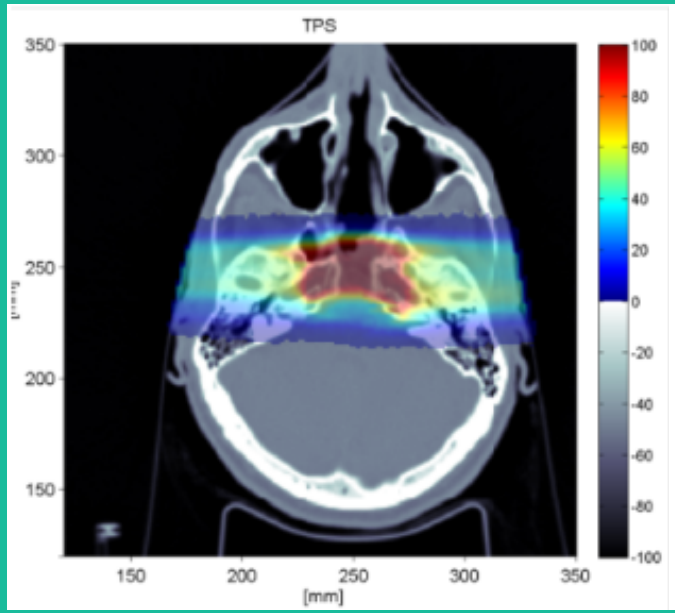

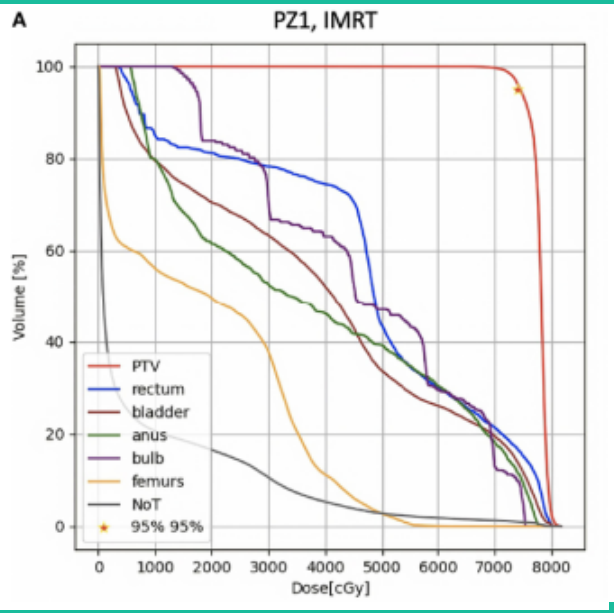

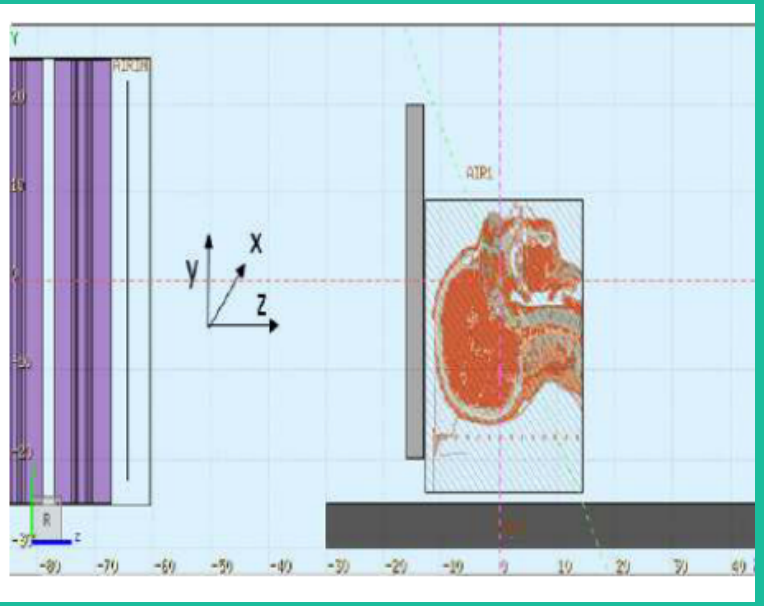

5: Treatment planning

Yunsheng Dong

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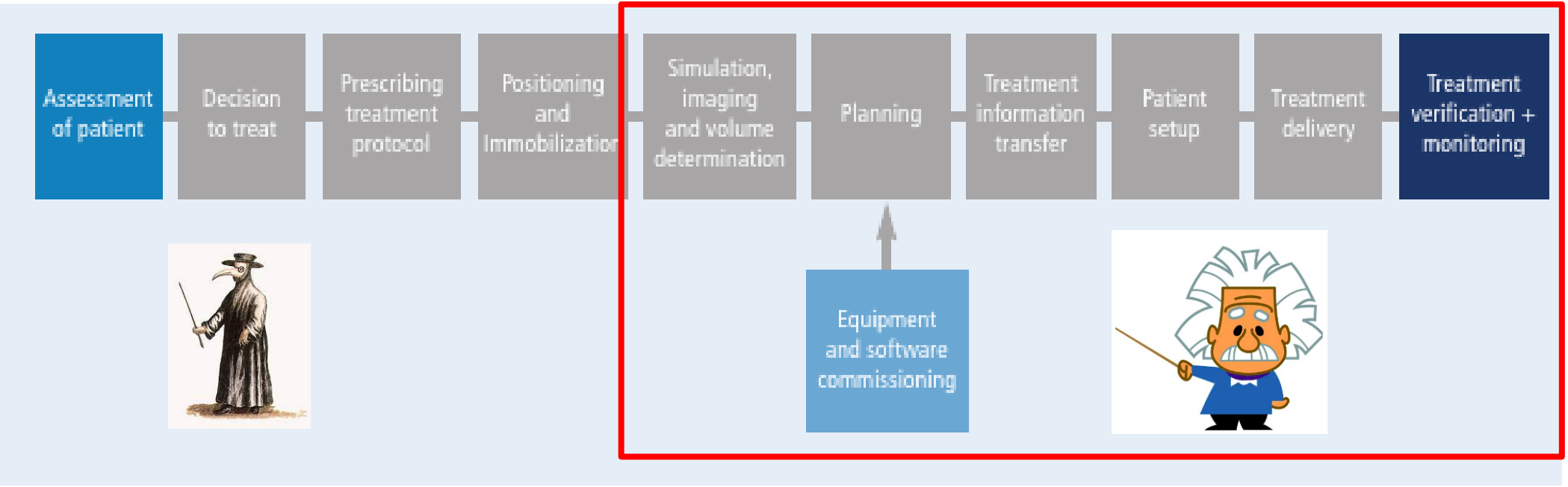
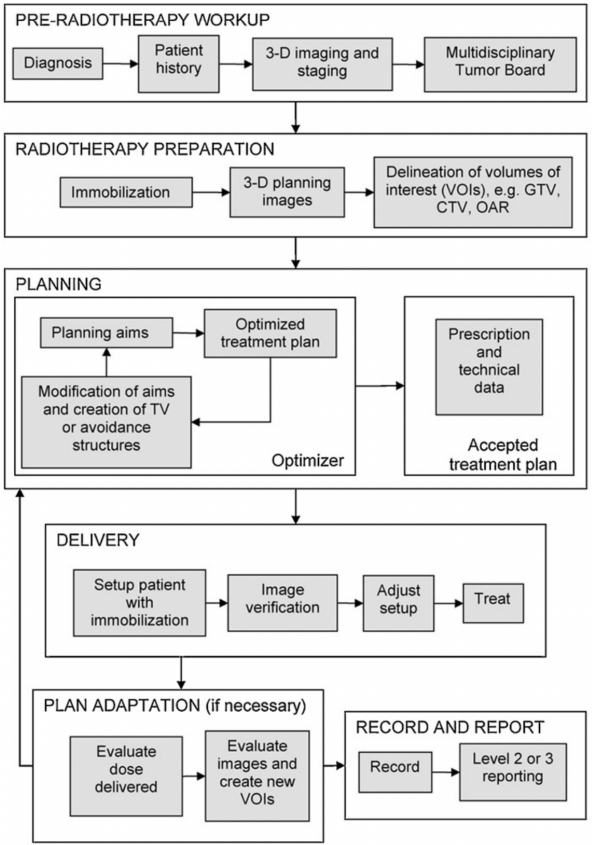
21/05/2024

