The Abdus Salam
**International Centre
for Theoretical Physics**

United Nations
Educational, Scientific and
Cultural Organization

IAEA
International Atomic Energy Agency

School on Medical Physics for Radiation Therapy:
Dosimetry and Treatment Planning for Basic and Advanced Applications
Trieste - Italy, 27 March - 7 April 2017
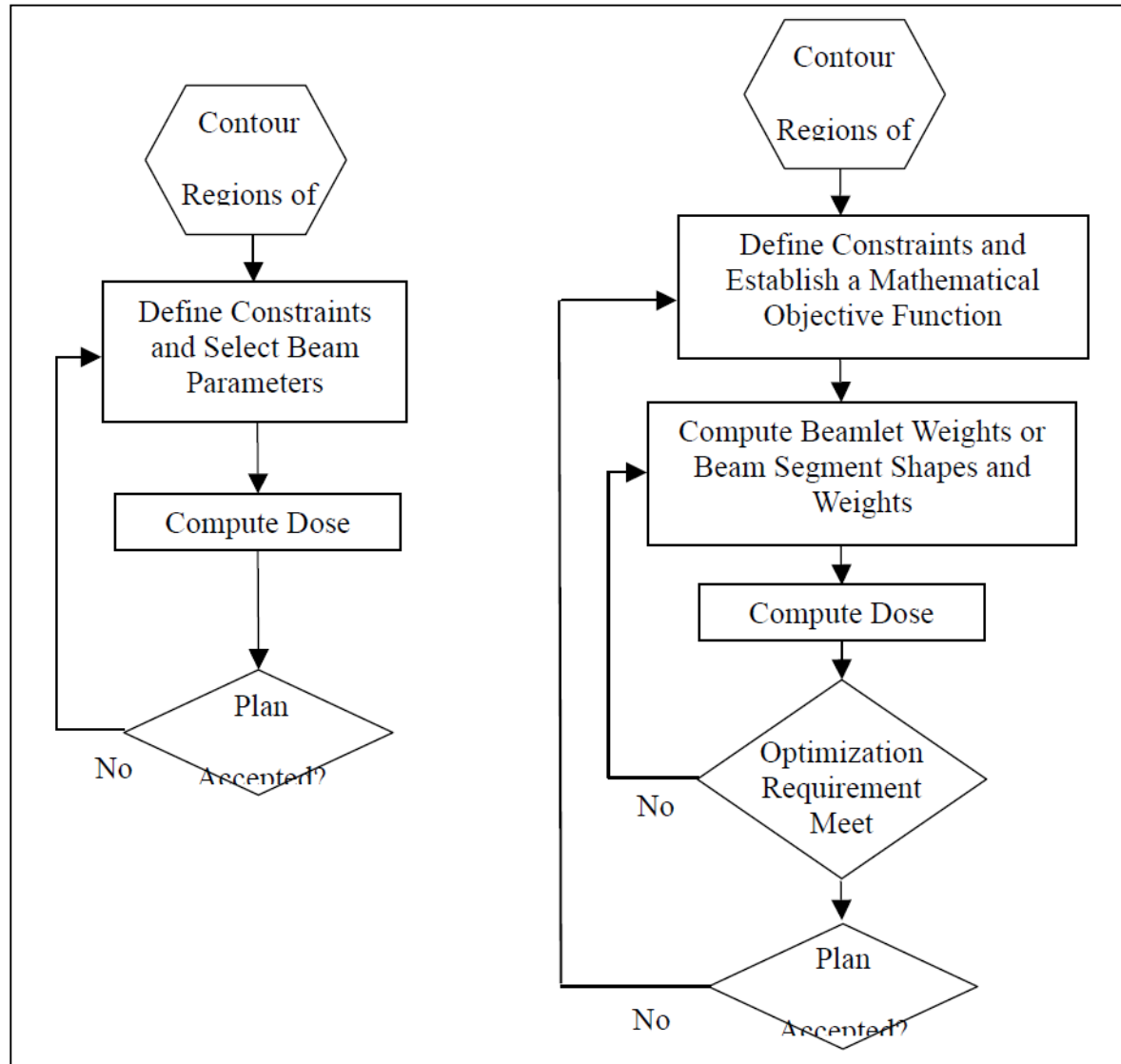
IMRT Planning:
Concepts and Recommendations of the ICRU report n. 83

Maria Rosa Malisan

Traditional vs IMRT planning

- In Traditional Optimization, **beam parameters** such as the direction, the presence of beam modifiers , and the shapes of the beams are established.

- The **beam attributes are iteratively modified** as necessary; then the resulting dose is computed.

- The key distinctions between Traditional and IMRT methods are:

  1) use of **mathematical objective functions** and incorporation of user-defined **dose-volume constraints**

  2) employment of an iterative computer based IMRT **algorithm to seek the optimal solution.**

- The beamlet weights or the weights of a series of beam segments are determined and the dose distribution that results is then computed.

Traditional vs IMRT optimization

Digital Dose Era

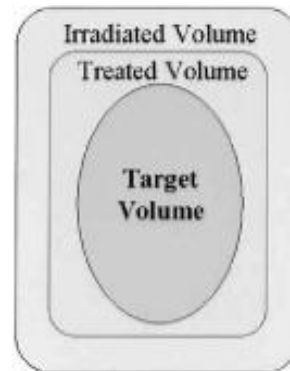IMRT is a digital dose distribution
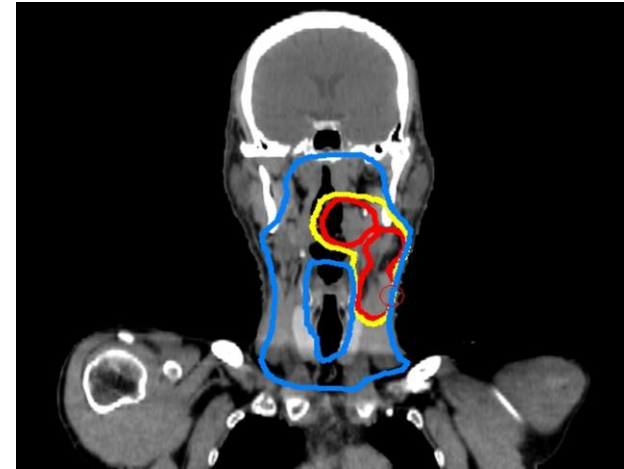
3D is an analogue dose distribution

Traditional vs IMRT planning

❖ Simple	❖ Complex
❖ No need of volume and OAR	❖ Target and OAR must be present
❖ Forward calculation	❖ Inverse calculation
❖ Give what you wish to target volume	❖ Requires dose-volume constraints and cost function
❖ Uniform fluence	❖ Non-uniform
❖ Exact solution	❖ Approximate solution
❖ Uniform dose	❖ High gradient dose
❖ Low MU	❖ High MU
❖ Analogue dose	❖ Digital dose
❖ Dose defined to volume but specified at isocenter	❖ Isocenter dose undefined and meaningless

New Issues about Volumes

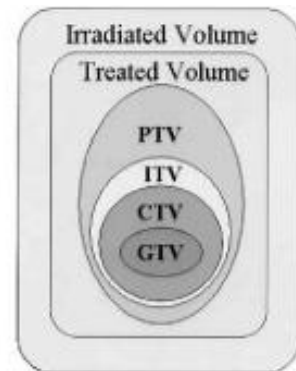- Multiple GTV :   anatomic vs functional
                       imaging;
                       before and during
                       treatment….

- GTV to CTV margins: clinical probability

- CTV to PTV margins: geometric probability,
                       overlapping volumes…

- ITV :   Internal Margin???

- OAR: open vs closed?

- Remaining normal tissues?

- PRV: serial vs parallel OAR
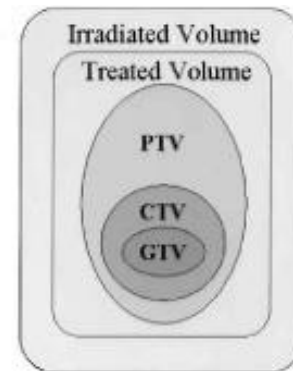
| Irradiated Volume	Irradiated Volume	Irradiated Volume
Treated Volume	Treated Volume	Treated Volume
Target Volume	PTV / CTV / GTV	PTV / ITV / CTV / GTV
(A) ICRU 29	(B) ICRU 50	(C) ICRU 62

New Issues for IMRT

- Single point dose prescription

- Single point dose reporting

- Biological metrics (e.g. EUD, TCP, NTCP…)

- Uncertainties in dose prescription and reporting

- More QA required

ICRU Guidelines

- the International Commission on Radiation Units and Measurements (ICRU) has been developing guidelines for prescribing recording, and reporting dose for radiation therapy.

