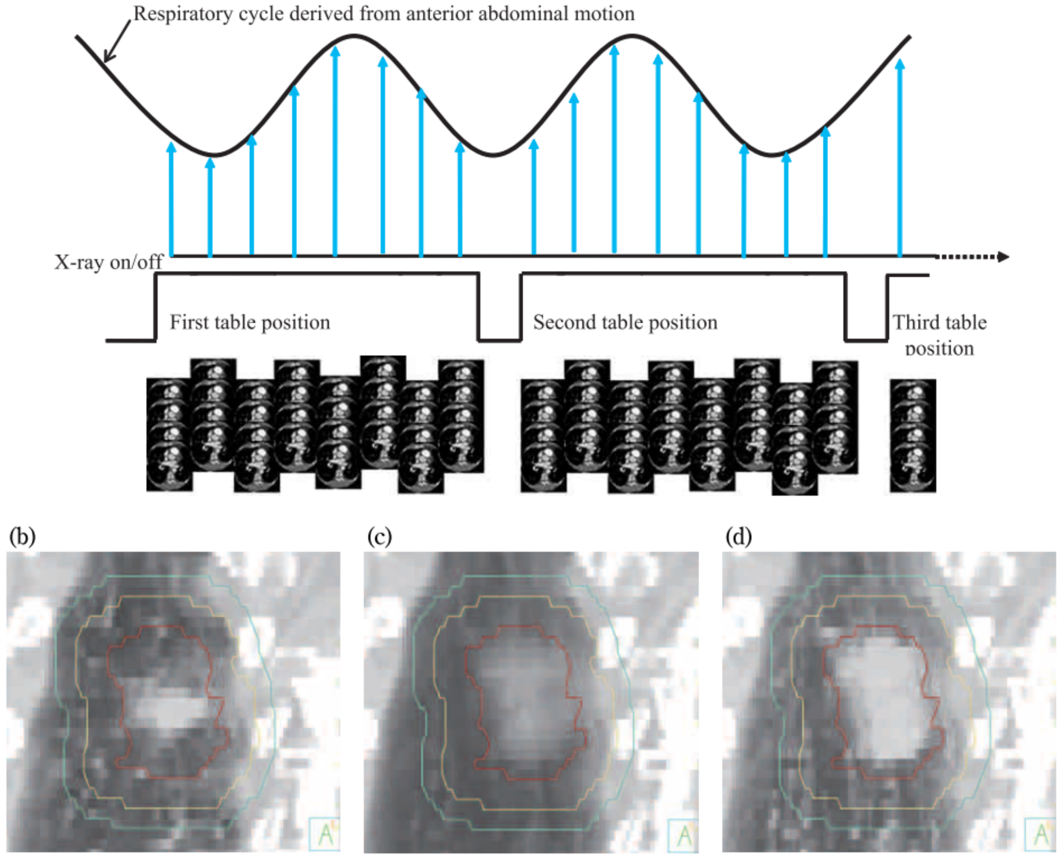


Figure 2 | Targeting radiotherapy before each fraction. Current IGRT practice focuses on the use of images acquired at the time of treatment to direct the placement of radiation fields within the body. These systems need to be highly integrated given the large number (25–40) of patients who are treated on a typical radiotherapy unit per day. Imaging, registration, and correction can be completed in a period of less than 5 min. Given the critical nature of these procedures, skilled individuals oversee the entire process and approve each image-guided adjustment according to criteria. Observed changes in disease and anatomy detected in these images is spurring the development of the adaptation paradigm'. Abbreviation: IGRT, image-guided radiotherapy.

Image guided radiation therapy

Organs in motion



- Every organ in the human body has internal movement, also the target of the RT is moving
- Four-dimensional CT (4DCT) was developed to define the ITV of the tumor in the lungs and liver, organs that both have large movements.
- In 4DCT, anterior abdominal motion is monitored as a surrogate of respiratory motion during CT scanning. All CT data has information on the respiratory phase derived from simultaneously monitored respiratory motion

Ref: doi:10.1002/mp.12679

Question:
Any idea about how to detect and track organs in motion?