Stages of radiotherapy treatment



From WHO radiotherapy risk profile

Stages of radiotherapy treatment



https://doi.org/10.1016/j.canrad.2011.04.003

Wikipedia definition

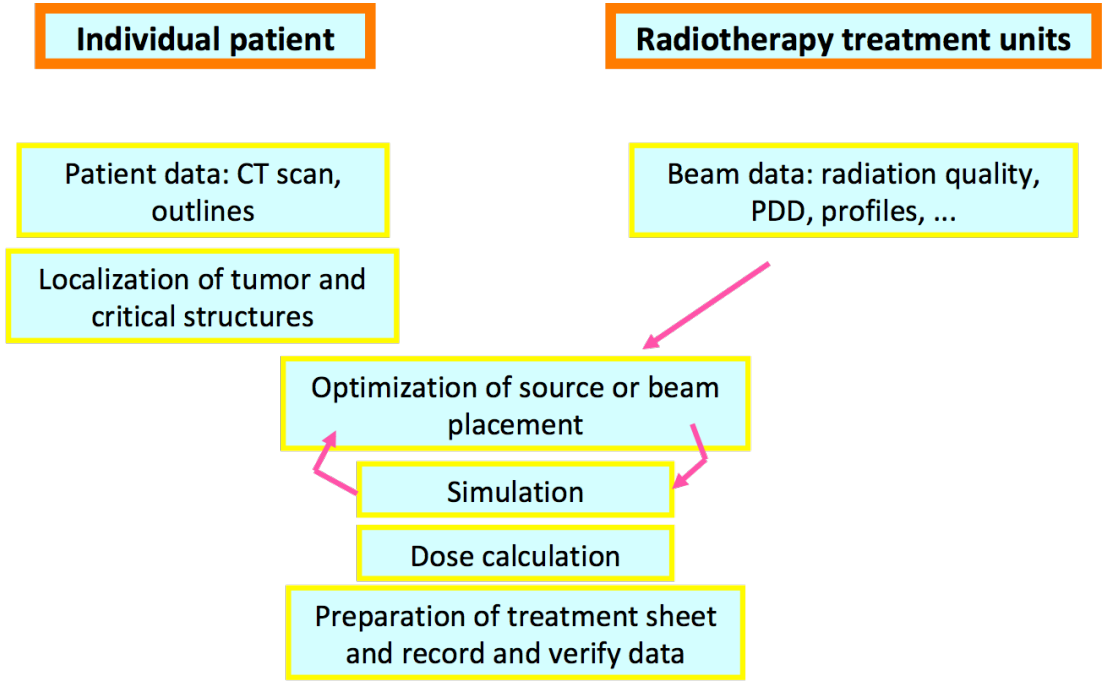
Radiation treatment planning

Article Talk

From Wikipedia, the free encyclopedia

In radiotherapy, **radiation treatment planning** (**RTP**) is the process in which a team consisting of radiation oncologists, radiation therapist, medical physicists and medical dosimetrists plan the appropriate external beam radiotherapy or internal brachytherapy treatment technique for a patient with cancer.

Goal of TP



- Treatment planning combines information of individual patients (e.g: disease site and size, organ at risk etc.) with data for the treatment units available in a particular department.
- This involves the optimization of the treatment approach for each individual patient.

CT scan

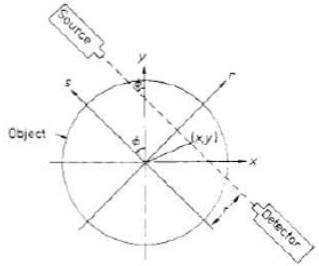
We define the **density function f(x,y)** as the planar distribution of linear attenuation coefficient μ of the body section, and the **projection** as the integral along a ray (r,ϕ) of f(x,y)

density function f(x,y)

$$f(x,y) = \mu(x,y)$$

Projection per r e ϕ

$$p(r,\phi) = \int_{r,\phi} f(x,y)\,ds.$$



- Volume definition is a prerequisite for meaningful 3D treatment planning and for accurate dose reporting
- **The first stage for the treatment planning is the imaging of patient tumour and surrounding healthy tissue**
- **Typically a CT is performed**
- Hey this picture on the left seems familiar…
  Yes, it has been borrowed (aka stolen) from the slides of prof. Colombo
  Yes, again… as done previously with the slides of prof. Veronese

(Old) Question:
How much dose is received with a CT scan?

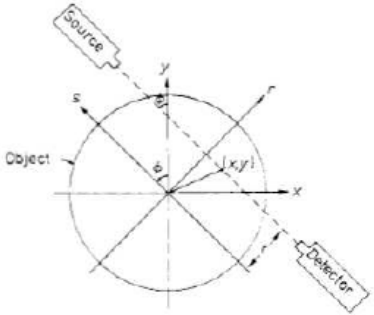
CT scan

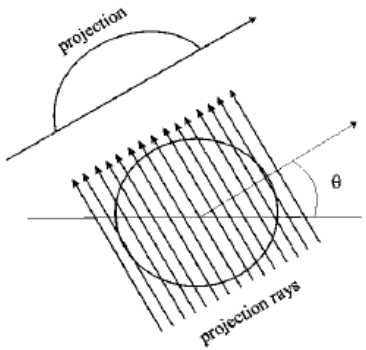
ABDOMINAL REGION 	Procedure	Approximate effective radiation dose	Comparable to natural background radiation for:
	Computed Tomography (CT)–Abdomen and Pelvis	7.7 mSv	2.6 years
	Computed Tomography (CT)–Abdomen and Pelvis, repeated with and without contrast material	15.4 mSv	5.1 years
	Computed Tomography (CT)–Colonography	6 mSv	2 years
	Intravenous Urography (IVU)	3 mSv	1 year
	Barium Enema (Lower GI X-ray)	6 mSv	2 years
	Upper GI Study with Barium	6 mSv	2 years

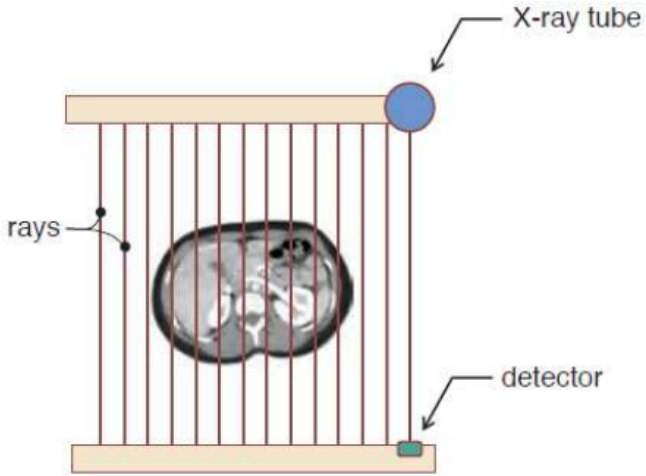
BONE 	Procedure	Approximate effective radiation dose	Comparable to natural background radiation for:
	Lumbar Spine	1.4 mSv	6 months
	Extremity (hand, foot, etc.) X-ray	Less than 0.001 mSv	Less than 3 hours

https://www.radiologyinfo.org/en/info/safety-xray

CT scan







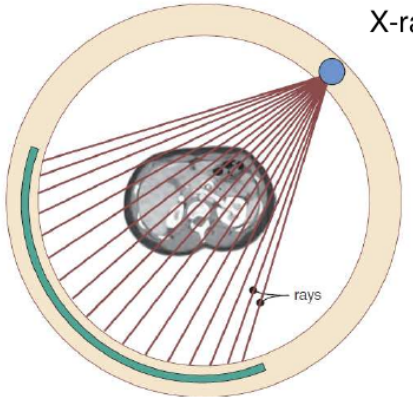
parallel beam projection

Projection al variare di r

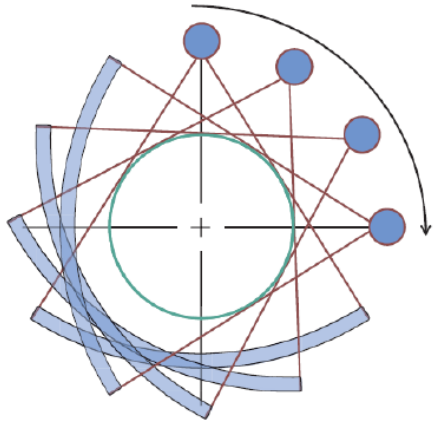
$$p(r,\phi) = \int_{r,\phi} f(x,y)\,\mathrm{d}s.$$

CT scan

Gantry Structure



Reconstruction Field of View



In the FOV the projections are sufficient to reconstruct the planar image

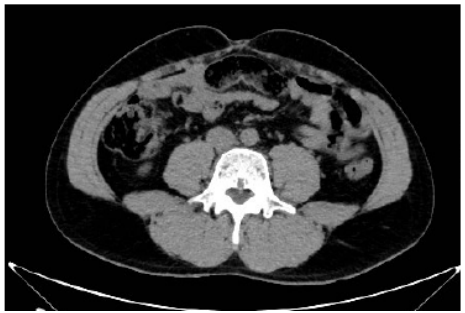
CT scan

Attenuation soft tissue

The primary constituent of soft tissue are carbon, hydrogen and nitrogen, that has (Z/A) = ½ , except hydrogen whereas it is 1. In reality the fluctuations of hydrogen content in tissue are very low and the contribution of the density dominates the equation.

$$\mu_{Compton} \propto \rho N \frac{Z}{A}$$

For hydrogenous tissue as adipose tissue the density (ρ≈0.94 g/cm3) is lower relative to soft tissue (ρ≈1) and it tends to dominate the formula : the consequence is that the fat appear darker respect soft tissue.