- The first set of guidelines (ICRU 29) was published in 1978 and was subsequently updated (ICRU 50, 1993; ICRU 62, 1999; ICRU 71, 2004; ICRU 78, 2007) to integrate the new development in RT including electron and proton beams .
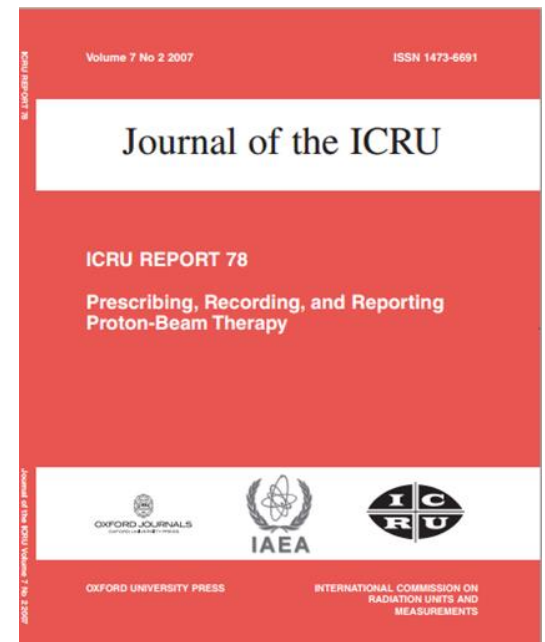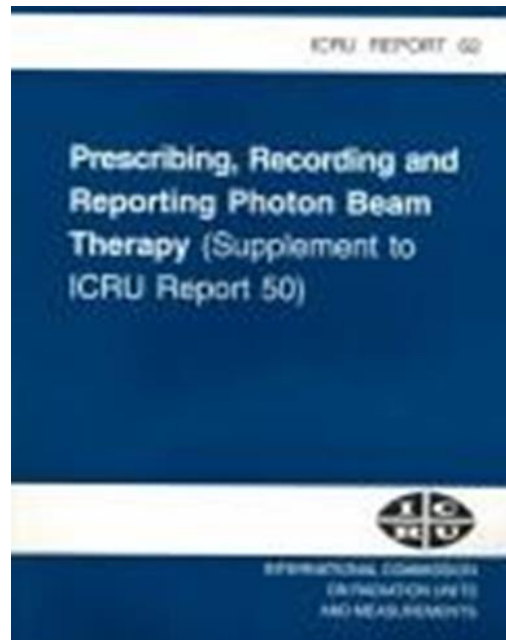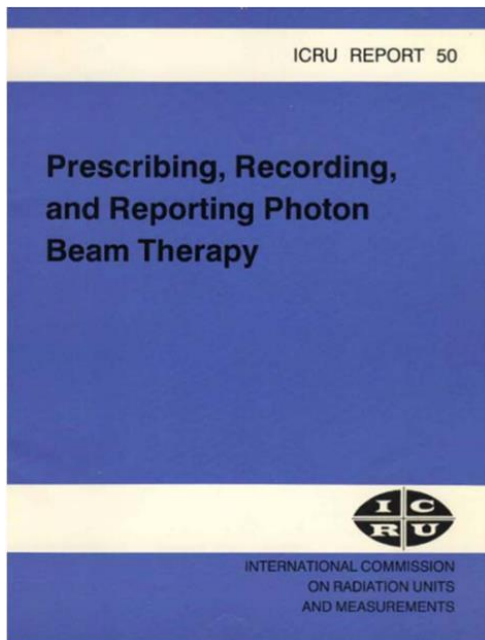
ICRU 83 (2010)

- There was a need to update these reports to take into account the new opportunities offered by IMRT.

- The ICRU report 83 provides the information necessary to <u>standardize</u> techniques and procedures and to <u>harmonize</u> the prescribing, recording, and reporting IMRT.

- New concepts are elaborated.

- Recommendations are given on the selection and delineation of the **targets volumes and organs at risk**.

- Concepts of **dose prescription and dose-volume reporting** have also been refined.

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Journal of the ICRU

ICRU REPORT 83

Prescribing, Recording, and Reporting Photon-Beam Intensity-Modulated Radiation Therapy (IMRT)

OXFORD JOURNALS
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OXFORD UNIVERSITY PRESS

INTERNATIONAL COMMISSION ON RADIATION UNITS AND MEASUREMENTS

What's relevant in ICRU 83 ?

- Revised classification of treatment volumes

- Dose prescription based on DVH

- New definitions of Dose $_{min}$ and Dose $_{max}$

- New *surrogate* of ICRU point

- Request for patient-specific QA

- New criteria for treatment accuracy

DEFINITION OF VOLUMES

- Because delineation of a GTV may vary according to the **diagnostic modality** (*e.g.*, clinical examination, anatomic imaging, functional imaging) used, a clear annotation is required.

- For example:

- **GTV-T (clin, 0 Gy)** : tumor GTV evaluated clinically <u>before</u> the start of the radiotherapy;

- **GTV-T (MRI-T2, 30 Gy)** : tumor GTV evaluated with a T2-weighted MRI scan <u>after a dose of 30 Gy</u> of external beam irradiation

- This approach avoids the introduction of new or potentially confusing terminology

  – *e.g. biological target volume (BTV), proliferative target volume (PTV), hypoxic target volume (HTV)…*

- and is able to cover all the different situations that might be encountered.

view from a laryngoscope
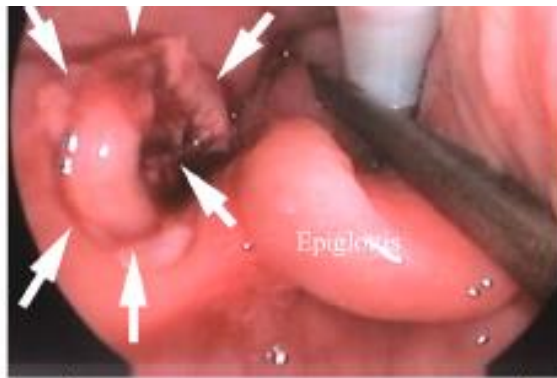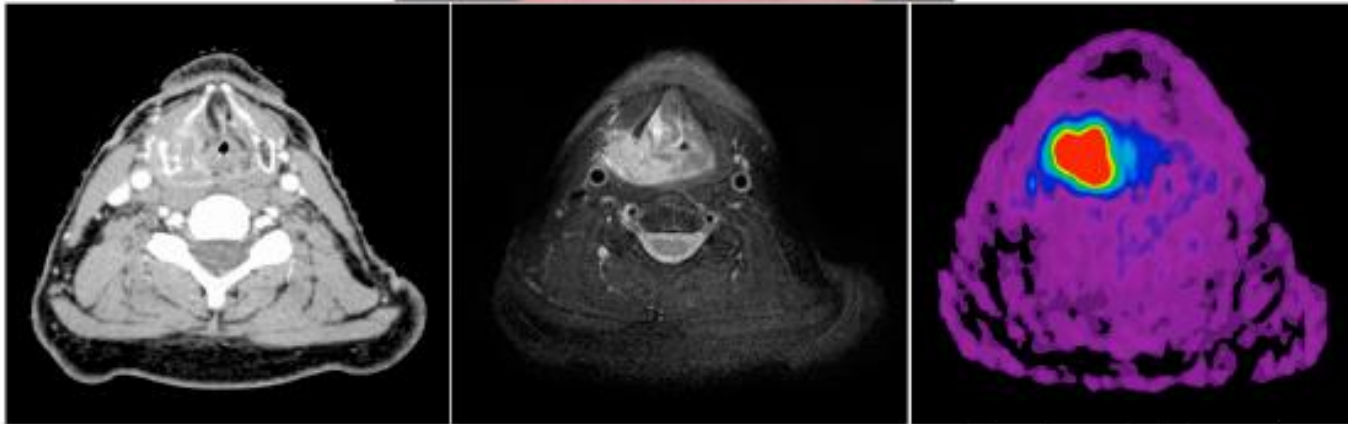
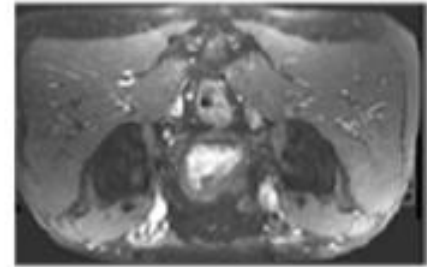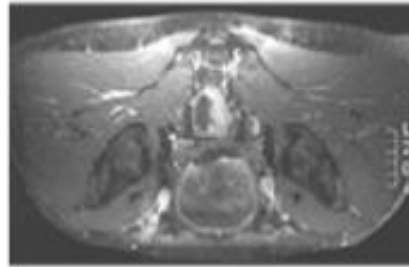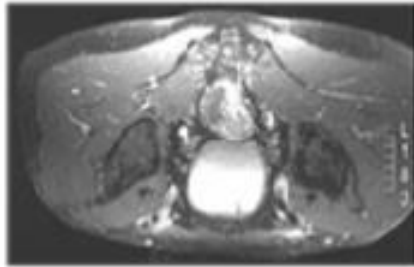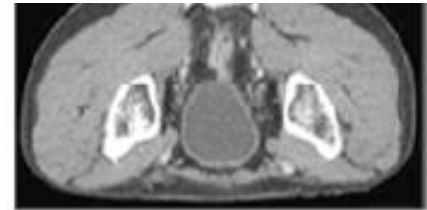|	contrast-enhanced CT	fat-sat T2-weighted MRI	FDG-PET
0 Gy			
20 Gy			