Organs in motion: external tracking systems

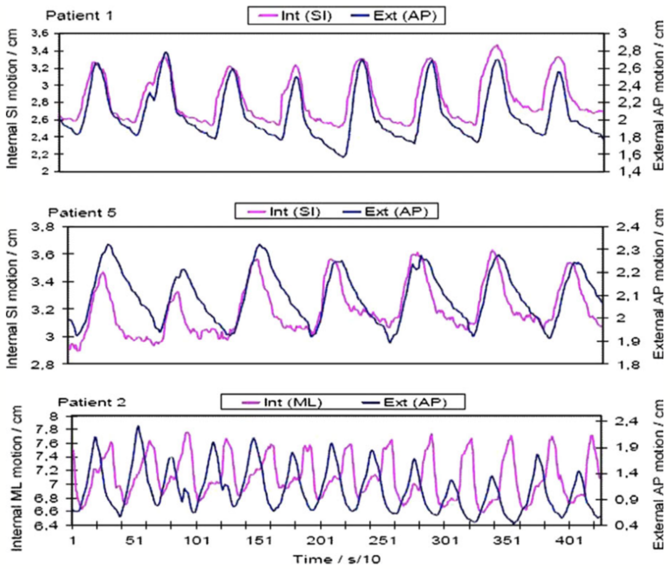


FIG. 1. Relationship between external marker (labelled Ext) and implanted fiducial marker (labeled Int) positions as a function of time in three different patients. The first case shows a good correlation between external and internal marker positions (upper panel); the second shows a slight delay in external marker position (middle panel); while the third shows low external/internal correlation and quite contrary respiratory phases (lower panel). With permission.[8] AP, anterior-posterior; SI, superior-inferior; ML, medio-lateral.

Two types of external tracking systems

- tagging points with artificial markers placed on the patient abdomen and captures motion using infrared cameras
- Monitoring of patient surface information by camera

they rely on the assumption that the observed external respiratory signal is well correlated with the actual internal tumor motion, which is not always the case

Organs in motion: internal tumor tracking

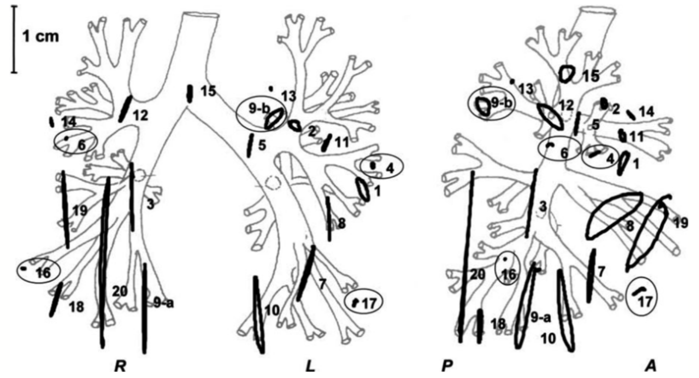


FIG. 3. Orthogonal projections (lines and ovals) of the trajectories of 21 tumors in (left) the coronal (LR-CC) and (right) the sagittal (AP-CC) plane. The tumors are displayed at the approximate position, based on the localization mentioned in the treatment chart. Tumors that were attached to bony structures are circled. With permission.[26]

TABLE I. Summary of the characteristics of fluoroscopic-based internal tumor tracking.

	Pros	Cons
Marker tracking	Easy to detect	Invasive
	Less computation	Marker migration
	High contrast	Tracking error at certain sites
Markerless tracking	Less invasive	Increased computation time
	No image artifact from marker	Lower contrast

Two types of internal tracking systems

- **Fiducial marker tracking:** use an irradiation system with >2 fluoroscopic imaging devices. The fiducial markers are inserted near to or in the tumor and are visible on the X-ray images

- **Markerless tracking**: detect 3d tumour tracking without fiducial markers, exploiting ML techniques

Organs in motion: other methods

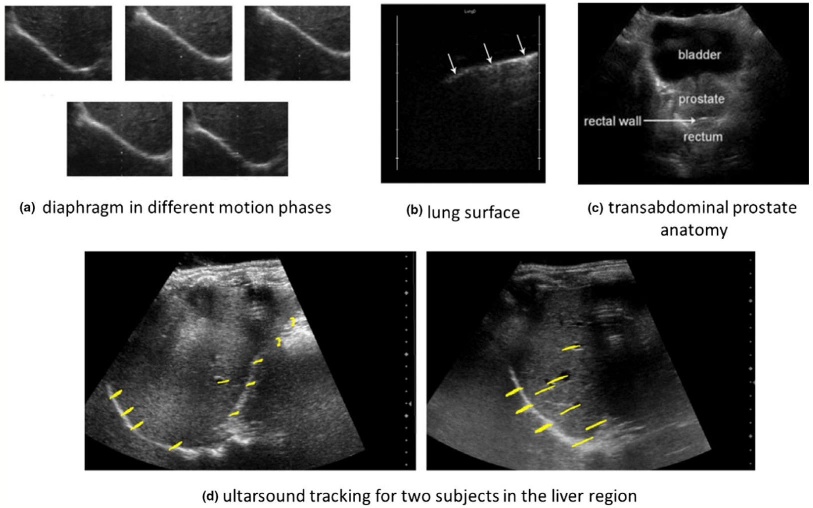


FIG. 8. Exemplary US images of different anatomical locations: (a) diaphragm,[46] (b) lung surface,[47] (c) prostate,[51] (d) liver.[48]

