An Insight in to IMRT Planning: Focus on ICRU 83

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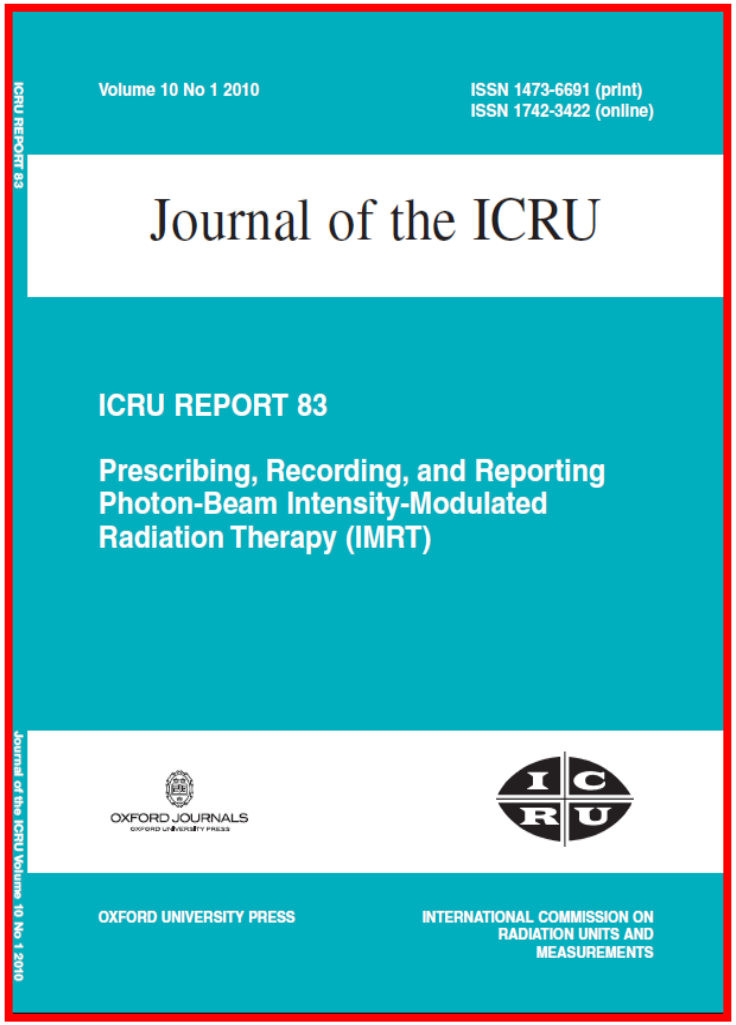

The present Report is based on concepts and definitions previously introduced in ICRU Reports 50 and 62

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Introduction

Routine Practice of Radiotherapy changed

Technological innovations -

- Diagnostic imaging
- Radiotherapy Technology
- Computer Science

Introduction

IMRT needs accurate anatomic delineation

- Most technically and intellectually challenging and time-consuming aspects of modern radiotherapy
- Requires an adequate specification of the tumor location and thorough knowledge of the processes of likely infiltration and spread
- Tissues containing tumor cells that are not delineated will not be adequately treated
- Sensitive structures not delineated may receive unacceptably high absorbed dose

Introduction

- Modern image-acquisition systems are increasing the sensitivity and specificity of tumor detection
- Functional and molecular imaging are emerging and provide new opportunities to understand the biology of both normal tissues and tumors

Introduction

Radiation-Induced Secondary Cancers

- Controversial subject
- Larger overall normal tissue volume is irradiated to a lower dose.