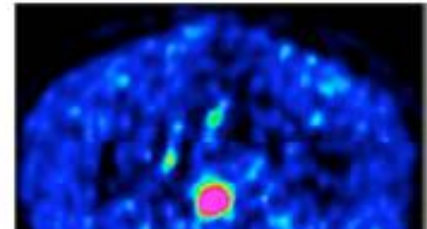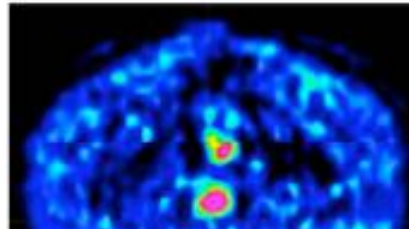**Comparison between various modalities for the definition of the primary HN GTV**
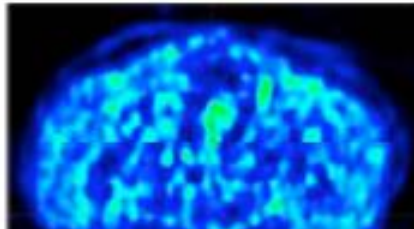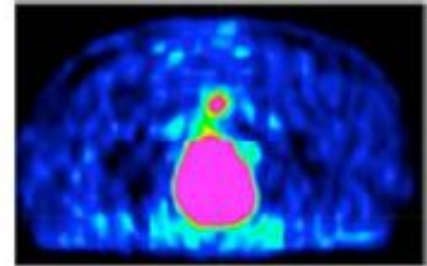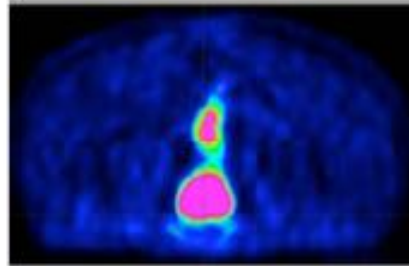
BEFORE   **DURING**   **AFTER RT**

MRI

PET CT
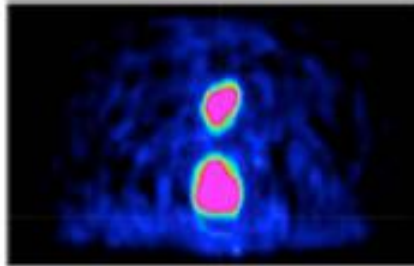
**Comparison among various modalities
for the definition of a primary rectal tumor GTV**

Organs at Risk

- The concept of **tissue organization is operationally useful for determining dose-volume constraints** and for the evaluation of the DVH's.

- From a functional point of view, tissue organization has been conceptually divided into "serial", "parallel" or "serial-parallel".

- **Serial organs**, or serial-like organs, (*e.g.*, spinal cord, nerve, the gastro-intestinal tract) consist of a chain of functional units, which **all** need to be preserved to guarantee the functionality of the tissue.

- **Parallel organs**, or parallel-like organs (*e.g.*, lung, parotid), consist of functional units **acting independently** of each other.

- Some organs such as the kidney have a mixed serial and parallel organization.

OAR Delineation

- **For serial-like organs**, the dose at or close to the **maximum dose** to a given volume is typically the best predictor of loss of function.

- In contrast, for **parallel-like organs** showing graded dose responses, **the mean dose or the volume** that receives a dose in excess of some defined value have been used as predictors of loss of function.

- This concept of tissue organization is also useful for the **delineation of OARs.**

- For serial-like organs, as the volume irradiated may have less impact on the assessment of the organ tolerance, **the extent to which these organs are delineated** will probably have a lesser importance for the patient's treatment

- However, to allow comparison between centers, it is very useful to follow guidelines,

- In contrast, for **parallel-like organs**, the volume assessment is crucial, and **complete organ delineation** is required.

Planning Organ at Risk (PRV)

- As is the case with the PTV, uncertainties and variations in the position of the Organs at Risk during treatment must be considered to avoid serious complications.

- For this reason, **margins have to be added to the OARs** to compensate for these uncertainties and variations, using similar principles as for the PTV.

- This leads, in analogy with the PTV, to the concept of Planning Organ at Risk Volume (PRV).

- A **margin around an Organ at Risk with a serial-like structure** (*e.g.,* spinal cord) is more clinically relevant than around Organs at Risk with parallel-like structure (*e.g.* liver, lung, parotid).

- For reporting, it is recommended that, as for the PTV, **the PRV be described by including the size of the margins applied** to the Organ at Risk in different directions.
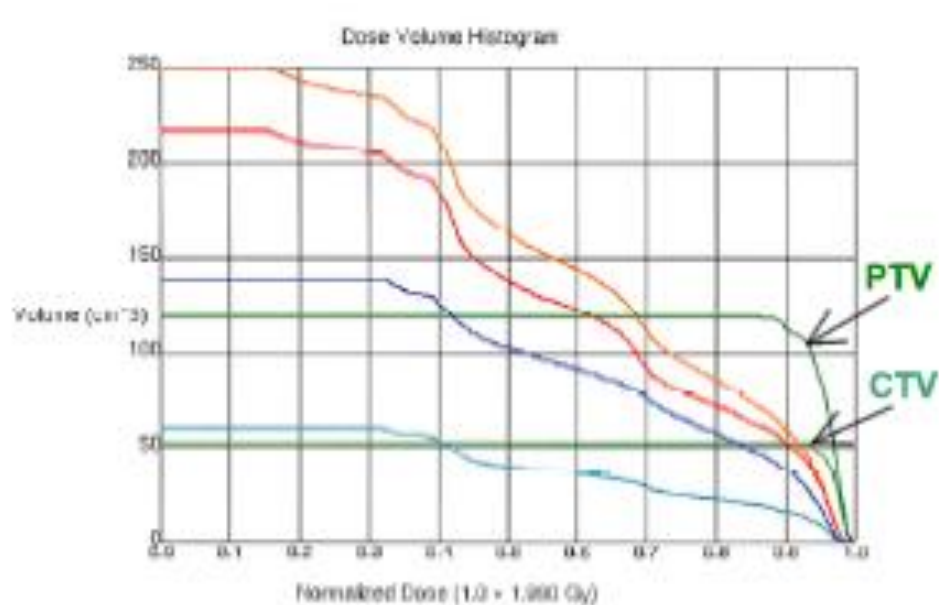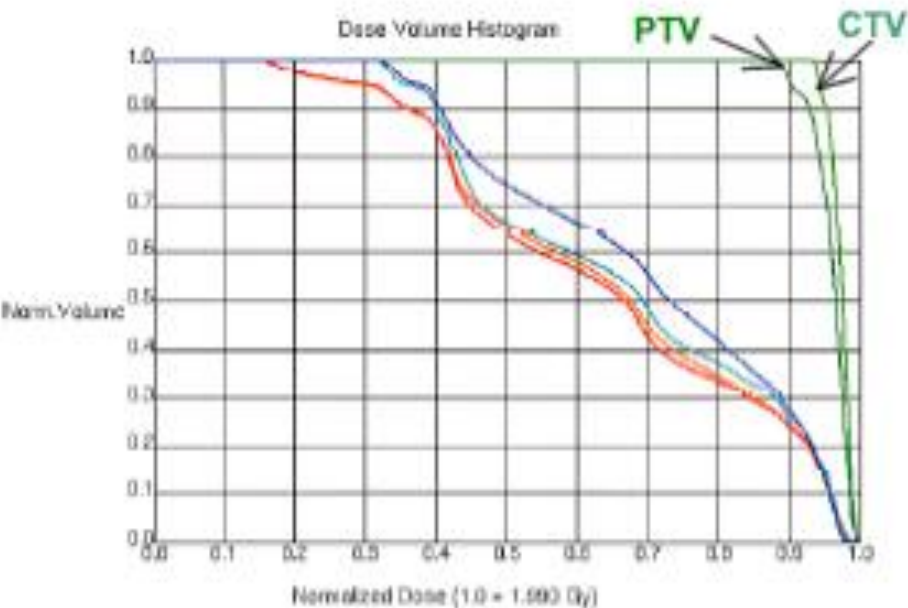
Relative and absolute DVH 's for a prostate cancer case comparing Rectum and Rectal Wall doses.

- The margin on the PRV was 0.5 cm as was the margin between PTV and CTV.

- The PRV margin for the rectal wall was only applied on the outside of the rectal OAR.

Overlap PTV-PRV

- The delineation of the PTV and the PRV will often result in one or more overlap regions.

- **It is recommended that the margins not be compromised for the PTV or PRV even if overlaps occur.**

- The practice of **shrinking the CTV-PTV margin** to accommodate an OAR is discouraged as it results in a deceptively better PTV dose homogeneity!

- To ensure sufficient normal tissue sparing, **priority rules** in the planning system can be used, or the **PTV or PRV can be subdivided** into regions with different dose constraints.