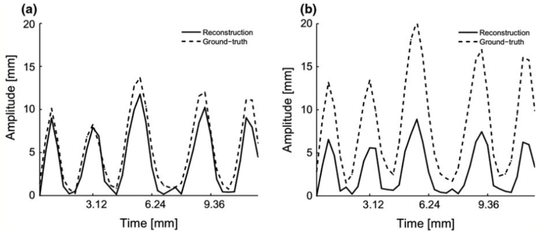


FIG. 9. US motion trace of two landmarks in the liver compared with manual ground truth.[48]

Other methods:

- **Ultrasound:** provide excellent contrast at high resolution for soft tissues apart from those shielded by the lungs or cranium
- **Magnetic resonance imaging:** 4DMR imaging allows studying irregularities in organ motion during free breathing over 10 min. Time-resolved 3D image sequences were reconstructed by retrospective stacking of dynamic 2D images using internal image-based sorting.

Question:
Any idea about how to deal with organs in motion?

Organs in motion: motion mitigation

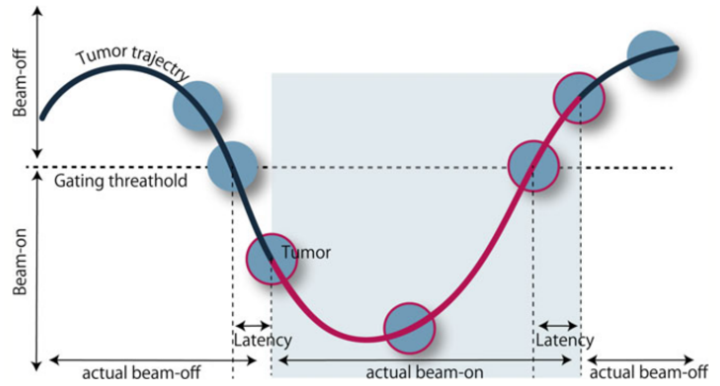
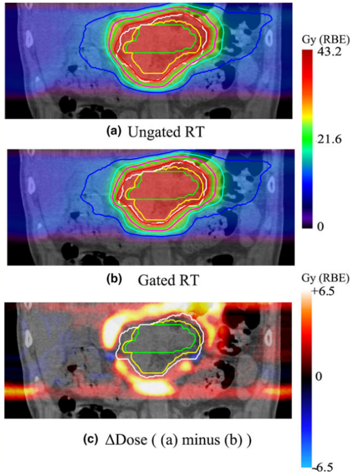
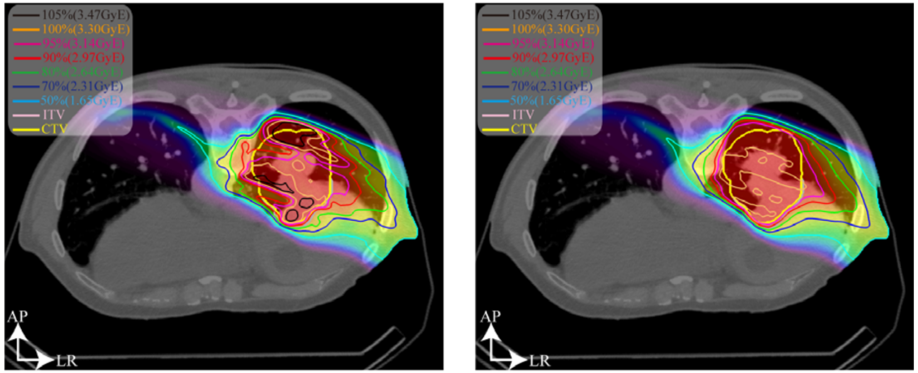


FIG. 13. Schematic drawing of the gated beam-on/off timing with gating latency time.





$1 \times PCR_L$ $8 \times PCR_L$

- **Gating:** synchronization of treatment beam irradiation or imaging with a gating signal. Proposed in 1980 and widely used now both for conv and hadrontherapy

- **Rescanning:** based on the statistical averaging of positional errors. Dose errors are smoothed out by irradiating the target volume multiple time.
  There are two main rescanning path: layered and volumetric