Optimized Treatment Planning For IMRT

Conventional vs IMRT

- Use of mathematical objective functions and incorporation of user defined dose – volume constraints
- Employment of iterative computer based IMRT algorithm to seek optimal solution

Constraint descriptors for optimization

- ‘Minimum’ absorbed dose to PTV
- ‘Maximum’ absorbed dose to OAR
- Dose volume specifications for both tumor and OARs
- Relative importance of each volume

- Optimizer converts the radiation oncologist's treatment goals into a set of beamlets of specified intensities and directions for delivery of the planned treatment
- Quality of resulting absorbed dose distributions and DVHs are highly dependent on the skill and experience of the planner

Special Considerations Regarding Absorbed-Dose and Dose–Volume Prescribing and Reporting in IMRT

- All centers are not well equipped with modern (“state-of-the-art”) techniques

Three levels of prescribing and reporting

- Level 1 recommendations
  - Minimum standards for prescribing and reporting
- Level 2 recommendations
  - Prescribing and reporting state-of-the-art techniques
- Level 3 recommendations
  - Optional research-and development reporting

The ICRU Reference Point and ICRU Reference Dose

- Absorbed dose at the point should be clinically relevant
- Point should be easy to define in a clear and unambiguous way
- Point should be selected so that the absorbed dose can be accurately determined
- Point should be in a region where there is no steep absorbed-dose gradient

The ICRU Reference Point and ICRU Reference Dose

- These recommendations will be fulfilled if the ICRU Reference Point is located-
  - Always at the center (or in a central part) of the PTV
  - When possible, at the intersection of the (treatment) beam axes

Level 1 prescribing & reporting

Inadequate for 3D CRT / IMRT –

- Absorbed-dose distribution within a PTV for IMRT can be less homogeneous
- Dose-reporting point in the region of high or low absorbed dose could be significantly misrepresent
- Monte Carlo calculations used to compute absorbed-dose distributions for IMRT. In Monte Carlo simulation, the statistical fluctuations in the results for small volumes make it difficult and uncertain to determine an absorbed dose at a point, whereas this is reasonably achieved in a volume

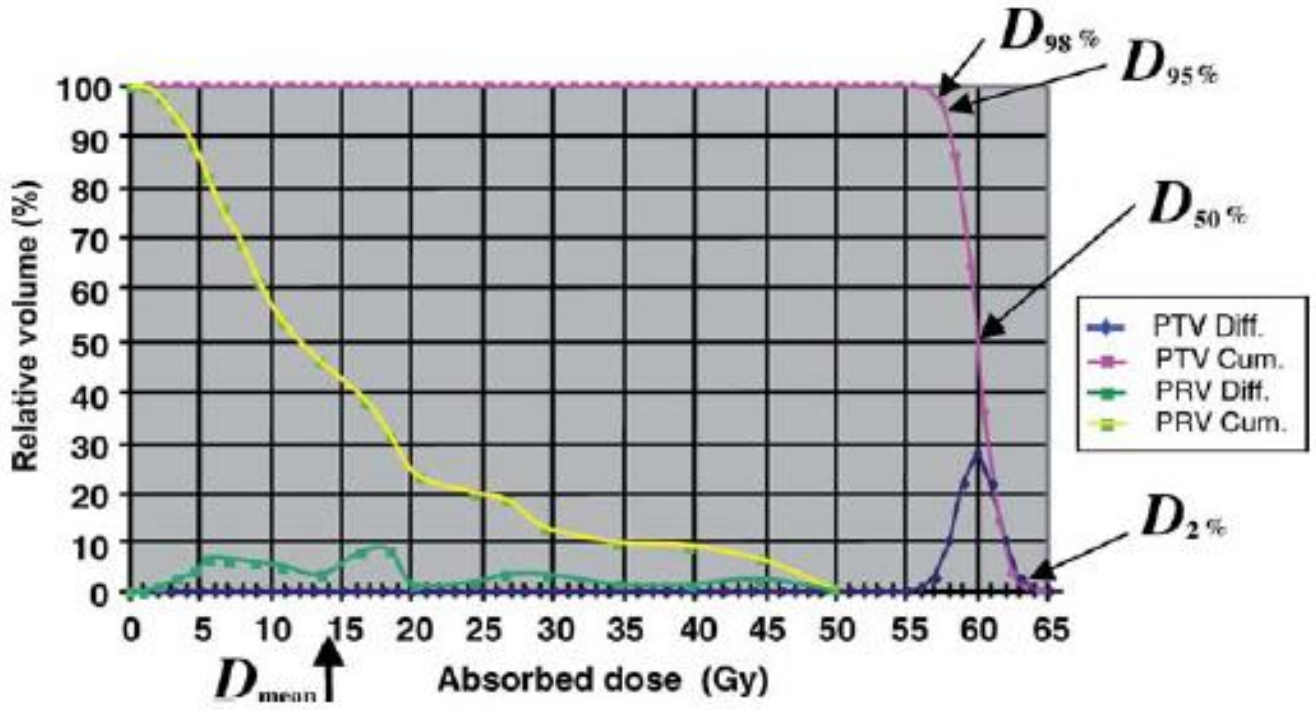
- From a single beam direction, IMRT can produce absorbed-dose gradients within a PTV much larger than those generated by a wedge
- Absorbed dose gradient at the boundary of a PTV as a result of multiple IMRT beams can be more than 10 %/mm, and a small shift in the field delivery can affect the reliability of using a single point to report the absorbed dose
- Modern treatment-planning systems have sufficient evaluation tools for Level 2 reporting to be the standard for use in IMRT