- In any case, it is recommended that the **dose be reported in the full PRV and PTV**.
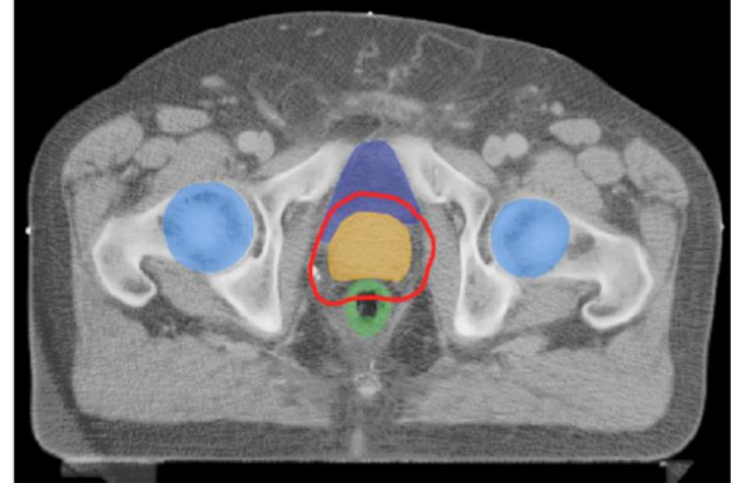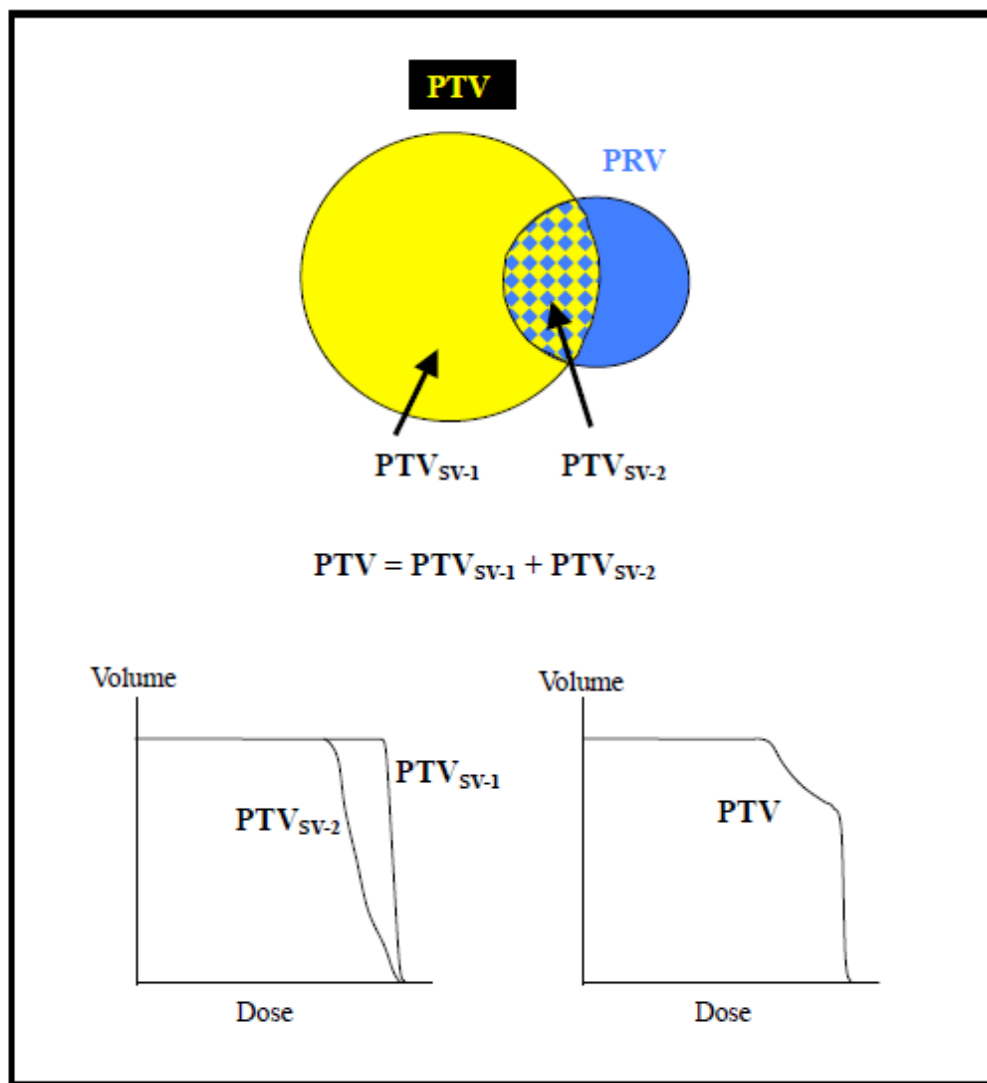
This sub-volume PTV can be used for planning purposes (beam arrangement and dose prescription), **but the dose should be reported for the whole PTV** (right DVH).

Ethmoid sinus IMRT
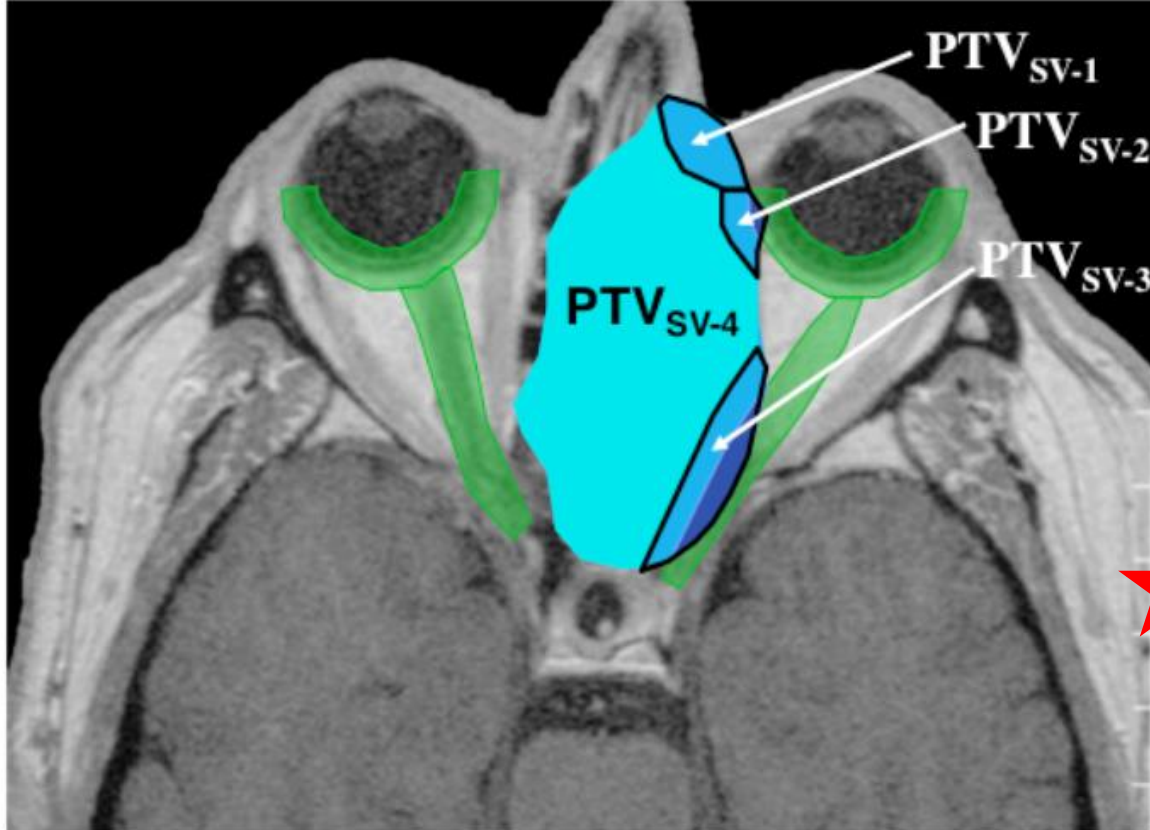
Planning aims

PTV
  median dose (D_{50}):   70.0 Gy
  near-min dose (D_{98}): $\geq$ 66.5 Gy
  near-max dose (D_2): $\leq$ 74.9 Gy
Optic nerves
  near-max dose (D_2): $\leq$ 60.0 Gy
Retina
  near-max dose (D_2): $\leq$ 50.0 Gy

Modification to planning aims

PTV
  PTV_{SV-1}
    near-max dose (D_2): $\leq$ 74.9 Gy
    near-min dose (D_{98}): $\geq$ 66.5 Gy
  PTV_{SV-2}
    near-max dose (D_2): $\leq$ 50.0 Gy
    near-min dose (D_{98}): $\geq$ 49.0 Gy
  PTV_{SV-3}
    near-max dose (D_2): $\leq$ 60.0 Gy
    near-min dose (D_{98}): $\geq$ 58.0 Gy
  PTV_{SV-4}
    median dose (D_{50}):   70.0 Gy
    near-max dose (D_2): $\leq$ 74.9 Gy
    near-min dose (D_{98}): $\geq$ 66.5 Gy
PRV optic nerves
    near-max dose (D_2): $\leq$ 60.0 Gy
PRV retina
    near-max dose (D_2): $\leq$ 50.0 Gy

⭐ PTV in the Build-Up region or extending outside the body
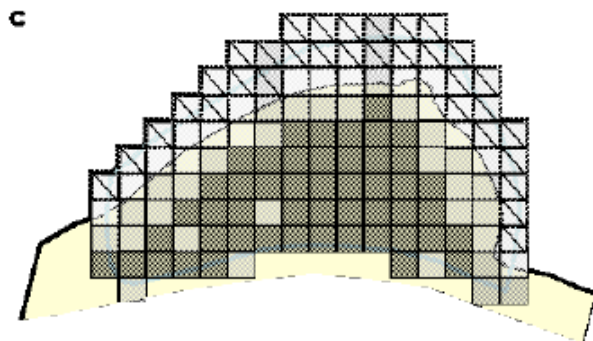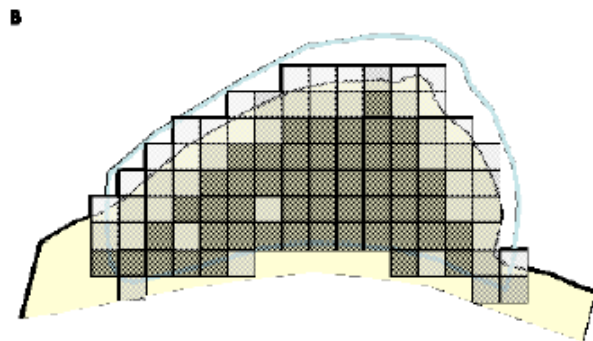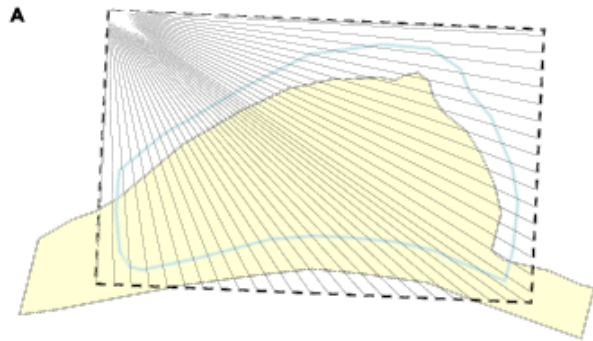
- a) beam's eye view (BEV) of **conventional tangential field** (dashed outline).