CT scan

Hounsfield Unit (HU)

The gray scale in CT is a a quantitatively meaninful value, called Hounsfield Unit (HU)

$$HU(x,y,z) = 1000\,\frac{(\mu(x,y,z) - \mu_w)}{\mu_w}$$

Where μ(x,y,z) is the average linear attenuation coefficient of each voxel at location (x,y,z) and μ_w is the linear attenuation coefficient of water.

voxel (x,y,z) contains water	HU = 0
voxel (x,y,z) contains air	HU = -1000
voxel (x,y,z) conteins bone	HU = 1000

For all x-ray tube voltages or spectrum, HU_{water}=0 and HU_{air}=-1000.

The other numbers changes at different kV.

CT calibration

CT segmentation into 27 materials of defined elemental composition (from analysis of 71 human CT scans)

Air, Lung, Adipose tissue

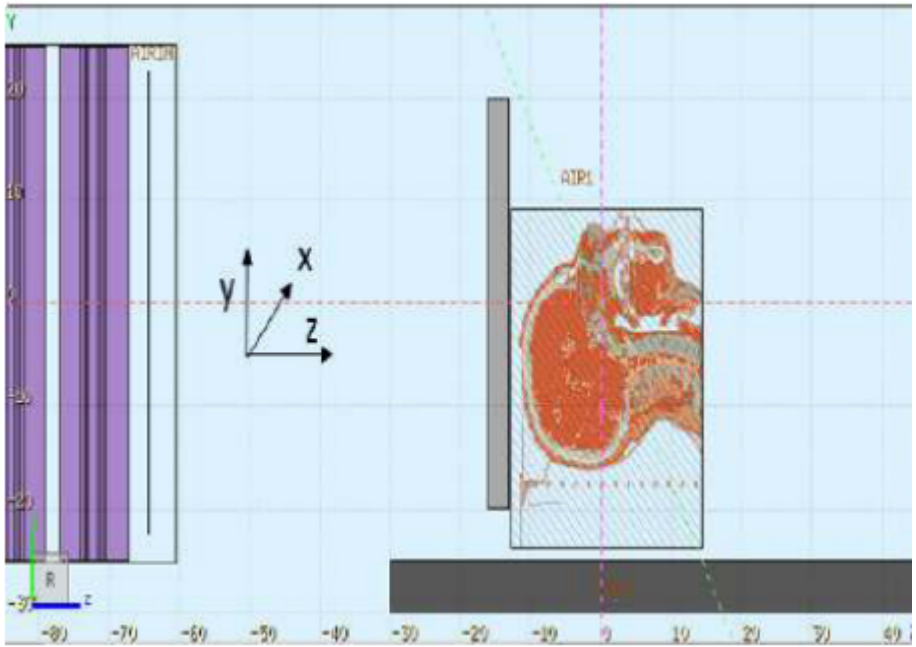
Soft tissue

Skeletal tissue

	w_j(pp)											
H	H	C	N	O	Na	Mg	P	S	Cl	Ar	K	Ca
−1000−−950			75.5	23.2						1.3		
−950−−120	10.3	10.5	3.1	74.9	0.2		0.2	0.3	0.3		0.2	
−120−−83	11.6	68.1	0.2	19.8	0.1			0.1	0.1			
−82−−53	11.3	56.7	0.9	30.8	0.1			0.1	0.1			
−52−−23	11.0	45.8	1.5	41.1	0.1		0.1	0.2	0.2			
−22−7	10.8	35.6	2.2	50.9			0.1	0.2	0.2			
8–18	10.6	28.4	2.6	57.8			0.1	0.2	0.2		0.1	
19–80	10.3	13.4	3.0	72.3	0.2		0.2	0.2	0.2		0.2	
80–120	9.4	20.7	6.2	62.2	0.6			0.6	0.3			
120–200	9.5	45.5	2.5	35.5	0.1		2.1	0.1	0.1		0.1	4.5
200–300	8.9	42.3	2.7	36.3	0.1		3.0	0.1	0.1		0.1	6.4
300–400	8.2	39.1	2.9	37.2	0.1		3.9	0.1	0.1		0.1	8.3
400–500	7.6	36.1	3.0	38.0	0.1	0.1	4.7	0.2	0.1			10.1
500–600	7.1	33.5	3.2	38.7	0.1	0.1	5.4	0.2				11.7
600–700	6.6	31.0	3.3	39.4	0.1	0.1	6.1	0.2				13.2
700–800	6.1	28.7	3.5	40.0	0.1	0.1	6.7	0.2				14.6
800–900	5.6	26.5	3.6	40.5	0.1	0.2	7.3	0.3				15.9
900–1000	5.2	24.6	3.7	41.1	0.1	0.2	7.8	0.3				17.0
1000–1100	4.9	22.7	3.8	41.6	0.1	0.2	8.3	0.3				18.1
1100–1200	4.5	21.0	3.9	42.0	0.1	0.2	8.8	0.3				19.2
1200–1300	4.2	19.4	4.0	42.5	0.1	0.2	9.2	0.3				20.1
1300–1400	3.9	17.9	4.1	42.9	0.1	0.2	9.6	0.3				21.0
1400–1500	3.6	16.5	4.2	43.2	0.1	0.2	10.0	0.3				21.9
1500–1600	3.4	15.5	4.2	43.5	0.1	0.2	10.3	0.3				22.5

Schneider et al PMB 45, 2000 [7]

CT calibration in treatment planning

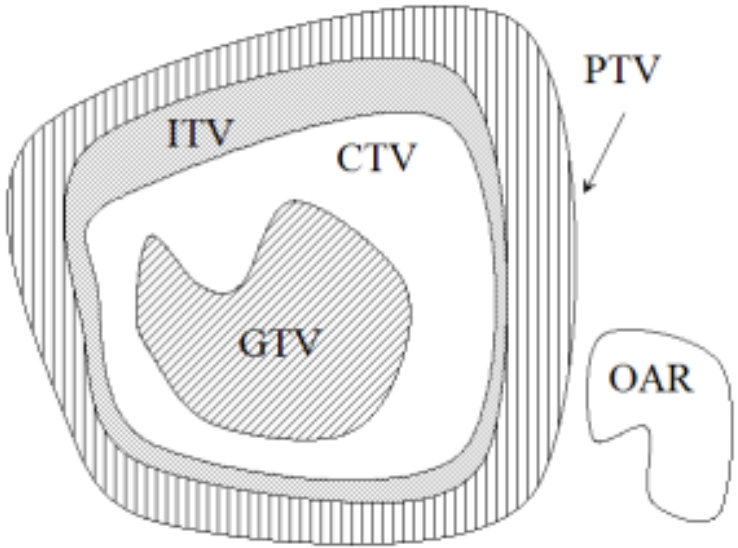


The conversion of HU to material density in the MC simulations is not straightforward:

- How to assign a realistic human tissue parameter (aka, material) for the MC calculation?
- How to handle the number of different HU values and the materials considered in MC? (1 HU~1 Material lead to computation memory and speed issues)
- How to preserve continuous and HU dependant information when the HU are segmented into intervals sharing the same tissue material?

Question:
Any idea/solution for the questions?