Level 2 Prescribing & Reporting for IMRT

- Based on absorbed-dose and volume information obtained from DVHs
- DVHs can lead to identification of clinically important characteristics of an absorbed-dose distribution
- Cumulative DVH / Differential DVH

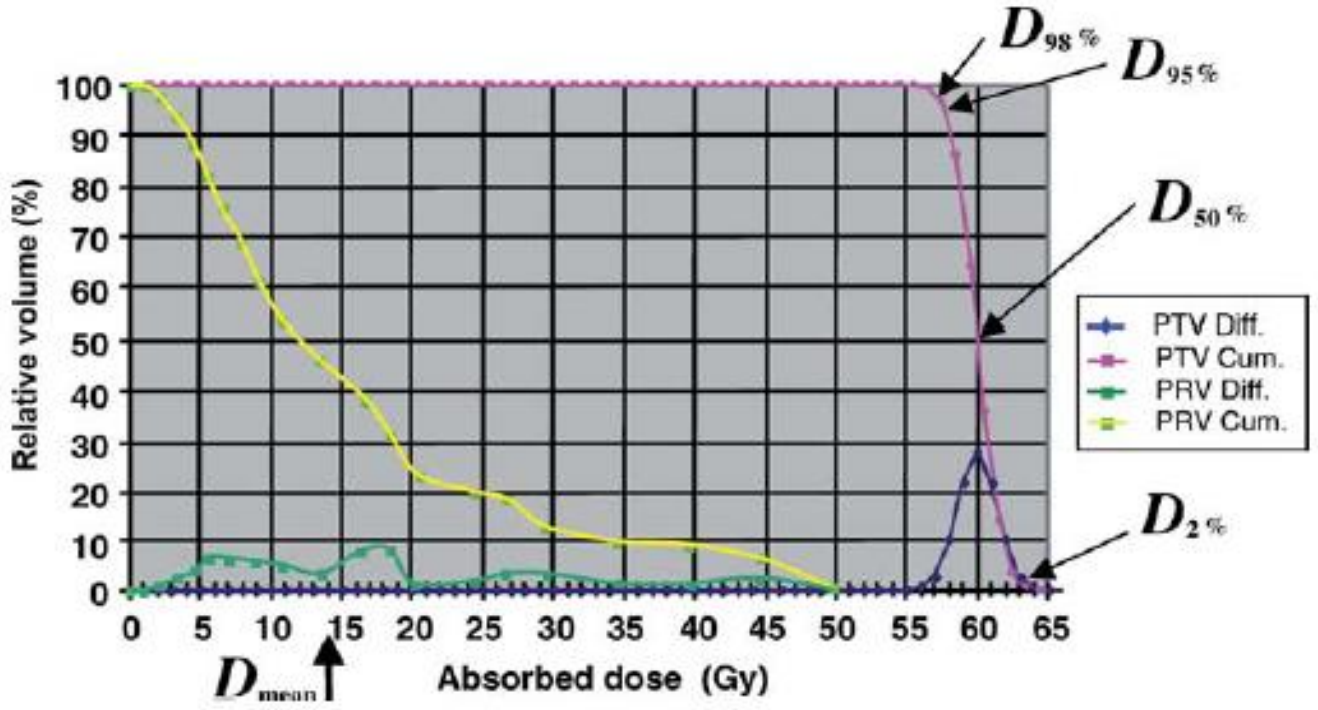
Cumulative DVH

Expressed as either the absolute volume / volume relative to the total structure volume, receiving at least a given absorbed dose, D.