- In blue, contour of PTV reaching outside the breast to secure flash;

- b) IMRT optimization is performed on the part of the **PTV a few mm inside the skin surface** to avoid (unwanted) dose compensation in the build-up region by the optimizer.

- No intensity is assigned to bixels projecting outside the BEV of the breast into the PTV. Flash is not secured;

- c) **creation of flash** by extending the same intensity values from the breast periphery to the regions of the PTV outside the breast BEV.

REMAINING VOLUME AT RISK (RVR)

- **RVR** = difference between the volume enclosed by the **external contour** of the patient and that of the **CTVs and OARs** on the slices that have been imaged.

- If it not specifically evaluated, there could be unsuspected regions of **high dose within the patient**, which would go undetected.

- The dose to the RVR might be useful in estimating the risk of late effects, such as **carcinogenesis** (important for younger patients!).

- Looking for high dose regions using the RVR DVH is, however, no substitute for a thorough **analysis on a slice-by-slice** basis to examine the dose distribution throughout the paths of the beams.
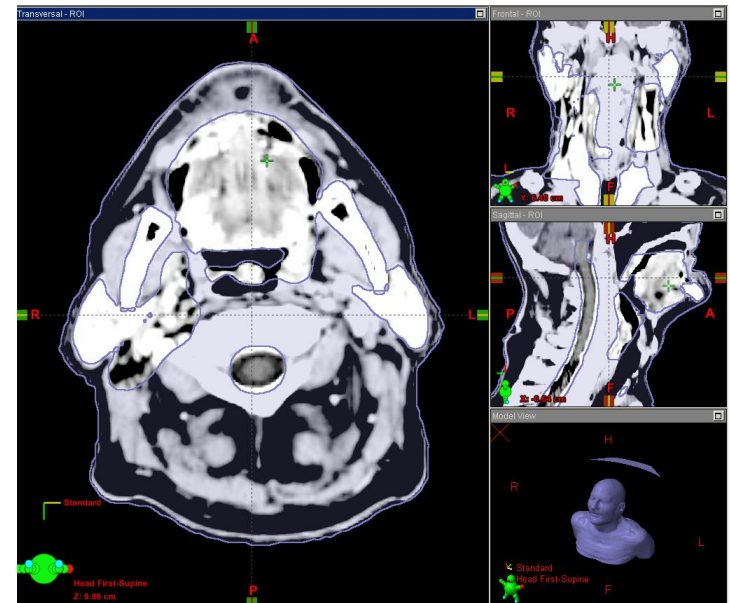
ICRU Levels of Reporting

- Historically, as a compromise, the ICRU identified 3 levels of prescribing and reporting:

- **Level 1:** minimum standards, <u>inadequate for IMRT</u>

- **Level 2:** standard level

- **Level 3 :** homogeneity, conformity and biological metrics and confidence intervals.

ICRU Point inadequate for 3DCRT &IMRT

- The dose distribution within a PTV for IMRT may be **less homogeneous** than in conventional radiation therapy and may contain significant dose variations.

- The selection of a dose reporting point that lies within a region of high or low dose would particularly **misrepresent the dose.**

- The **dose gradient at the boundary** of a PTV as a result of multiple IMRT beams can be more than 10 % per millimeter and a small shift in the field delivery may affect the reliability of using a single point to report the prescription.

- Modern TPS's have sufficient evaluation tools for Level 2 reporting to be the standard for use in IMRT.

Level 2 recommendations

- Level 2 prescribing and reporting implies that the treatments are performed using **computational dosimetry and three-dimensional imaging.**

- At this level it is assumed that all volumes of interest (*e.g.*, GTV, CTV, PTV, OAR, PRV) are defined using, for example, a series of CT or MRI sections and that 3D dose distributions are available and include **heterogeneity corrections**.

- It is expected that DVHs for all volumes of interest are routinely computed.

- It is also assumed that a complete QA program is in place to ensure that the prescribed treatment is accurately delivered.

Dose-volume specification
D_V, $D_{near\text{-}min}$, $D_{near\text{-}max}$

- Reporting of minimum dose should be replaced by the better-determined **near-minimum dose $D_{98\%}$,** also designated as $D_{near\text{-}min.}$

- Other dose-volume values, such as $D_{95\%}$, may also be reported but should not replace the reporting of $D_{98\%}$.

- Analogously, it is recommended to report the **near-maximum dose $D_{2\%}$** as a replacement for the "maximum dose".

- Both recommendations serve the same purpose, **to report a dose that is not reliant on a single computation point.**

- The radiation oncologist may judge that the "maximum dose" defined by ICRU 50 is clinically relevant and this value may be reported.

PTV Median Dose D50%

- The report does not recommend any particular V value of D_V for a prescription. However, **the median dose, $D_{50\%},$** is likely to be a good measure of a <u>typical dose</u> in a relatively homogeneously irradiated tumor.

- As shown by *Das et al, 2008*, the median dose has been shown to be computed accurately by many commercial TPS's, and its value is easy to determine from a cumulative dose-volume histogram.
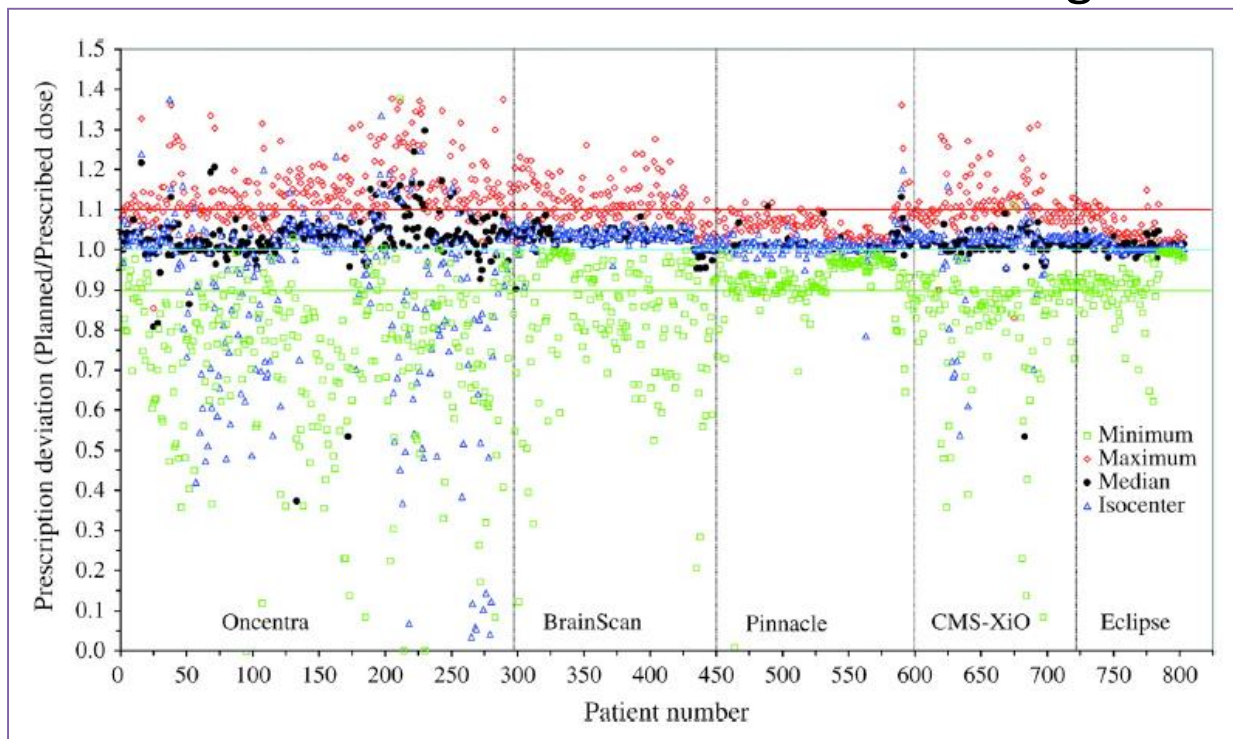
PTV Median Dose $D_{50\%}$

- The original rationale for **reporting the dose at the ICRU reference point and reporting of $D_{50\%}$ are very similar**, *i.e.*, reporting an absorbed dose that is largely representative of the absorbed dose to the PTV.