Stereotactic irradiation

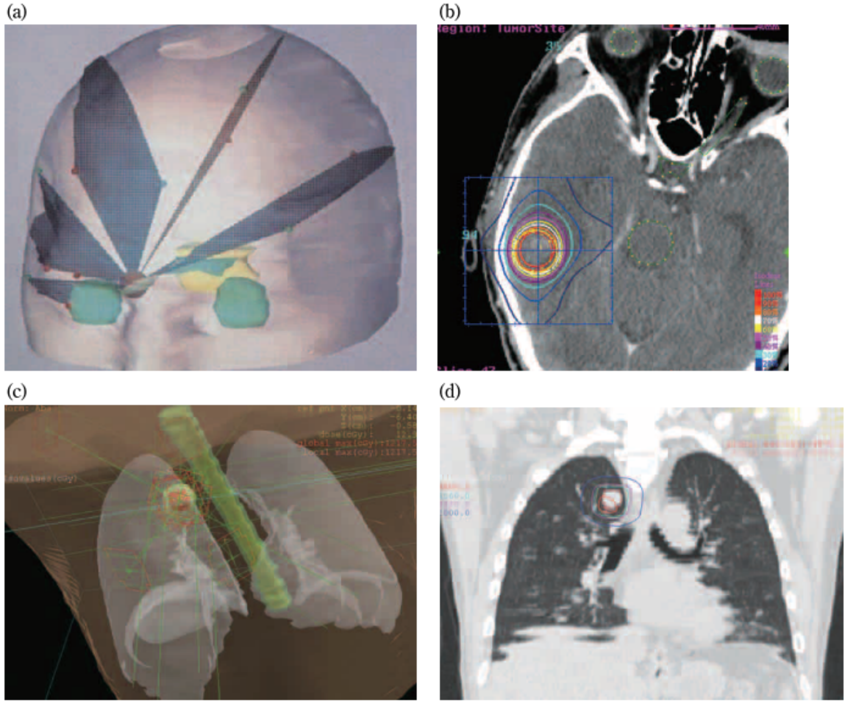


Figure 5. Stereotactic irradiation
(a) Tracks of radiation beams in small volume multiple arcs radiation therapy (SMART) using linear accelerator for brain tumor
(b) Dose distribution demonstrated on a CT axial image in SMART for metastatic brain tumor.
(c) Beam arrangement in non-coplanar static multiple portals irradiation for lung cancer
(d) Dose distribution demonstrated on a coronal CT image in stereotactic radiation therapy for lung cancer

a highly precise treatment method that focuses a narrow ionizing radiation beam on the target from various directions.

- involves the use of an immobilization system to minimize isocenter deviation within ±2 mm in a treatment for brain tumours and ±5 mm for the tumours in other body organs
- STI enables the delivery of a large dose of radiation to the target in a single fraction or a small number of fractionations
- The main target for STI is the metastatic brain tumour

Intensity Modulated Radiation Therapy

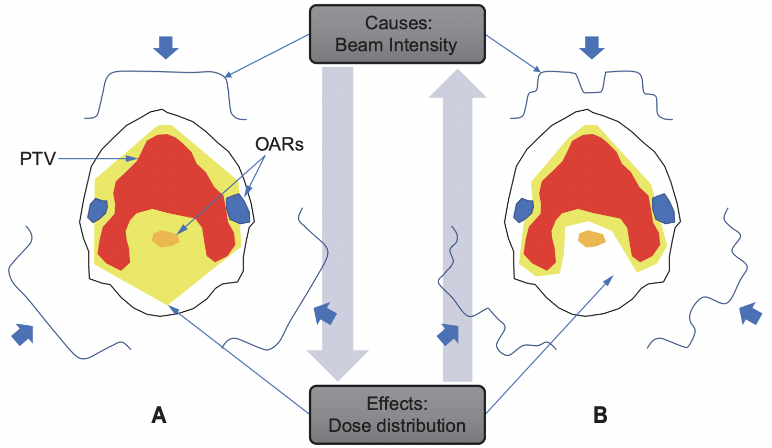


Fig. 1. Comparison of the principle of 3D-CRT (A) and IMRT (B) with illustrations of forward vs. inverse planning. Considering the dose calculation problem of radiation therapy in terms of the concept of causality, while the causes are beam parameters including energy, direction, size, and intensities, the effects are dose distributions. Therefore, conventional planning, in which the beam parameters are given first and the dose distributions are calculated, is 'forward' planning. By contrast, intensity-modulated radiation therapy planning, in which the beam intensities are calculated to provide the given objectives and constraints on dose distributions to the target volume and organs at risk (OARs), is termed 'inverse' planning. 3D-CRT, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiation therapy; PTV, planning target volume.