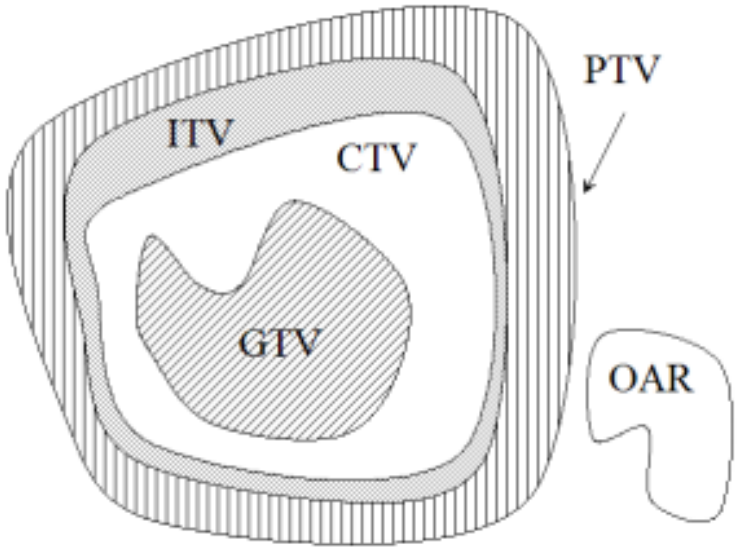
Tumour contouring



Once the CT has been taken, The following volumes have been defined as principal volumes related to 3D treatment planning:

- **Gross Tumour Volume (GTV)**: is the gross palpable or visible/demonstrable extent and location of malignant growth (ICRU 50)
- **Clinical Target Volume (CTV)**: is the tissue volume that contains a demonstrable GTV and/or sub-clinical microscopic malignant disease, which has to be eliminated. This volume thus has to be treated adequately in order to achieve the aim of therapy, cure or palliation" (ICRU 50).

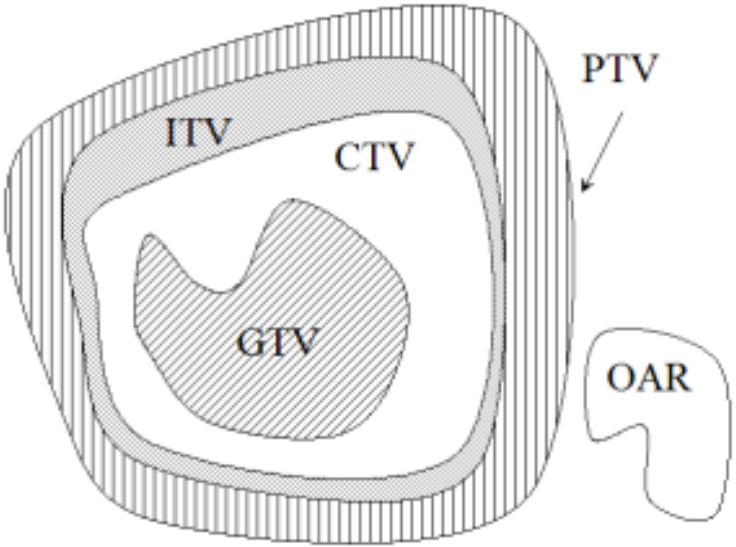
Tumour contouring



The CTV often includes the area directly surrounding the GTV that may contain microscopic disease and other areas considered to be at risk and require treatment (e.g., positive lymph nodes). The CTV is usually stated as a fixed or variable margin around the GTV, in some cases it is the same as GTV

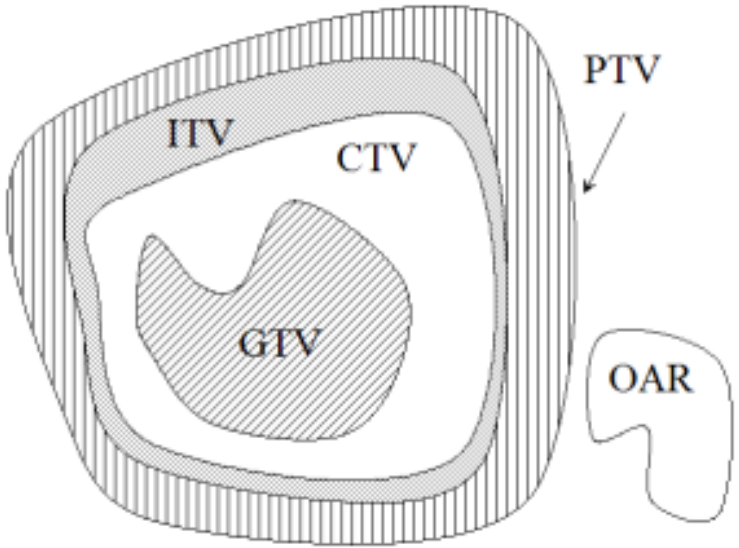
- **Internal Target Volume (ITV)**: is the CTV plus an internal margin, designed to take into account the variations in the size and position of the CTV

Tumour contouring



- **Planning Target Volume (PTV)**: is a geometrical concept, and it is defined to select appropriate beam arrangements, taking into consideration the net effect of all possible geometrical variations, in order to ensure that the prescribed dose is actually absorbed in the CTV (ICRU 50)
  PTV includes the internal target margin (ICRU 62) and an additional margin for set-up uncertainties, machine tolerances and intra-treatment variations.
  The PTV is linked to the reference frame of the treatment machine.
  It is often described as the CTV plus a fixed or variable margin (PTV=CTV+1cm)

Tumour contouring



The PTV depends on the precision of such tools as immobilization devices and lasers, but does NOT include a margin for dosimetric characteristics of the radiation beam (i.e., penumbral areas and build-up region) as these will require an additional margin during treatment planning and shielding design

- **Organ at Risk (OAR)**: is an organ whose sensitivity to radiation is such that the dose received from a treatment plan may be significant compared to its tolerance, possibly requiring a change in the beam arrangement or a change in the dose

The machine

All the following machine parameters need to be considered and modelled in the TPS

- Beam description (quality, energy)
- Beam geometry (isocentre, gantry, table)
- Field definition (source collimator distance, applicators, collimators, blocks, MLC)
- Physical beam modifiers (wedges, compensator)
- Dynamic beam modifiers (dynamic wedge, arcs, MLC IMRT)
- Normalization of dose

Cost function

Input data:

The first step of the TPS concerns the acquisition and manipulation of computed tomography (CT) data scan and contours data relative to the PTV and the organs at risk (OARs), to generate a three-dimensional digital model of the irradiation region

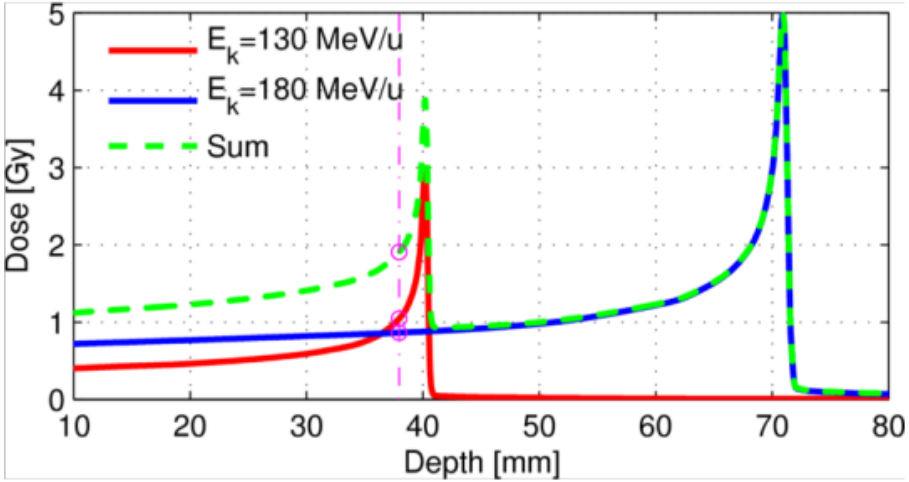
The cost function:

Then, one can start defining a cost function to minimize to optimize the whole treatment
e.g.:

$$X^2 = \sum_{i \in m_T} [D_i^b - D_T]^2 + \sum_{i \in OAR} [D_i^b - D_{OAR}]^2$$

where
-D_i is the biological dose delivered on the i^{th} voxel
-D_{OAR} is the total dose that can be delivered on the OAR
-D_T is the total dose prescribed to the tumour

Cost function



Evaluation of the dose release:

The TPS have to compute the biological dose released on each voxel from all the PB.