- However, numerically the values could probably differ to a small extent **depending on the dose distribution in the PTV**.
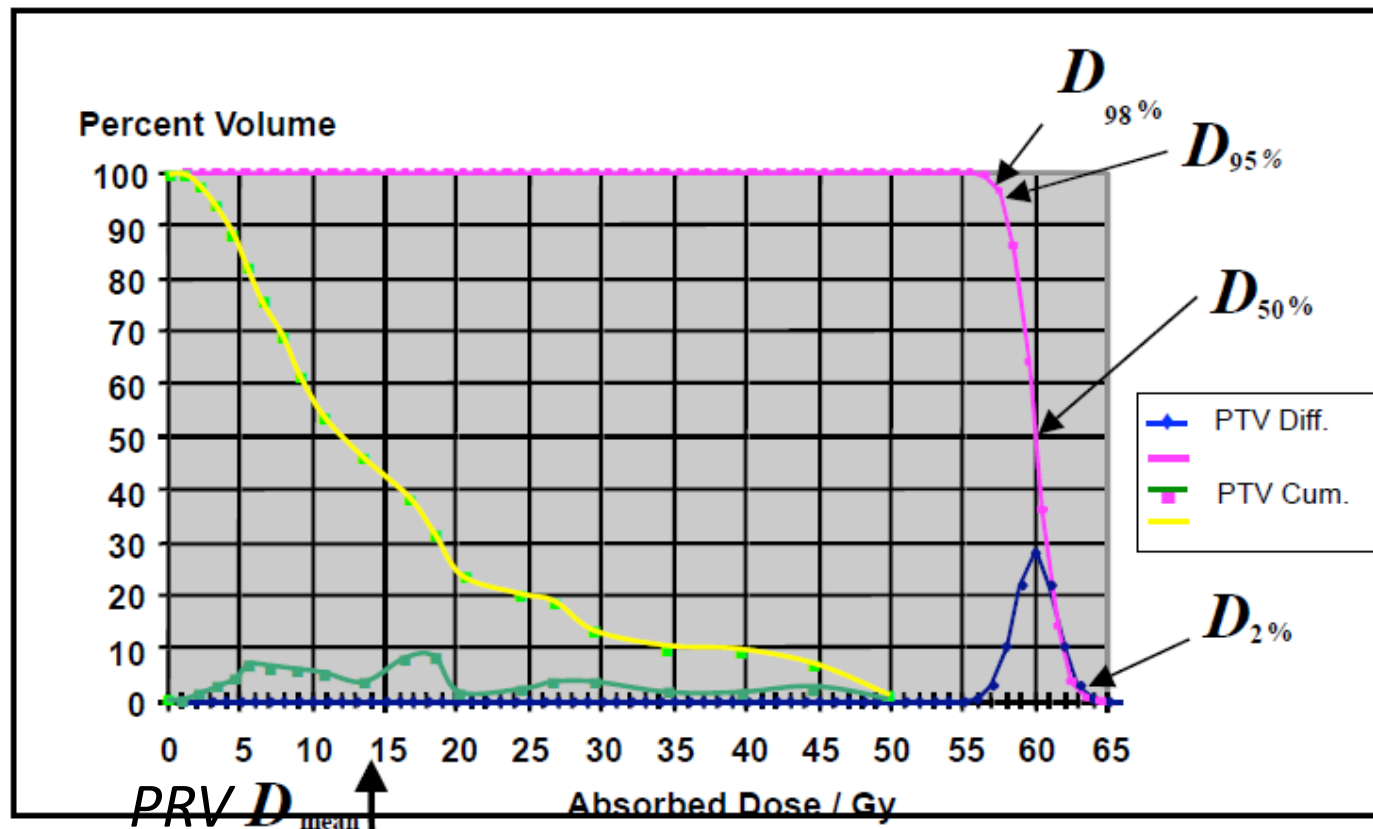
Dose-Volume Reporting

- It is strongly recommended that **if the method of prescription is changed** from a point-dose to a dose-volume approach, **the impact** on the dose received by patients should be determined.
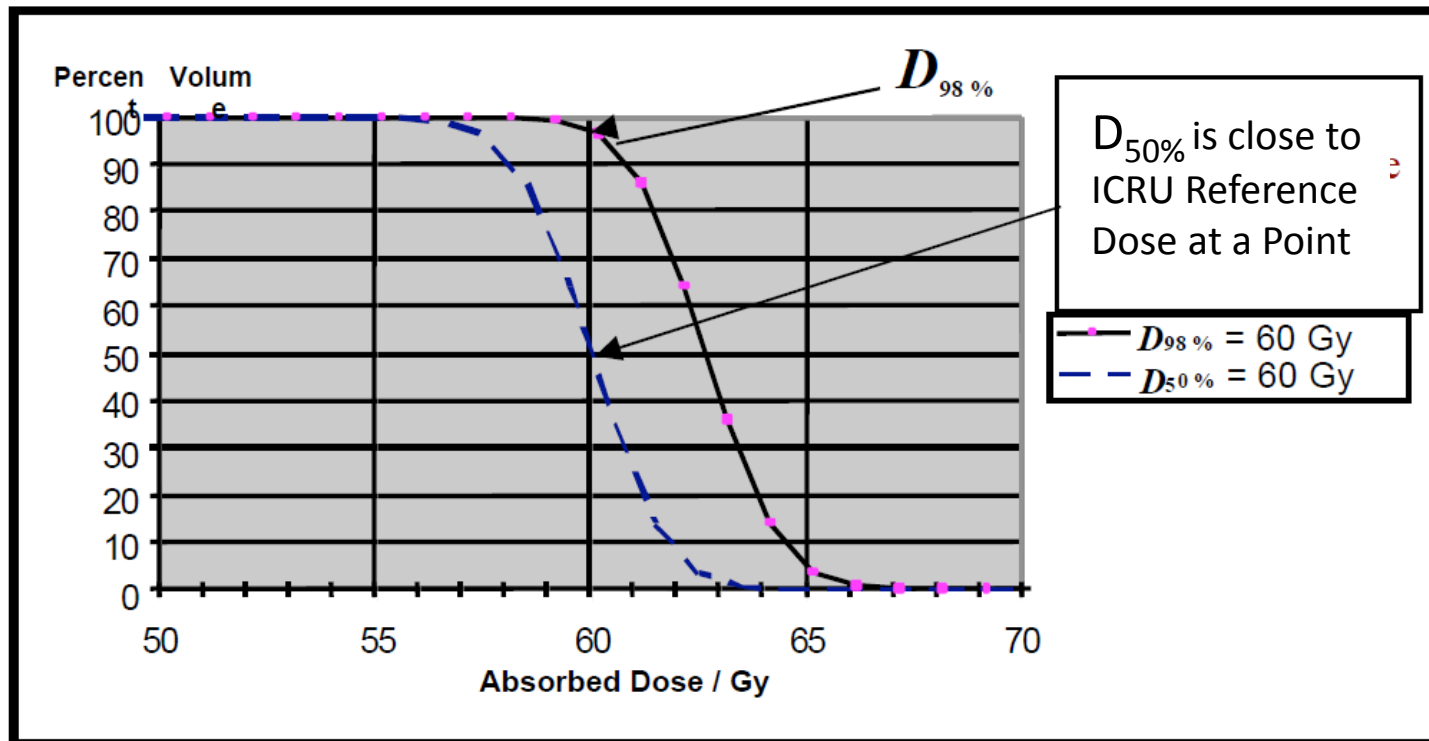

The prescription to the ICRU Reference Point and to $D_{50\%}$ would be nearly equivalent, with $D_{98\%}$ =57 Gy. If instead prescription was set to $D_{98\%}$, this would have amounted to about a **5 % increase in the dose** to a typical point in the PTV, $D_{50\%}$ in this example.

DOSE-VOLUME REPORTING SPECIFIC TO THE OAR AND PRV

- For **"serial-like" OAR's** (e.g. spinal cord, intestines, optic nerve…), **$D_{2\%}$** is to be reported and the entire organ should be delineated.

- A high estimate of $D_{2\%}$ will result if only those portions of the organ that receive a high dose are delineated.

- Care should be taken in a **change from maximum dose $D_{0\%}$** or another maximum-like dose-volume specification to the near-maximum dose $D_{2\%}$.

- For example, the RTOG Protocol 0615 for nasopharyngeal cancer set the **$D_{1\%}$ dose at 50 Gy for the spinal cord PRV** but placed a constraint such that the **spinal cord** itself would have a maximum dose **$D_{0\%}$ of 45 Gy**.

- Replacing $D_{1\%}$ or $D_{0\%}$ in this protocol by $D_{2\%}$, might require these doses to be **significantly reduced** depending on the gradient of the DVH curve for the spinal cord at high doses.