Differential DVH

- Symmetric and unimodal (i.e., having onlyone peak),
- Median (D50 %) and mean absorbed doses are nearly identical.



- Thus the absorbed dose is computed throughout the PTV, and no particular point, such as the ICRU Reference Point, is favored

- What does D95% mean?
  - D95 % is the minimum absorbed dose that covers 95 % of the volume of the PTV
- The volume V, that DV is based on should be reported textually or as a subscript value
- The report does not recommend any particular value of V in D_V for a prescription
- For consistency, the reporting of the median absorbed dose, D50 %, is recommended in addition to any other D_V that the radiation oncologist believes to be clinically relevant

- Various dose regions can be identified using isodose contours
- Radiation oncologist should not rely solely on the DVH for treatment
- Careful inspection of the absorbed dose distributions slice-by-slice to make sure that the PTV is being adequately irradiated

- In previous ICRU Reports
  - “maximum absorbed dose” the high absorbed dose in at least a given minimum volume of the tissue (ICRU, 1993).
- In the present Report
  - “near-maximum absorbed dose”- D2%, as a replacement for the “maximum absorbed dose”.

Dose–Volume Reporting Specific to the OAR and PRV

- Serial Structure - Dmax
- Parallel-like structures
  - Recommended that more than one dose–volume specification be considered for reporting
  - Entire organ be contoured so that meaningful values of Dmean and V_D can be determined

- Not clear serial-like or parallel-like structure
  - At least three dose– volume specifications should be reported
  - Include D_{mean}, $D_{2\%}$, and a third specification V_D.
- When feasible, the whole organ should be delineated. When not feasible, a clear description of the delineation criteria should be reported.

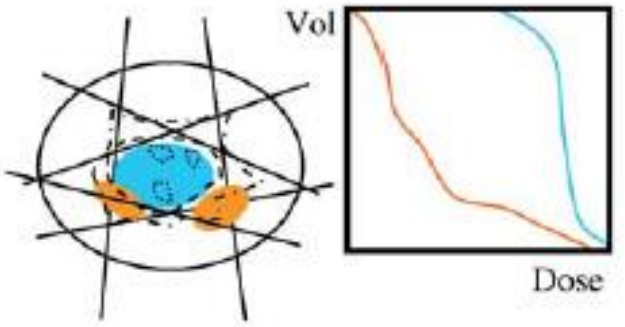
Level 3 Prescribing & Reporting for IMRT

- Describes techniques and concepts that are under development, and have not yet reached a stage at which they are sufficiently established to recommend their use in routine practice
  - Dose Homogeneity and Dose Conformity
  - Clinical and Biological Evaluation Metrics
  - Equivalent Uniform Dose

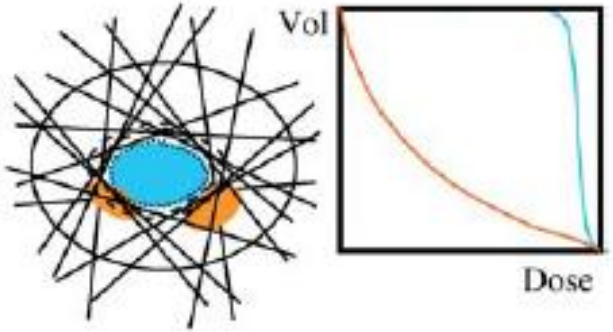
Dose Homogeneity and Dose Conformity

- Independent specifications for quality of the absorbed dose distribution
- Dose homogeneity
  - Uniformity of the absorbed-dose distribution within the target volume
- Dose conformity
  - Degree to which the high-dose region conforms to the target volume, usually the PTV