IMRT is an irradiation technique that has achieved a marked improvement **in three dimensional dose convergence** on a target, by **modulation of the beam intensity** distribution within a field

- IMRT considered the most successful development in radiation oncology since the introduction of computed tomography (CT) into treatment planning (1980s)
- IMRT can deliver a higher radiation dose to a target while reducing the dose to the surrounding normal tissue
- Use of **inverse planning** with respect to traditional 3D-CRT

Intensity Modulated Radiation Therapy

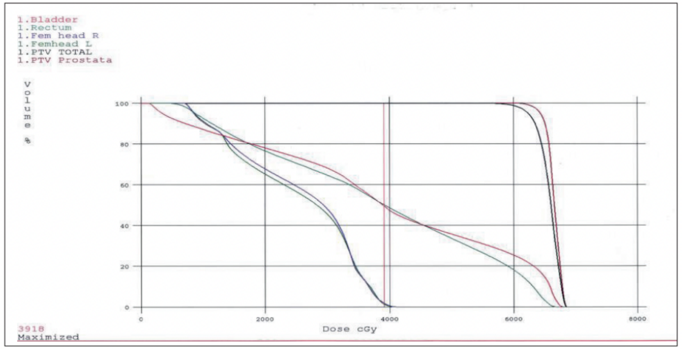


Figure 1. A case of IMRT treatment plan DVH

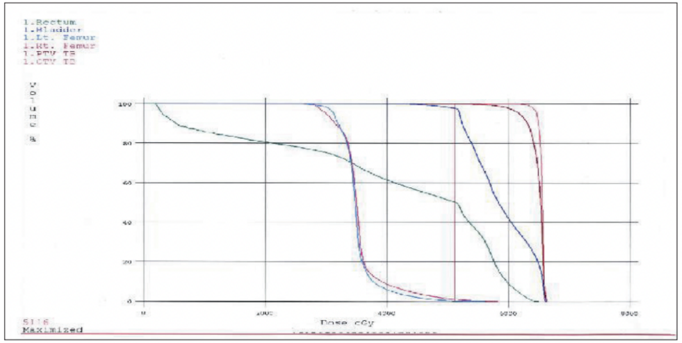
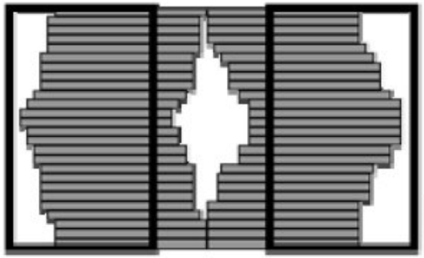


Figure 2. A case of 3D CRT treatment plan DVH

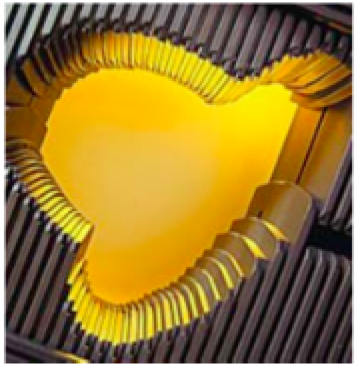
- In IMRT, optimal intensity modulation is produced by continuous irradiation using various irregular fields with the multi-leaf collimator configuration being based on intensity maps calculated using TPS
- Possibility to produce a horseshoe shaped dose distribution
- IMRT becomes an effective irradiation method for the patients where the organs at risk such as spinal cord and salivary glands locate beside the target

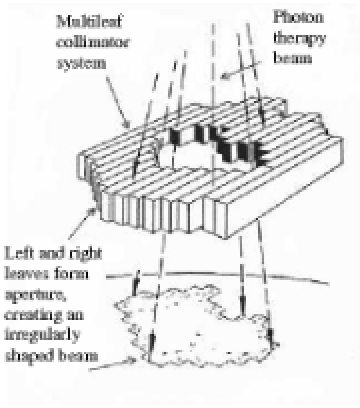
Intensity Modulated Radiation Therapy



Collimatore multilamellare

collimatore costituito da (50+50) lamelle che vengono retratte per lasciare un *foro* con forma uguale al tumore