The contribution can come from different PB of the same field, and from PB of different fields

Different fields often are required to avoid OAR and to minimize the damage to the healthy tissues

Cost function

Considering the physical and biological dose, the cost function can be rewritten as:

$$X^2 = \sum_{i \in V}^{cond} [RBE_i * \sum_l (d_i^l * f_l) - D_T]^2$$

Where
d_i^l is the physical dose released by the l^{th} beam on the i^{th} voxel

F^l is the fluence of the l^{th} beam

RBE_i is the mean average RBE of the i^{th} voxel.
(average of the contribution of all the beams that contribute to the i^{th} voxel

WEPL

In order to evaluate the beam energies etc and reconstruct the SOBP, the Water Equivalent Path Length (WEPL) has to be computed

Conventional one-dimensional scaling of pencil beam

If the two ionization potentials are nearly the same

$$\rho_w \left(\frac{Z}{A}\right)_w z_w = \rho_m \left(\frac{Z}{A}\right)_m z_m$$

z_m: depth in the medium
z_w: depth water.

z_m can be expressed using the **Water Equivalent Path Length** approach:

$$z_m = \frac{\rho_w \left(\frac{Z}{A}\right)_w}{\rho_m \left(\frac{Z}{A}\right)_m} z_w = S_m^w z_w$$

If the ratio of stopping power between water and the medium $S^w_m z_w$ is assumed to be independent of the proton energy one easily derives the scaling relation:

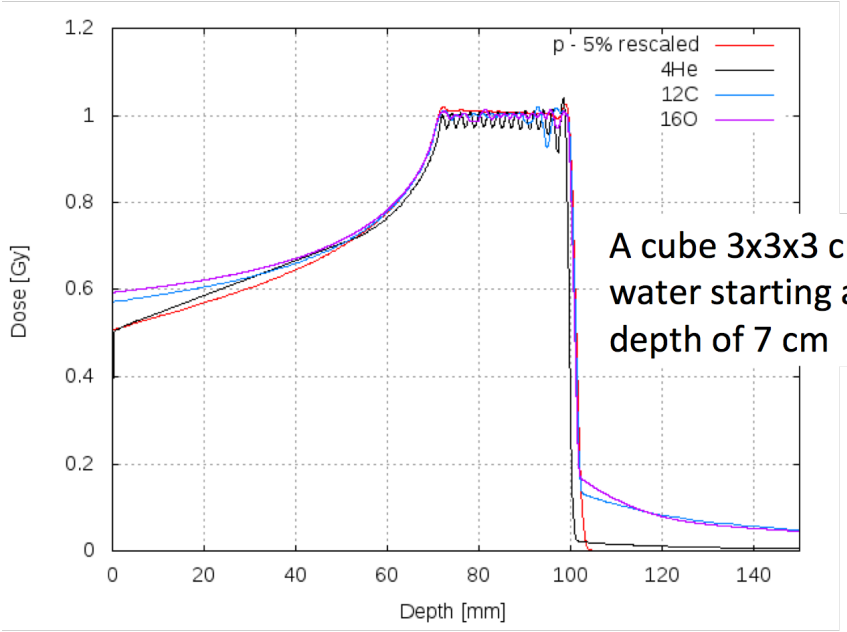
$$D^m(z, E_0) \approx \frac{\rho_m^w}{S_m^w} D^w\left(z \frac{1}{S_m^w}, E_0\right)$$

This 1D path length scaling, is transferred to the lateral fluence $L^m(r,z,E_0)$ accounting for multiple Coulomb scattering:

$$L^m(r, z, E_0) = L^w\left(r, \frac{z}{S_m^w}, E_0\right)$$

WEPL

Syngo TPS calculation (HIT)



Thanks to
A. Mairani

A cube 3x3x3 cm^3 in water starting at a depth of 7 cm

From patient CT to water equivalent material:
Here it is possible to compare the dose release of different beams

Real case for protontherapy

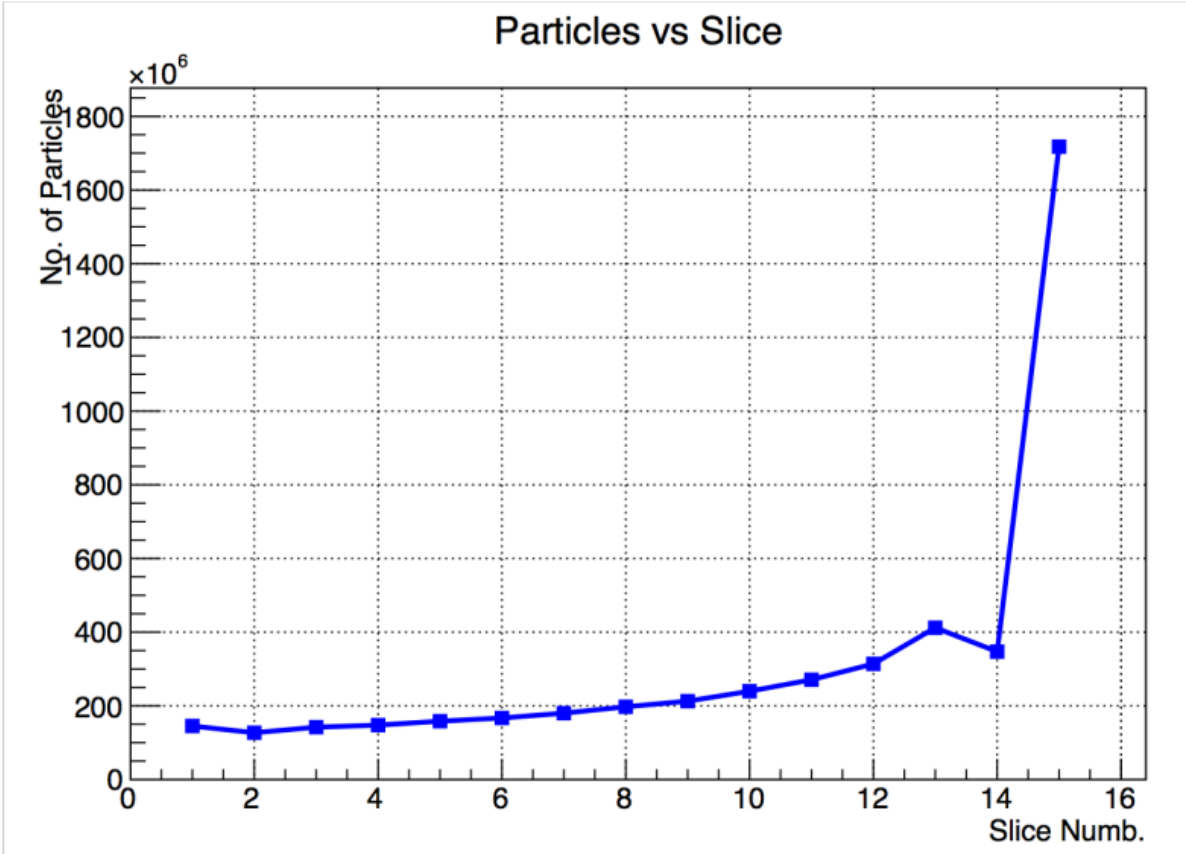
Beam spacing ΔX, ΔY is 3 mm, ΔZ is 2 mm
15 “slices” (energies) from 97.53 to 116.85 MeV
121 beams/slice
Total no. of particles: 4.77915E+09

Last slice (116.85 MeV) at ~10 cm of depth:
$\sigma_{x,y}$ = 1.37 cm at isocenter
1.71766E+09 total particles,
1.4196E+07 particles/beam (1.2780e+08 particles in 0.3 cm x 1 cm^2)

First slice (97.53 MeV) at ~7 cm of depth:
$\sigma_{x,y}$ = 1.61 cm at isocenter
1.45296E+08 total particles,
1.412E+06 particles/beam (1.0807e+07 particles in 0.3 cm x 1 cm^2)

Question:
why the number of particle per slice is almost always smaller for the initial slices?