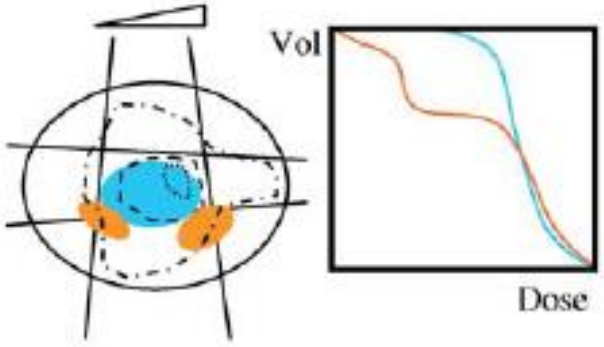
Dose Homogeneity and Dose Conformity



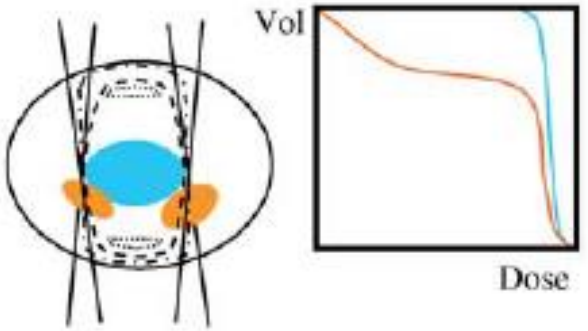
Low homogeneity–high conformity



High homogeneity–high conformity



Low homogeneity–low conformity



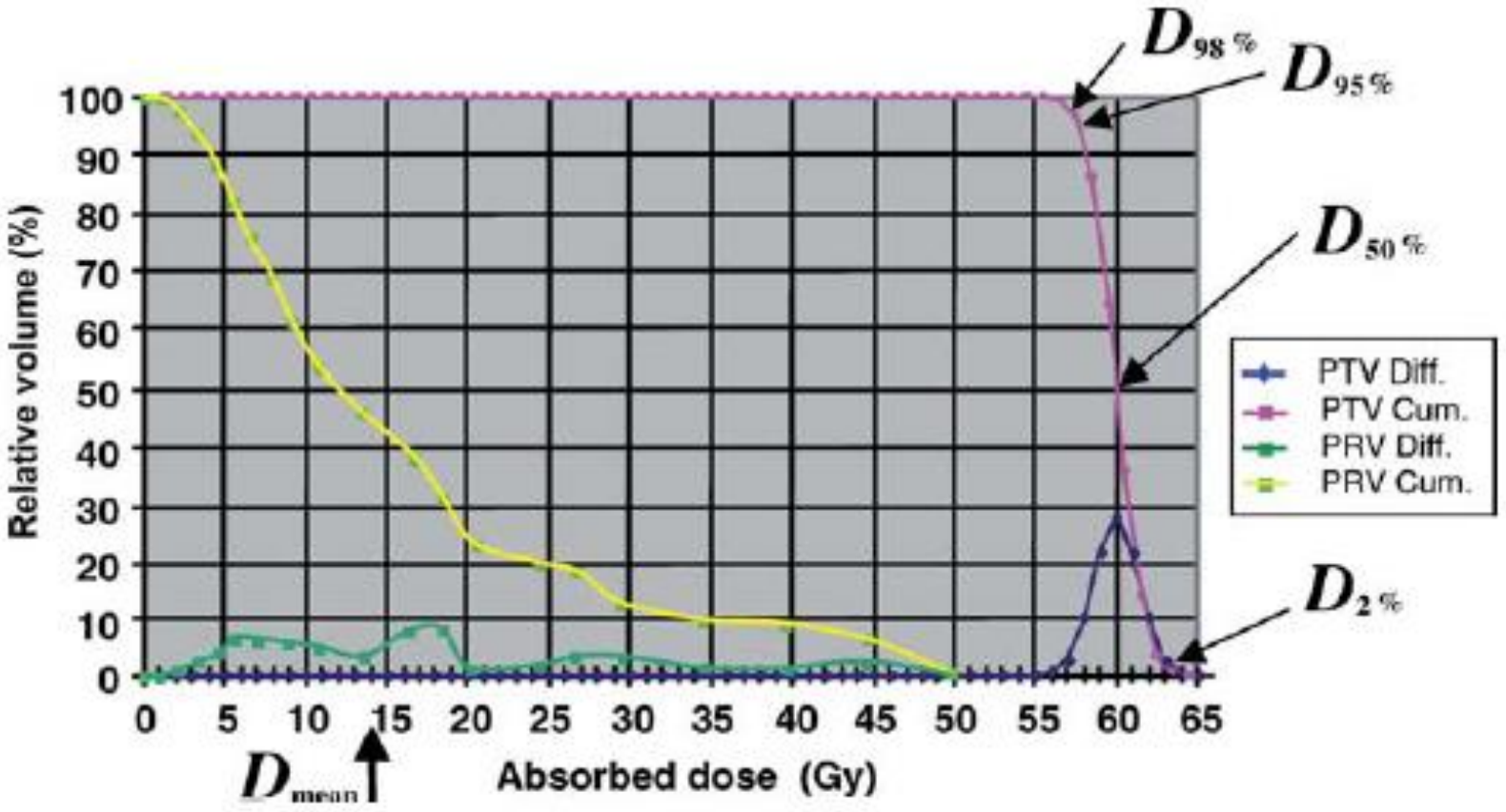
High homogeneity–low conformity

Dose Homogeneity and Dose Conformity

- A perfectly homogeneous dose to the PTV would be characterized by a spike (a delta function) in the differential DVH or a vertical drop of the cumulative DVH line for the PTV at that absorbed dose

Homogeneity Index

- $HI = \frac{D2\% - D98\%}{D50\%}$
- HI of zero indicates that the absorbed-dose distribution is almost homogeneous
- D50 % is suggested as the normalization value because reporting of D50 % is strongly recommended in Level 2 reporting



- D2 % is 63 Gy, D50 % is 60 Gy, and D98 % is 57 Gy
- HI is equal to 0.1

Definitions of volume

Gross Tumor Volume

<u>Reasons to describe and report the GTV in a complete and accurate way</u>

- For staging
- Adequate absorbed dose must be delivered to the whole GTV to obtain local tumor control
- Evaluation of regression of GTV- redefining CTV and PTV during the course of treatment
- Changes of the GTV during treatment might be predictive of treatment outcome

Gross Tumor Volume

Reporting GTV

- Location and tumor extent according to the TNM/AJCC
- Methods used to delineate the GTV
- Any changes occurring in the GTV during treatment to be quantified with anatomic- and/or functional-imaging techniques

Gross Tumor Volume

Reporting GTV

Recommended that the absorbed dose and/or the time when the GTV is evaluated or measured with respect to the start of treatment be indicated

In post-operative case, complete surgical resection (R0 or R1 resection), there is no GTV to define, and only a CTV needs to be delineated

Clinical Target Volume

- Volume of tissue that contains a demonstrable GTV and/or subclinical malignant disease with a certain probability of occurrence considered relevant for therapy

Clinical Target Volume

Delineation of the CTV based on

knowledge of anatomical pathways

regarding probability of

microscopic tumor infiltration

into the surrounding normal tissues and/or nodes

Clinical Target Volume

- **NO CTV** in benign tumor GTV since no risk of microscopic or metastatic tumor infiltration into the regional nodes
- In the case of post-operative irradiation (after R0 or R1 resection), there is **NO GTV**, only CTV will be selected and delineated.