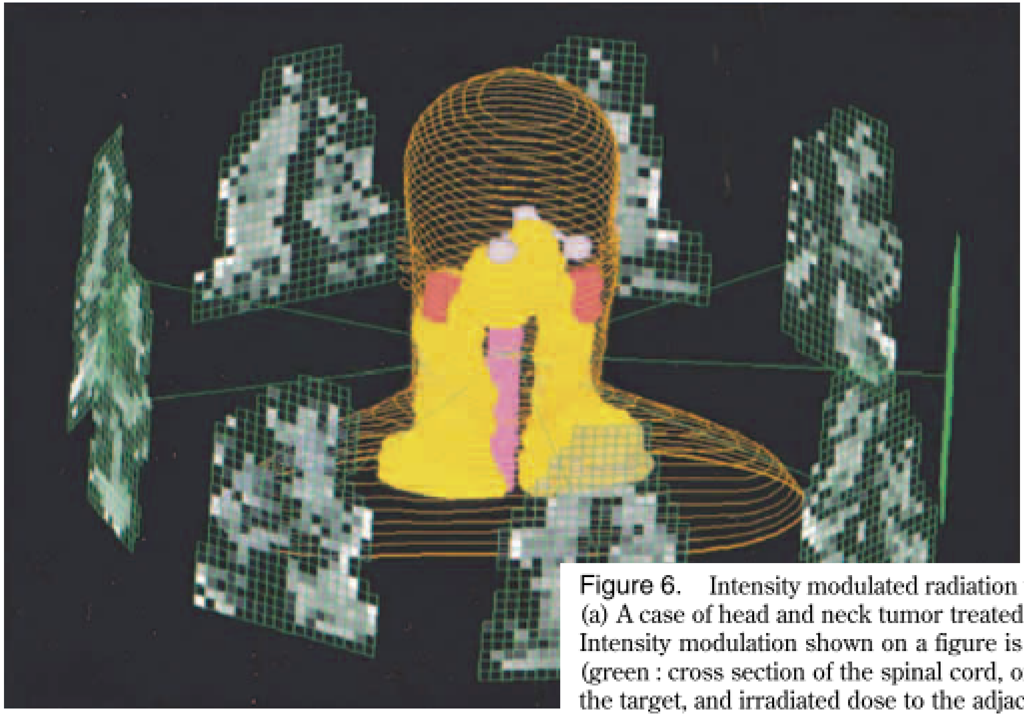




(b)

Intensity Modulated Radiation Therapy

(a)



(b)

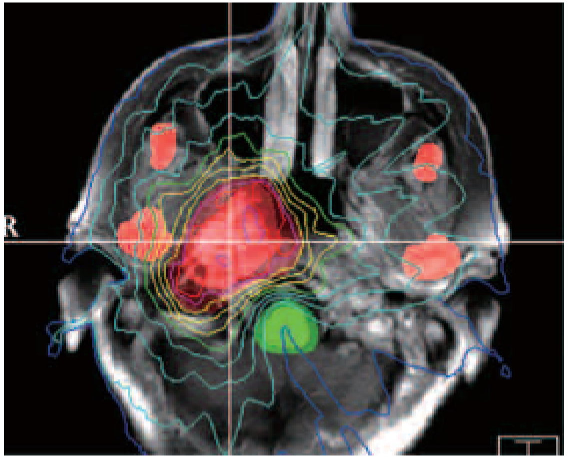
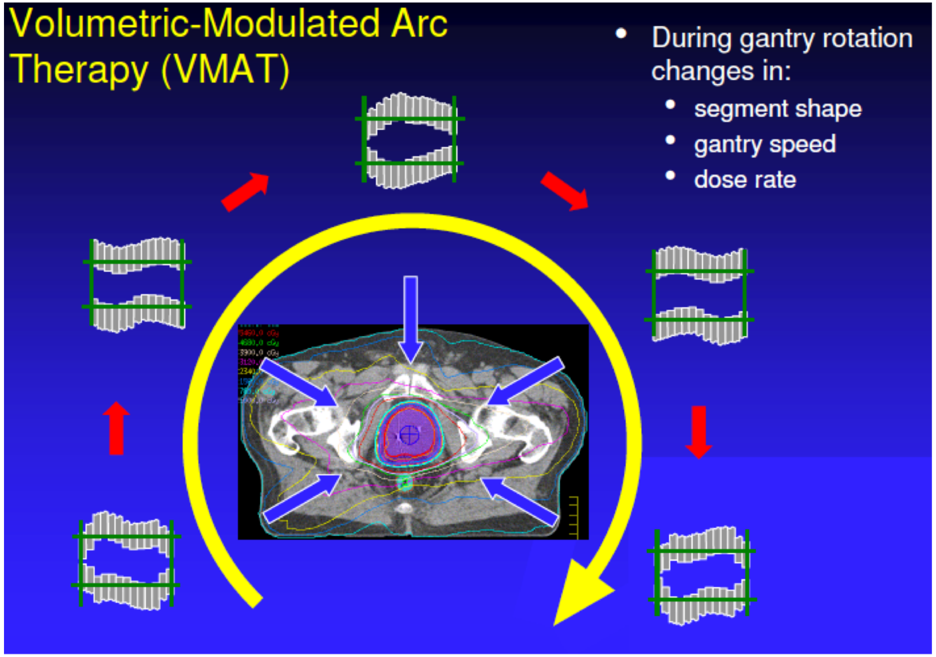


Figure 6. Intensity modulated radiation therapy
(a) A case of head and neck tumor treated by intensity modulated radiation therapy (IMRT) with 9 beams (cited from reference 7), Intensity modulation shown on a figure is performed in every beam. (b) Dose distribution chart on an axial image of CT in IMRT (green : cross section of the spinal cord, orange : cross section of the salivary glands), IMRT realize conformal dose distribution to the target, and irradiated dose to the adjacent normal tissue can be reduced. IMRT becomes an effective irradiation method for the patients where the organs at risk such as spinal cord and salivary glands locate beside the target.