Real case for protontherapy



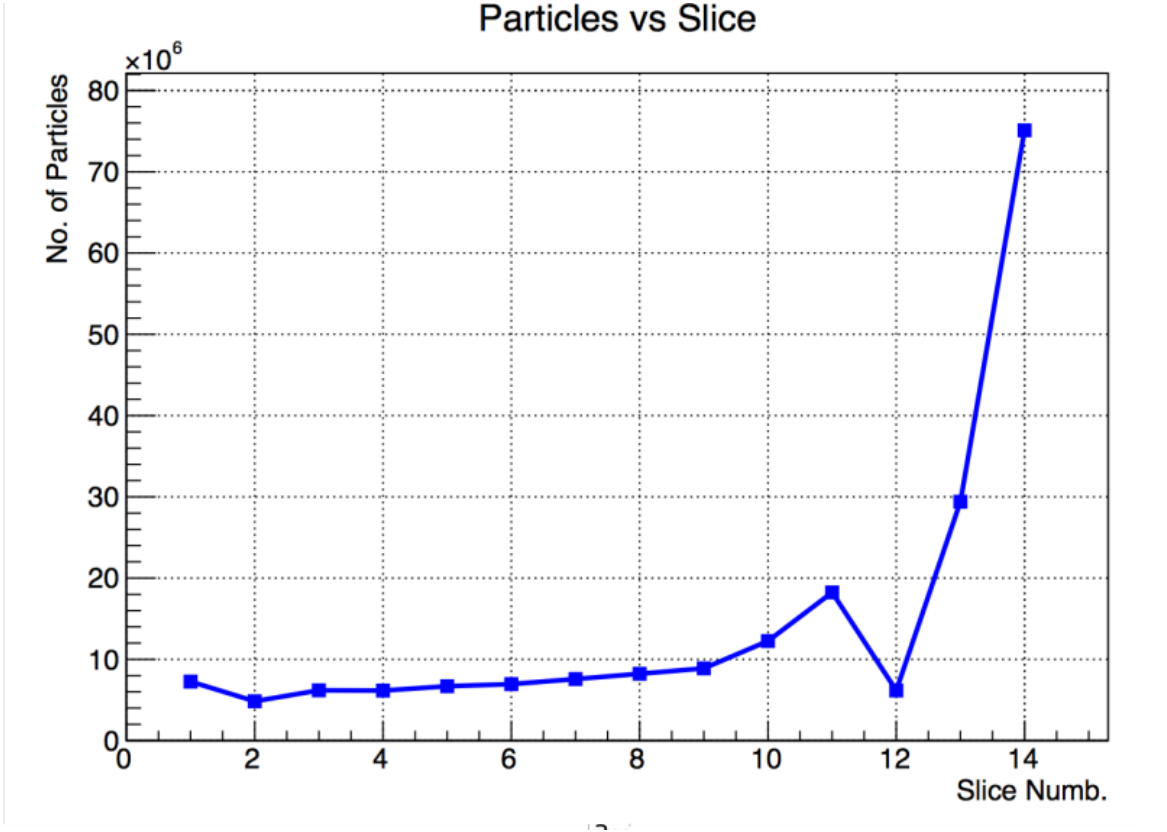
Real case for heavy ion therapy

Beam spacing ΔX, ΔY is 2 mm, ΔZ is 2 mm
14 “slices” (energies) from 186.57 to 223.56 MeV/u
225 beams/slice
Total no. of particles: 2.03959E+08

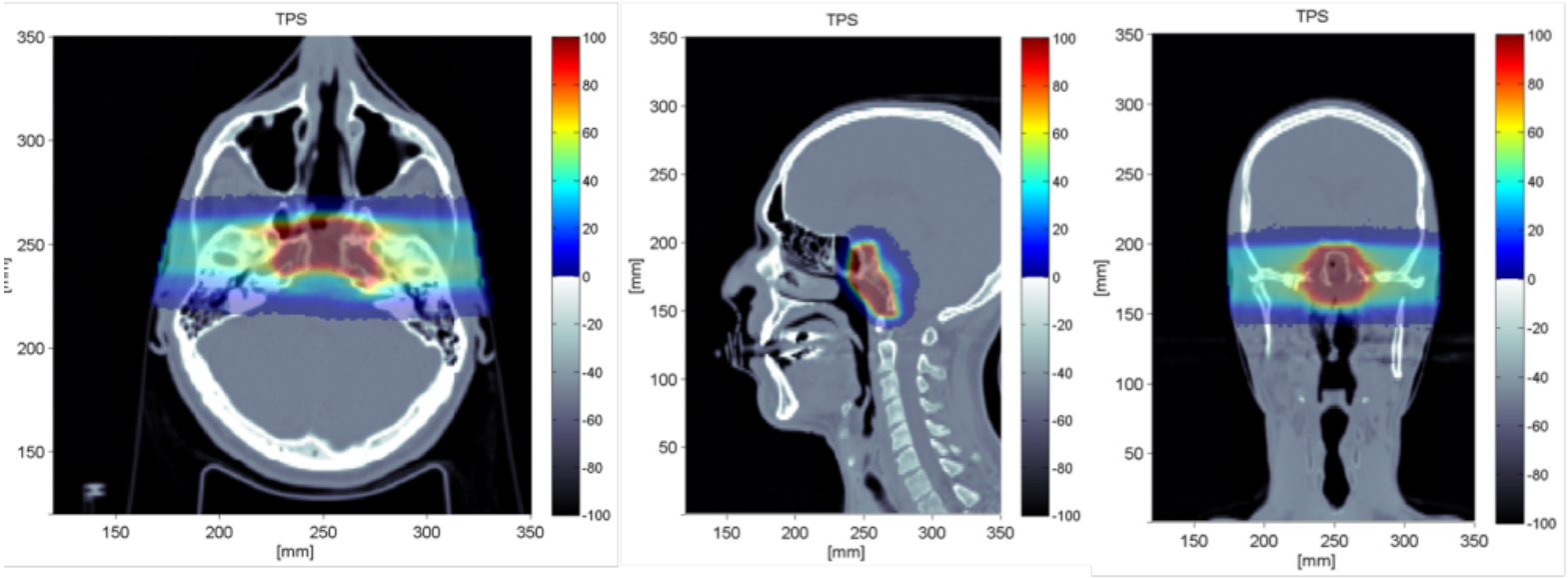
Last slice (223.56 MeV/u) at ~10 cm of depth:
$\sigma_{x,y}$ = 0.64 cm at isocenter
7.5102E+07 total particles,
3.33787E+05 particles/beam (8.345E+06 particles in 0.2 cm x 1 cm^2)

First slice (186.57 MeV) at ~7 cm of depth:
$\sigma_{x,y}$ = 0.69 cm at isocenter
7.2631E+06 total particles,
3.2280E+04 particles/beam (8.07E+05 particles in 0.2 cm x 1 cm^2)

Real case for heavy ion therapy



Real case for heavy ion therapy



Dose prescription as calculated by Syngo TPS

Beam1 = 272 571 648 particles
Beam2 = 239 598 608 particles

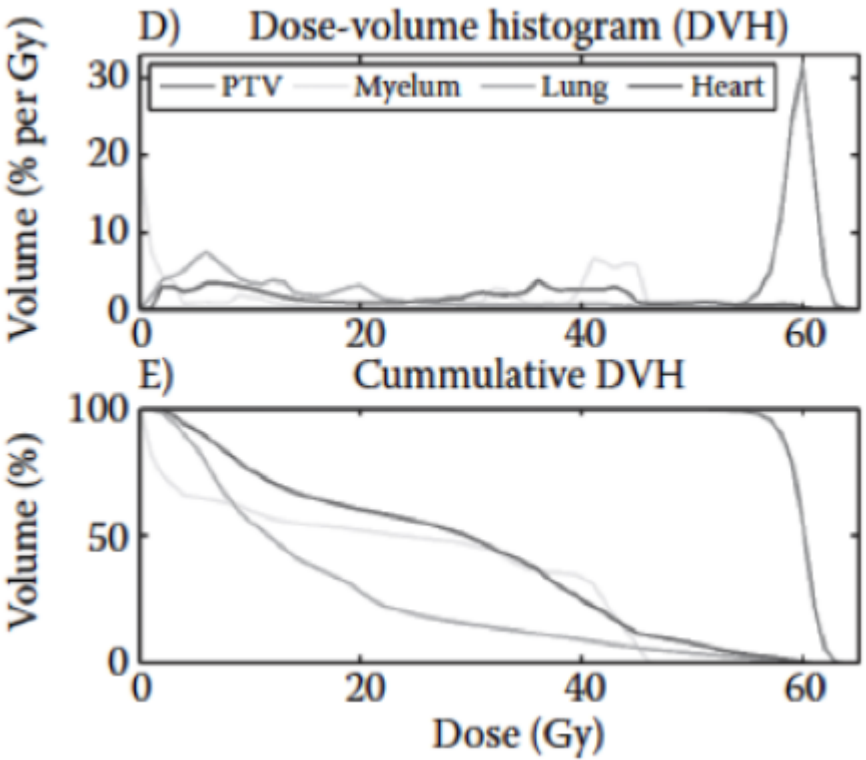
Real case for heavy ion therapy

Treatment Description: Beam 1

Energy Slice [n]	Nominal Beam Energy [MeV/u]	Spots per Slice [n]:
1	137.28	2
2	140.72	2
3	144.10	3
4	147.43	3
5	150.71	5
6	153.94	7
7	157.12	8
8	160.26	10
9	163.35	15
10	166.41	28
11	169.43	71
12	172.41	103
13	175.37	163
14	178.28	219
15	181.17	249
16	184.03	236
17	186.86	234
18	189.66	235
19	192.43	231
20	195.18	229