ITV

- Defined as the CTV plus a margin taking into account uncertainties in size, shape, and position of the CTV within the patient

PTV

- Used for absorbed-dose prescription and reporting
- To ensure prescribed absorbed dose will be delivered to CTV despite geometrical uncertainties (organ motion and setup variations through out the treatment)
- Delineation of GTV and CTV are independent of the irradiation technique, the delineation of the PTV is dependent on the technique
- To reduce the CTV-to-PTV margin has always been a temptation

PTV overlaps OAR / PRV

- PTV margins should not be compromised, to ensure accurate reporting of absorbed dose to the PTV
- Treatment-planning software achieves sufficient dose sparing of the OAR
- Using priority rules in optimizer planning systems
- Alternatively, subdivision of the PTV into regions with different prescribed absorbed doses (PTV-subvolumes)
- Dose reporting be done for the whole PTV - under dosage may reflect lower probability of adequate absorbed-dose coverage to the CTV

PTV margins

- Vary from center to center
- Depends upon
  - Use of patient-immobilization devices
  - Application of quality-assurance programs
  - Skill and experience of the radiation therapy technologists
  - Use of image-guidance systems
- Other uncertainty-reduction techniques can significantly alter the size of the required margins

PTV margins

- The PTV margin surrounding the CTV should be three-dimensional
- Many authors have proposed approaches to calculate the margins on the basis of systematic and random uncertainties
- PTV extends close to or even outside the patient's skin (how to overcome limitation)
  - Use of bolus
  - PTV sub-division
  - Relaxation of the absorbed-dose objectives for planning

OAR

Functional tissue organization

- Serial organs / serial-like organs
  - Spinal cord, nerves
- Parallel organs / parallel-like organs
  - Lung, parotid
- Mixed serial and parallel organization
  - Kidney (glomerulus has a more parallel organization, whereas the distal tubules are more serially organized)

OAR

- Functional tissue organization is useful for determining dose–volume constraints and for evaluating DVH
- Serial-like organs
  - Absorbed dose at or close to the maximum absorbed dose to a given volume is typically the best predictor of loss of function
- Parallel-like organs
  - Graded absorbed-dose responses
  - Mean absorbed dose or the volume that receives an absorbed dose in excess of some defined value have been used as predictors of loss of function

OAR

Reporting

- To allow comparison between centers, it is very useful to follow guidelines
  - Delineate spinal cord (head-and-neck tumors) from its junction with the brain stem to D1
  - For prostate cancer to delineate the rectum starting at anus to where the rectum turns horizontally into the sigmoid colon
  - Parallel-like organs- complete organ delineation
- In all instances, the volume of the organ delineated should be recorded. This is particularly important when DVHs are reported in terms of relative volumes

Planning organ at risk volume

- Analogy to PTV
- Uncertainties and variations in the position of the OAR during treatment
- A margin around an OAR with a serial-like structure (e.g., spinal cord) is more clinically relevant than that around an OAR with a parallel-like structure (e.g., liver, lung, parotid).

TREATED VOLUME

- Volume enclosed within a specific isodose envelope, with the absorbed dose specified to achieve tumor eradication or palliation within acceptable complications
- In report, value of isodose selected to define the TV should either absolute dose or relative to the prescribed absorbed dose
- Significance - Evaluate causes for local recurrences (inside / outside TV)

Remaining Volume at Risk

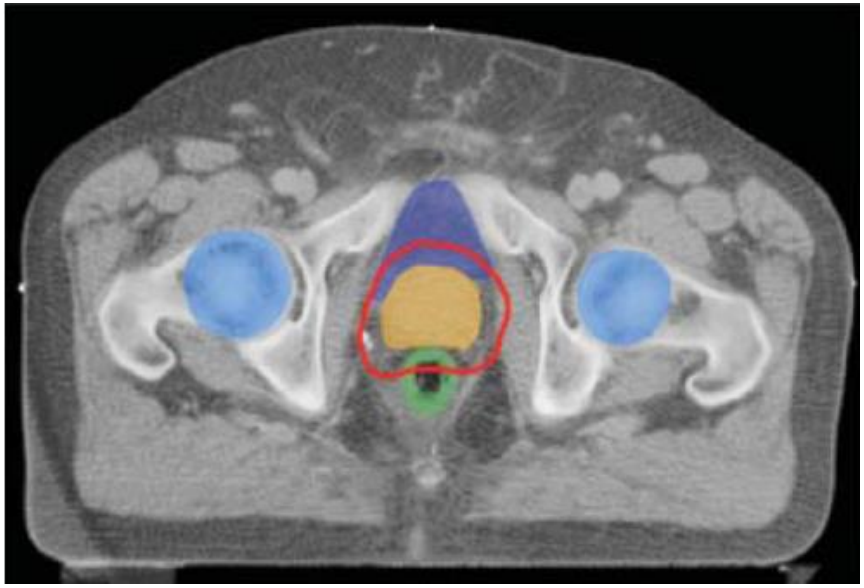
- Difference between the volume enclosed by the external contour of the patient and that of the CTVs and OARs on the slices that have been imaged
- Significance
  - Unsuspected regions of high absorbed that would otherwise go undetected
  - Estimating the risk of late effects, such as carcinogenesis
  - For younger patients who can expect a long life span