Change from D_{max} to $D_{near-minimum}$
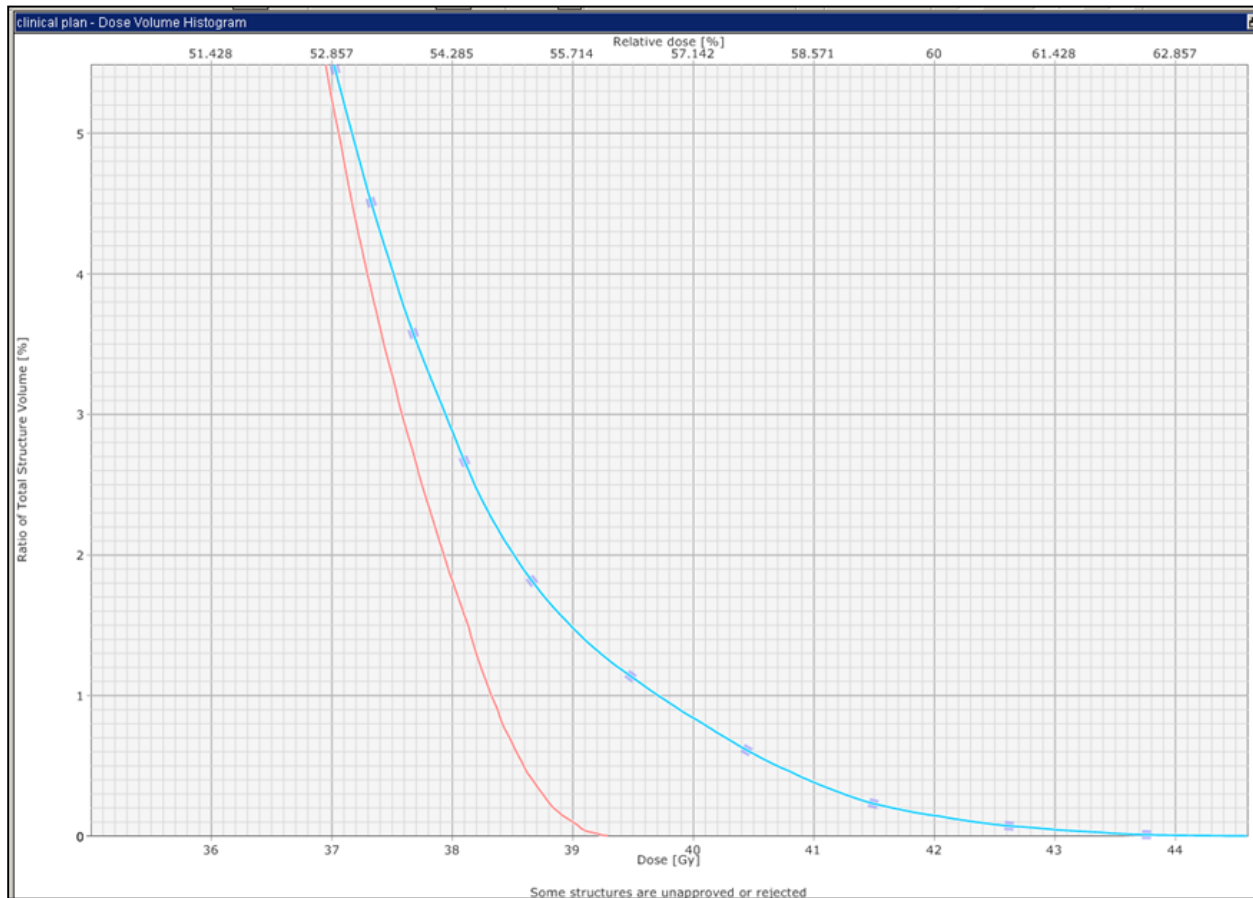
	D0%	D1%	D2%
Spinal Cord	39.3	38.3	37.9
PRV SC	44.7	39.7	38.5

DOSE-VOLUME REPORTING SPECIFIC TO THE OAR AND PRV

- For **parallel-like structures** (e.g. parotid, lung, kidney, liver...) it is recommended that **more than one dose-volume specification** be considered for reporting.

- The **mean dose** in parallel-like structures may be a useful measure of dose in an organ at risk.

- It is recommended that **both D_{mean} and V_D** be reported, where the subscript D is a dose, which if exceeded within some volume, has a high probability of causing a serious complication.

- For example, the incidence and severity of lung pneumonitis is well correlated with $V_{20\ Gy}$, the volume of normal lung receiving more than 20 Gy.

DOSE-VOLUME REPORTING SPECIFIC TO THE OAR AND PRV

- Because most organs are not clearly a serial-like or parallel-like structure (e.g. heart) **at least 3 dose-volume specifications** should be reported.

- These would include D_{mean}, $D_{2\%}$, **and a third specification** V_D that correlates well with a dose D, which if exceeded within some volume has a known high probability of causing a serious complication.

- Normal tissues limits as defined in **QUANTEC** should be used.

Parotid Scoring

Parotid Scoring		
No Variation	Minor Variation	Major Variation
Mean dose to either parotid is at or less than 26.0 Gy *or*	40% of either parotid receives less than, or equal to 30.0 Gy	**Failure to achieve either** No Variation or Minor Variation
50% of either parotid receives less than 30.0 Gy *or*		
20 cc of the combined parotid glands receive less than 20.0 Gy		

REPORTING OF SOFTWARE VERSIONS FOR TREATMENT PLANNING AND DELIVERY

- Dose-calculation algorithms are expected to improve for the foreseeable future as Monte Carlo dose-calculation algorithms become more accessible.

- In addition, beam characterization and algorithms to account for collimator leaf shape and extra-focal radiation (scatter from the head of the treatment unit) are under development.

- As part of Level 2 reporting it is important to note the **make, model and software version of the TPS** and on the **optimizer software** used.

- It is usually relevant to report details of the **treatment delivery software** too.

Level 3 recommendations

- Level 3 reporting describes **techniques and concepts** which are **under development**.

- They have not yet reached a stage where they are sufficiently established to recommend their use in routine practice.

- Examples include the use of concepts such as TCP, NTCP or EUD

- It is recommended that all information required at Level 1 and 2 should be incorporated when reporting at Level 3.

- It is recognized that procedures at Level 3 may be added to Level 2 in the future.

$$TCP = \prod_i \exp[-n_i SF(D_i, d_i)] \qquad NTCP = 1 - (1 - p(D))^N$$

$$EUD = \left(\sum_i v_i D_i^a \right)^{1/a}$$

Dose homogeneity and dose conformity

- Dose homogeneity and dose conformity are independent specifications of the quality of the dose distribution.

- **Dose homogeneity** characterizes the uniformity of dose distribution within the target volume.

- **Dose conformity** characterizes the degree to which the high dose region conforms to the target volume, usually the PTV.
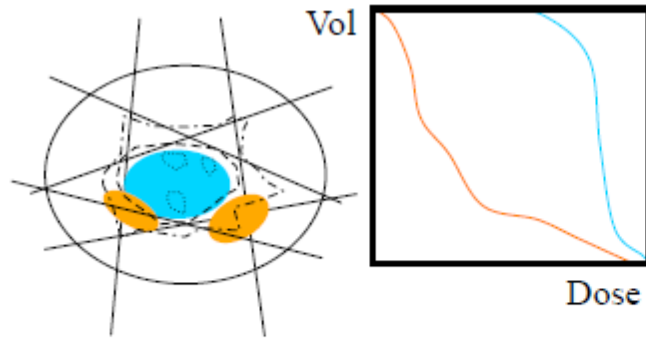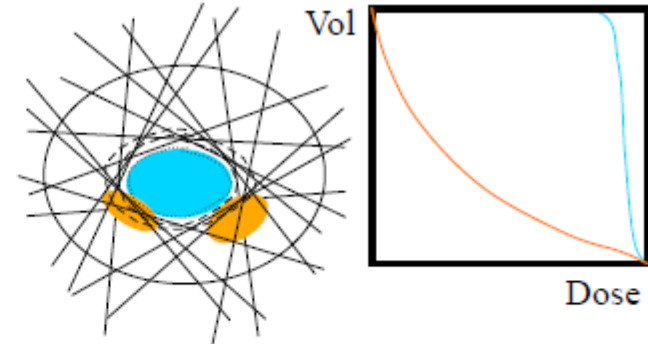
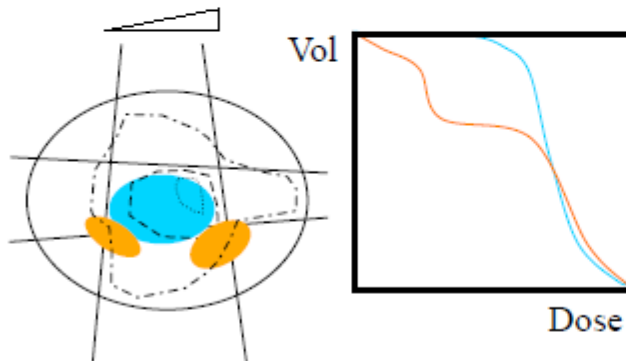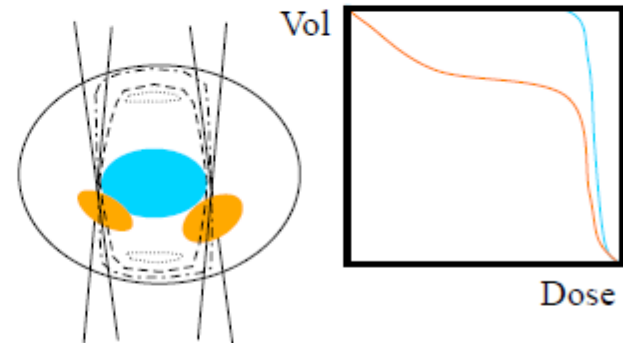# Dose homogeneity and dose conformity

Homogeneity Index

- The following definition for homogeneity index is suggested:

$$HI = (D2\ \% - D98\ \%) / D50\ \%$$

- An **HI = 0** indicates that the dose distribution is almost homogeneous.

- $D_{50\ \%}$ is suggested as the normalization value because reporting of $D_{50\ \%}$ is strongly recommended in Level 2 reporting.

- The ICRU **previously** recommended that the dose values in the PTV be confined **within 95 % to 107 %** of the prescribed dose.