Energy Slice [n]	Nominal Beam Energy [MeV/u]	Spots per Slice [n]:
21	197.91	232
22	200.61	228
23	203.29	193
24	205.95	181
25	208.58	174
26	211.19	186
27	213.79	180
28	216.36	172
29	218.91	166
30	221.45	154
31	223.96	135
32	226.46	123
33	228.94	105
34	231.34	88
35	233.79	72
36	236.22	49
37	238.63	33
38	241.03	14
39	243.42	4

Dose volume histogram



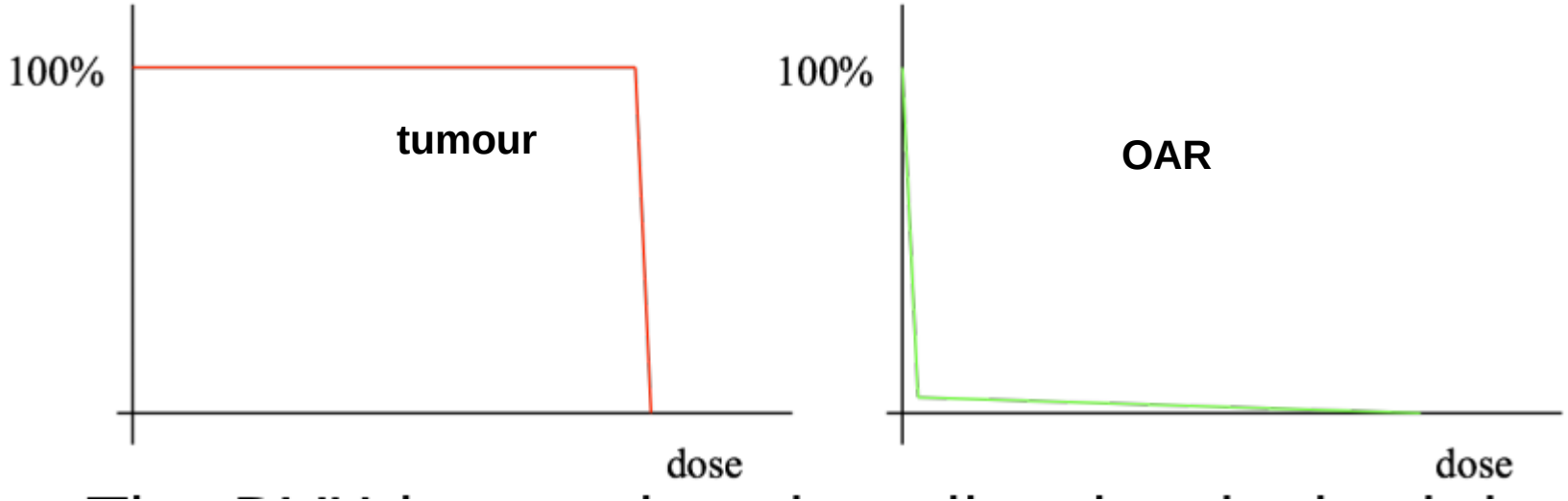
In the process of improvement of the quality of radiotherapy, the volumes of organs at risk exposed to significant doses has significantly decreased, resulting in increased inhomogeneities in the dose distributions within these organs. This has increased the importance of identifying volume effects in normal tissues.

The Dose Volume Histogram (DVH) is used to evaluate a treatment plan, compare different techniques and estimate the Tumour Control Probability (TCP)

- **Differential DVH: what volume received a particular dose?**
- **Cumulative DVH: what volume received at least a particular dose?**

Dose volume histogram

Ideally, the best DVH is when:
the tumour volume received a high homogeneous dose and the critical organs received low dose to most of the structures

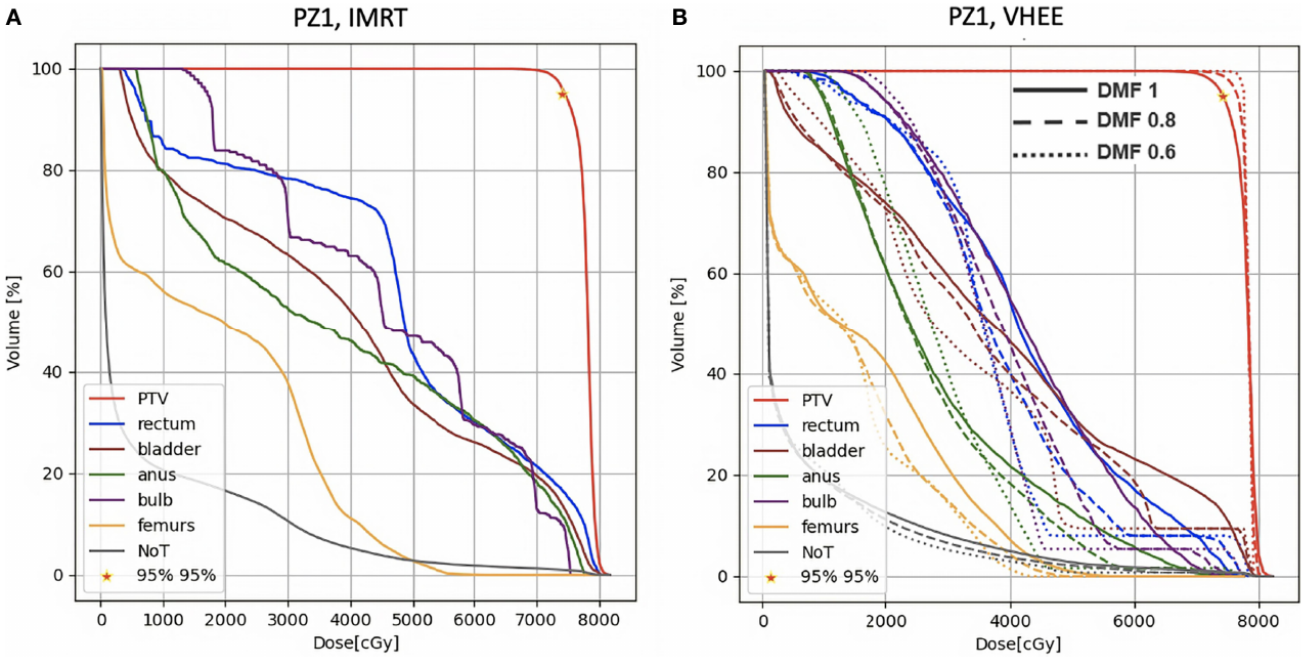


Dose volume histogram

- 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

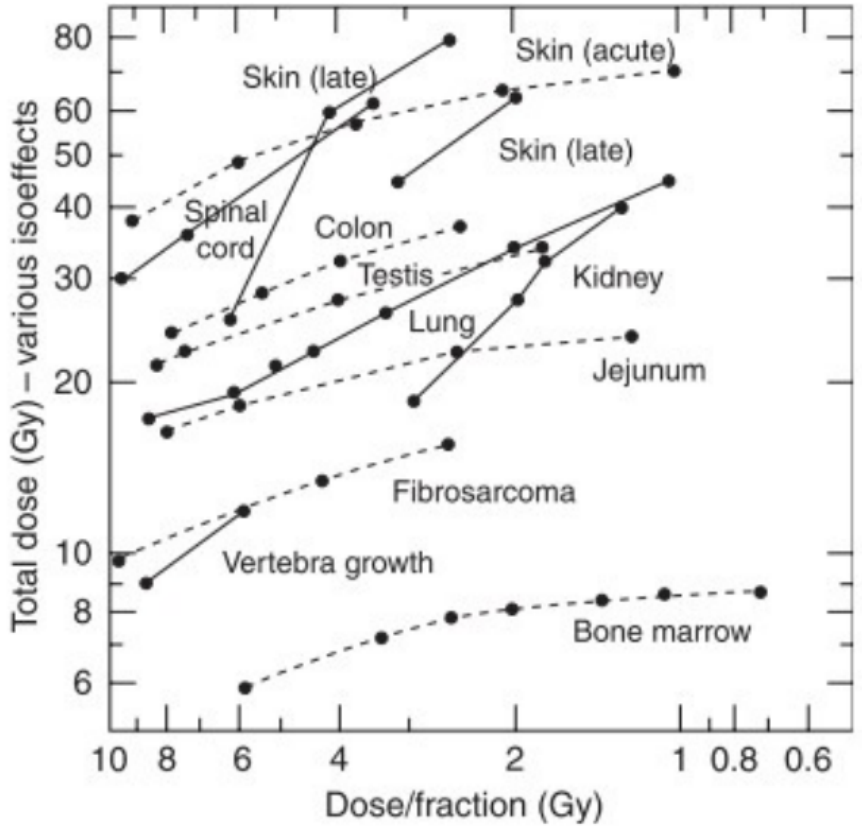
- Usually this is not possible, so there are different constraints to be fulfilled (given by the prescriptions)
- The TPS have to optimize the DVH fulfilling the constraints