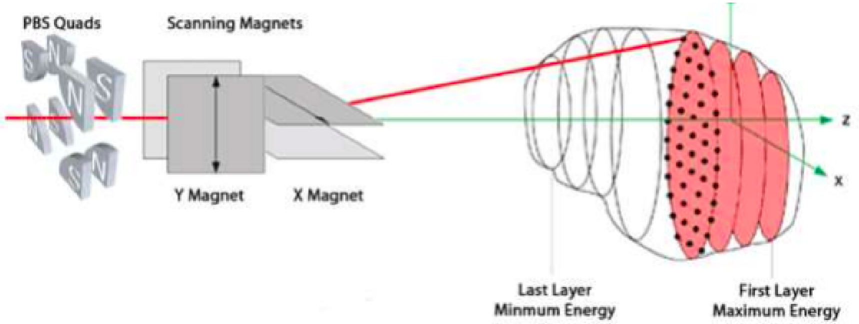
Volumetric Modulated Arc Therapy

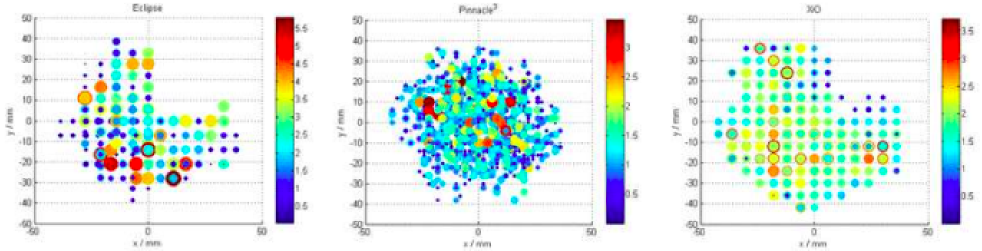


VMAT is a type of IMRT technique in which the modulation of beam intensity is achieved by regulating the dose-rate and a multi-leaf collimator dynamically with a **rotating gantry** in a linear accelerator.

- VMAT requires shorter treatment time than conventional IMRT (VMAT~2 minutes)
- Higher precision with respect to IMRT
- First VMAT treatments in ~2010

Pencil beam scanning



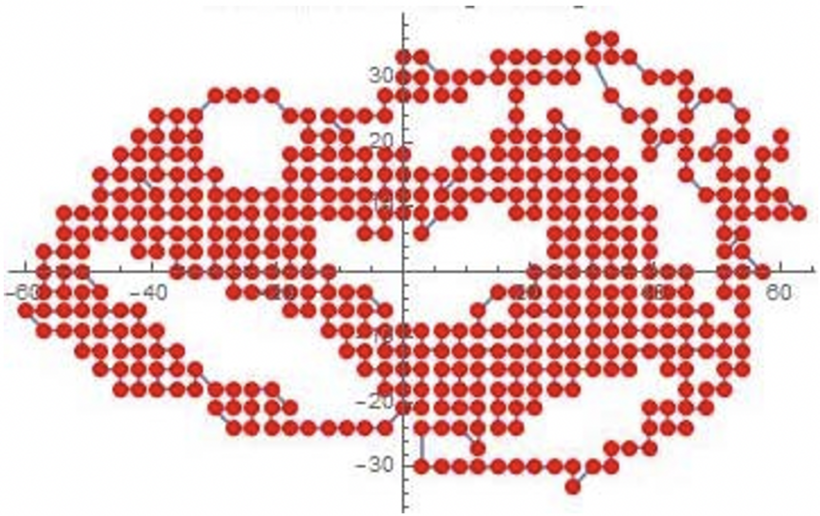


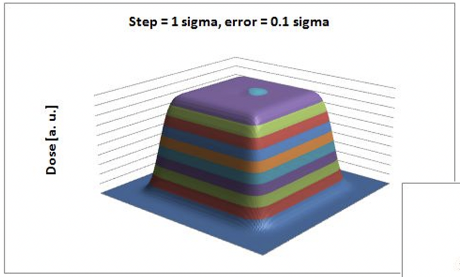
In hadrontherapy the gold standard is the Pencil beam scanning technique