Planning Aims, Prescription, and Technical Data

Planning aims

- D_V (absorbed dose in fraction V of the volume) and V_D (volume receiving at least an absorbed dose D)
- Conflicts in the planning aims
- Priority ranking by clinician
- Constraints and objectives modified (are not fixed) to achieve an acceptable plan in accordance with the treatment aims

Planning aims for treatment of a prostate adenocarcinoma



Planning aims

PTV: median absorbed dose (D_{50} %) of 74 Gy
near-min absorbed dose (D_{98} %) of 70 Gy
near-max absorbed dose (D_2 %) of 79 Gy

PRV rectum: D_{40} % ≤ 65 Gy
D_{30} % ≤ 70 Gy
D_5 % ≤ 75 Gy

PRV bladder: near-max dose (D_2 %) of 70 Gy

PRV femoral heads: D_5 % ≤ 50 Gy

- PTV overlaps with PRV rectum & PRV bladder giving rise to conflicts in the planning aims
- Resolution by using different dose-constraints on the overlapping region between the PTV and the PRVs

Special Situations - Use of Planning Aims

Planned absorbed dose in buildup region and in a PTV extending outside the body contour

- Dose-computation algorithms cannot accurately compute absorbed dose in buildup regions
- Underdosage of CTV near the skin
  - Clinically unacceptable
    - Bolus applied
  - Clinically acceptable
    - Subdivision of the PTV into a number of subvolumes
    - Acceptable absorbed-dose range of the PTV planning aim is relaxed (drawback of lacking spatial control over the underdosed region)

Special Situations - Use of Planning Aims

Overlapping volumes and conflicting absorbed dose objectives

- Aim - controlled under dosage of a volume inside the PTV, a controlled over dosage of a volume inside the PRV, or both
- By changing the importance of the constraints (priority ranking)
- Enable PTV and PRV delineation intact

Special Situations - Use of Planning Aims

Unexpected high absorbed dose to part of the remaining volume at risk (RVR)

- Why?
  - Absorbed-dose objectives for planning are imposed for PTVs and PRVs only
- May be, maximum absorbed dose of the plan can be in RVR
- Overcome - Planning aims applied to RVR (same as additional OAR)

Treatment plan

- Optimized absorbed-dose distribution accepted
- Prescription and technical data finalized
- Prescription
  - Description of volumes of interest, absorbed dose and/or dose–volume requirements for PTV, fractionation scheme, normal-tissue constraints, and the absorbed-dose distribution(s) planned.
  - Though acceptable, can be different from original planning aim
- Technical data
  - Details of beams, beam segments, aperture shapes or multi leaf-collimator settings, monitor units per beam segment, positioning and immobilization parameters for the patients on the couch, etc.

Take home message

- Dose-reporting has moved from single-point to volume-based absorbed-dose specification
- Minimum & maximum absorbed doses not recommended for reporting, but replaced by near-minimum (D98 %) and near-maximum (D2 %)
- Median absorbed dose D50 %, should be reported (considered to correspond best with the previously defined dose at the ICRU reference point)

Take home message

- IMRT possible due to modern imaging and computer technology
- Appropriate patient-specific quality control is necessary to ensure patient receives prescribed dose as accurately as possible

Decades of clinical experience in conventional therapy has to be interpreted in context of IMRT