Dose volume histogram



Question:
Which one is better?
IMRT or VHEE with DMF=1?

Normal tissue



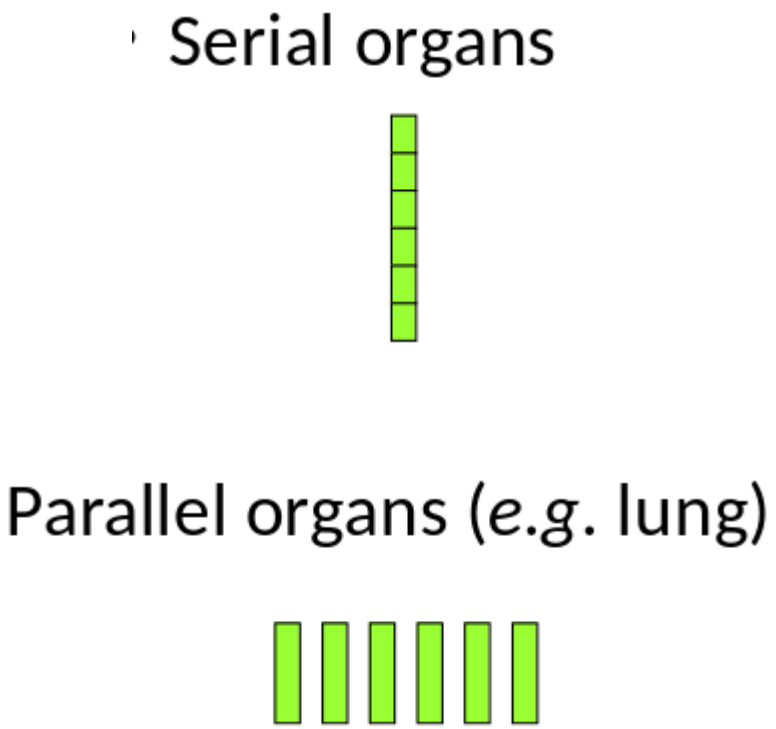
Sparing of normal tissues is essential for good therapeutic outcome

- The radiobiology of normal tissues may be even more complex as the one of tumours:
- different organs respond differently
- there is a response of a cell organization not just of a single cell
- repair of damage is in general more important

Functional subunits

- Structural tissue tolerance depends on cellular radiation sensitivity and is independent of volume irradiated.
- Functional tolerance depends on tissue organization and functional reserve capacity
- Tissue may be considered to have functional subunits (FSU, from Withers et al. 1988), where each subunit perform some function of that organ
- FSU is the largest tissue volume, or unit of cells, that can be regenerated from a single surviving clonogenic cell.
- Functional subunits are sterilized independently by irradiation
- The number of FSUs that are sterilized, and hence the severity of the damage, depends on their intrinsic radiosensitivity, and on dose and other radiobiological parameters

Serial and parallel organs



The clinical consequences are dependent on the arrangement of the FSU within the exposed organ

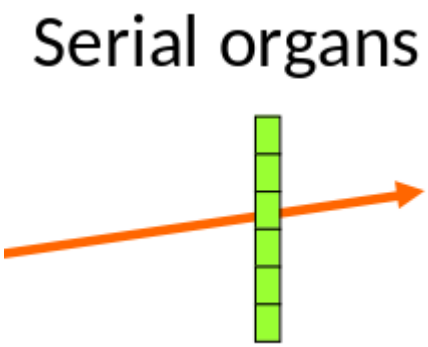
Serial organs:

- **The function of the entire organ depends on the function of each individual FSU**
  E.g.: spinal cord and gastrointestinal tract

Parallel organs

- **each FSU performs its function relatively independently of the others.**
  E.g.: the lung, liver and kidney

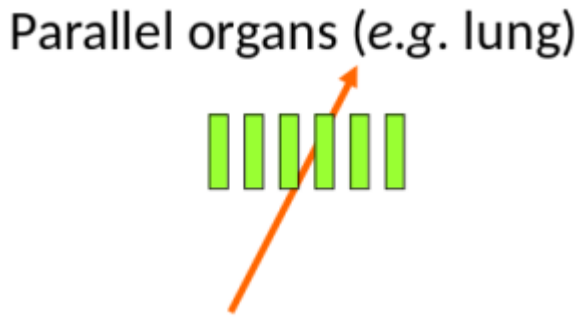
Sparing of normal Serial and parallel organs



Serial organs:

- **Inactivation of only one FSU results in clinical side-effects in a binary response**
- The risk of complications is highly dependent on ‘hot spots’
- The dose distribution within the entire organ is less relevant.

Serial and parallel organs



Parallel organs

- A clinical radiation effect is observed only if the number of surviving FSUs is too low to sustain the physiological organ function
- A threshold volume must be considered in treatment planning, which must not be exceeded but within which large doses may be administered.
- The risk of complications depends on the distribution of the total dose within the organ rather than on individual ‘hot spots’

Serial and parallel organs

- The purely parallel or serial organization of an organ, however, represents the extreme cases. In reality, no organ is organized simply as a chain of FSUs
- **The actual portrait is much more complicated. E.g.:**
- one component of late radiation effects is the response of the (micro)vasculature, and individual small vessels may be considered as serially arranged, which introduces a serial factor into parallel arranged tissue
- The relative seriality model, does not take into account the influence of cellular migration and regeneration from outside the irradiated area
- There could be regional differences in radiation sensitivity within one organ
- Many organs, such as the brain, are better described by an intermediate type of organizational structure which is neither serial/tubular nor parallel. Specific areas of the brain perform specific functions. The clinical tolerance of brain tissue is therefore much more dependent on which area of brain is irradiated than the total volume irradiated.

Mathematical modelling

- The modelling of volume effects on the basis of their serial or parallel organization is useful and explains the apparent paradox that relatively radiosensitive organs, such as kidney and lung, can sustain the loss of more than half their total mass without significant loss of function, whereas relatively radioresistant tissues such as spinal cord can be functionally inactivated by the irradiation of only a small volume.
- Theoretical models have been developed to estimate NTCP for partial volume irradiations and inhomogeneous dose distributions.
- Lyman (1985) and extended into Lyman–Kutcher–Burman (LKB) model: a power-law relationship was assumed between the tolerance dose for uniform whole or partial organ irradiation, where the parameter n (the exponent of the partial volume) describes the volume dependence of the tolerance dose. When $n \rightarrow 1$, then the volume effect is large and the tolerance dose increases steeply with decreasing volume, and when $n \rightarrow 0$ then the volume effect is small.
  The LKB model is currently one ofthe most commonly used models for predicting normal-tissue complication probability.

Mathematical modelling

- relative seriality model of Källman et al (1992): an extra parameter, s (the ‘degree of seriality’), is introduced to describe the functional organization of a tissue. A near- zero value of s represents a parallel structure and an s value close to unity represents an organ with a serial organization
- Withers et al., (1988) model: an organ can be divided into physiologically discrete compartments or FSUs. This model allows for the spatial distribution of FSUs in the tissue to be non-uniform. The radiation response of each independent FSU is determined by Poisson statistics and the functional architecture of FSUs determines the organ’s response to partial volume irradiation


Questions?

CERN Knowledge Transfer

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