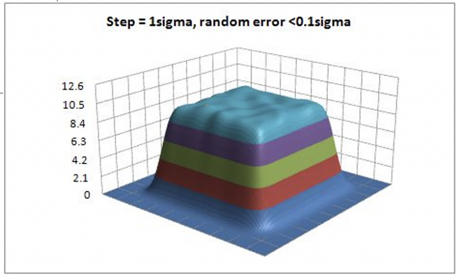
- Small pencil beams (a few mm)
- Scanning magnets to position the beam in the transversal plane
- Beam energy to position the beam in the longitudinal plane
- Possibility to use Gantry that change the beam position as in VMAT

Pencil beam scanning

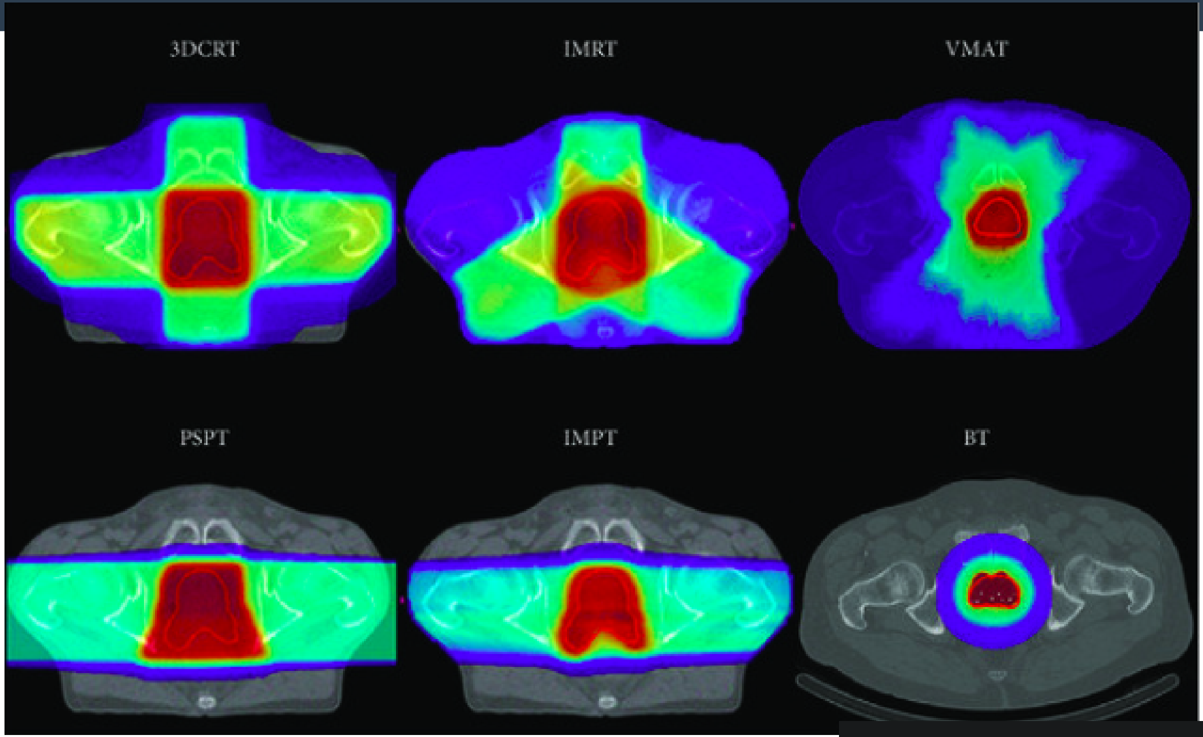
Slices can have complex shapes







Summary



Examples of dose distribution of a 3DCRT, IMRT-5, VMAT, PSPT, IMPT, and a BT treatment plan calculated on the same patient. The red surface represents the high-dose regions, the yellow surface the intermediate-high-dose regions, the dark blue surface the low-dose regions, and the azure blue surface the intermediate-dose regions. 3D-CRT: 3-dimensional conformal radiotherapy; IMRT: intensity modulated radiotherapy; VMAT: volumetric modulated arc therapy; PSPT: passively scattered proton therapy; IMPT: intensity modulated proton therapy; BT: brachytherapy.

Hadrontherapy vs conv rt

	Photon	Proton	^{12}C
Accelerator	Linac	cyclo/syncrotron	syncrothron
cost	low	medium	high
Depth-dose profile	slow exp. decrease	Bragg peak	Bragg peak
Interactions	Photoelectric+Compton +p.p.	Ionization + Nuclear int.	Ionization + Nuclear int.
Dose conformity	IMRT+VMAT	PB+gantry	PB+gantry
LET (KeV/µm)	Low (0.2)	Medium (0.5-10)	High (10-140)
Ionization density Mean distance (nm)	High (130)	Medium (15-90)	Low (0.3-4)
RBE	1 (by definition)	1.1	3-6, varying
OER	1-3	1-3	~1
Number of fractions	~30	~30	~15

Questions?