- With IMRT **these constraints may be unnecessarily confining** if the avoidance of normal tissue is more important than target dose homogeneity.
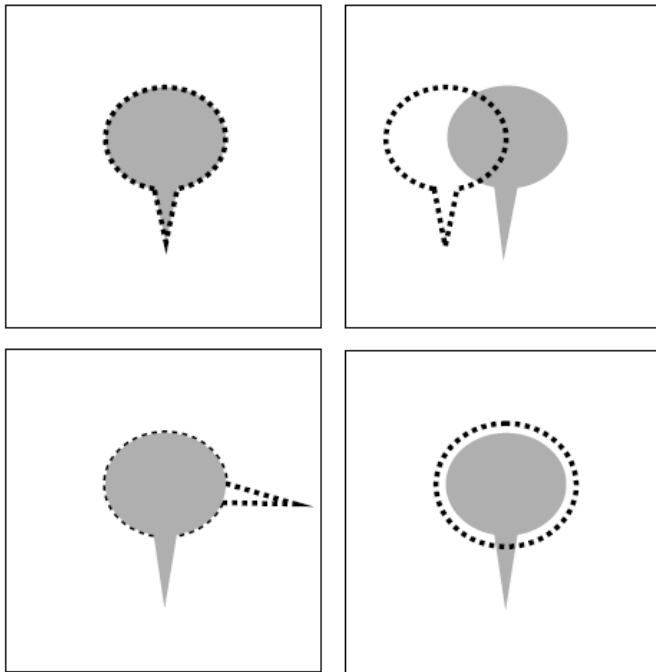
Conformity Index

- A variety of indices have been proposed to characterize the degree of dose conformity of the **Treated Volume (TV) to the PTV** using a single parameter.

- For example in ICRU 62:

Conformity Index = TV $_{prescr}$/ PTV $_{volume}$

- In using any of these index formulations, it is recommended that $D_{98\ \%}$ be used for delineating the TV (with the exception of the Conformity Index, where there is a requirement that the TV include the entire PTV).

- However, because of the increasing availability and use of DVH formats for reporting dose information, the applicability of any of the above indices for reporting results of IMRT, is likely to be limited.

CONFORMITY INDEX: A REVIEW

Loïc Feuvret, M.D.,* Georges Noël, M.D.,* Jean-Jacques Mazeron, M.D., Ph.D.,*†
and Pierre Bey, M.D.*‡

Lomax and Scheib proposed an index taking into account exclusively the irradiation of healthy tissues:

$$Healthy\ tissues\ conformity\ index = \frac{TV_{RI}}{V_{RI}}$$

where TV_{RI} **target volume** covered by the reference isodose, and V_{RI} volume of the reference isodose.

van't Riet *et al.* proposed an index called **conformation number (CN)**:

$$CN = \frac{TV_{RI}}{TV} \times \frac{TV_{RI}}{V_{RI}}$$

where TV = target volume. The CN ranges from 0 to 1, where 1 is the ideal value.

Clinical and biological evaluation metrics

- Biological-based evaluation metrics are interesting research quantities but clinically **they should be used with caution.**

- They are based not only on dose and volume, both of which can be physically defined, but also to some extent on clinical observations and/or biological models.

- All biological models have **uncertainties** in the values of the parameters chosen.

- As biological models become more used in research studies as prescription and evaluation quantities their possible role will become better defined.

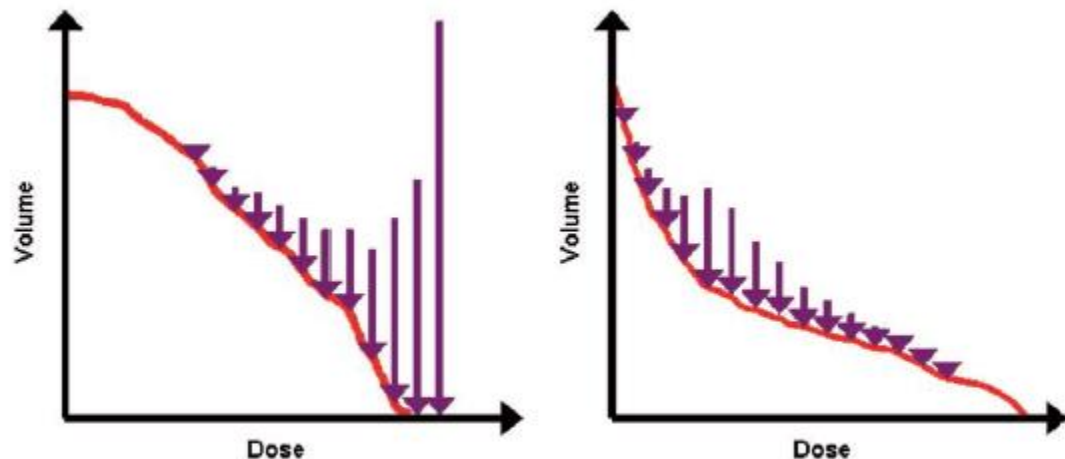- Eventually the models may be used directly as **objective functions in IMRT optimization**.

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Figure 1. Weights of "virtual" DV objectives representing the same volume effect as a serial-type cost function (a) or a parallel-type cost function (b).

Clinical and biological evaluation metrics

- ICRU 83 recommends that biologically-based quantities be explored as **evaluation metrics** to provide additional quantitative tools for radiation oncology.

- As with plan optimization, either EUD or TCP/NTCP models can be used.

- The EUD has the advantage of fewer model parameters, as compared to TCP/NTCP models.

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AAPM

The Use and QA of Biologically Related Models for Treatment Planning

Report of AAPM Task Group 166 of the Therapy Physics Committee

March 2012

- If biologically-based metrics are to be reported, the assumptions used in the models, their **parameters, and the model itself must be unambiguously specified**.

Model-based dose calculation

- Recently, model-based dose-calculation algorithms, such as the convolution/superposition method or Monte Carlo simulation have been adopted and provide accurate absorbed-dose calculations even in situations of tissue heterogeneity such as the lung.

- It is recommended that **the users ensure** that TPS's have the ability to **compute the absorbed dose accurately** for **small fields, inhomogeneous tissues**, and in regions in which there is **electronic disequilibrium**.

Use correction for heterogeneities
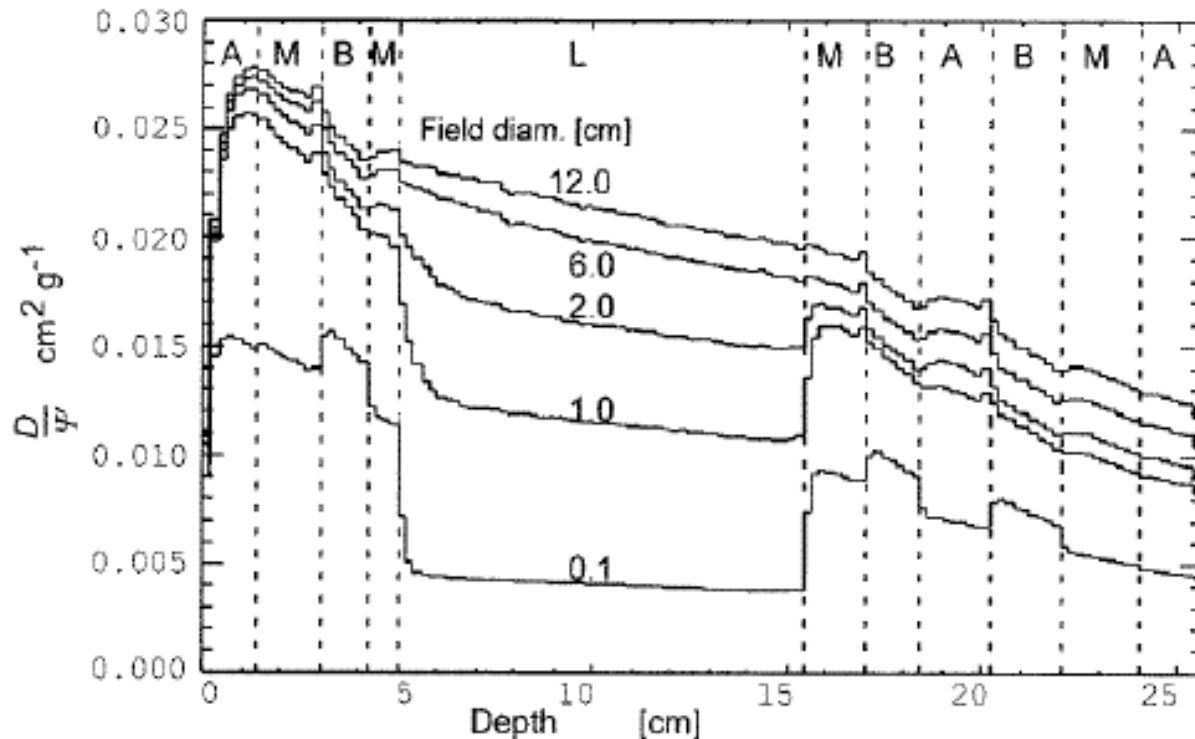
A = adipose

B = bone

L = lung

M = muscle

4MV X

- Even more perturbations in dose would result at **small field sizes for higher energy beams** because the range of charged particles would be even longer.

- IMRT demands the ability to determine the dose accurately for small fields especially for heterogeneous tissues.

Calculate dose to water

- The new algorithms can calculate **dose per energy fluence** in water-equivalent material of any density from **first principles**.

- For soft tissues in photon beams the difference between the dose in soft tissue and water is small, but considerable deviations exist for bone, and also to some degree for phantom materials.

- As the main sensitive volume for radiation impact is living cells, which are largely composed of water, it is recommended that the dose for photon beams should be reported as **the dose in a small mass of water in tissue.**

- As in Attix's cavity theory, the correction is made by a scalar multiplication using a ratio of average mass collision stopping powers of water to the medium.

Summary

- More emphasis on **statistics**

- Prescribing and reporting with **dose-volume specifications**

- **No longer use** ICRU-Refrence Point

- Need to report **median dose D$_{50\%}$**

- Use **model-based dose calculations**

- Include the effect of tissue **heterogeneities**

- Report dose to small mass of **water**, not dose to tissue

T.R. Mackie and V. Gregoire

Thank you !

Any questions?

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