ICRU RECOMMENDATIONS FOR GYNECOLOGICAL BRACHYTHERAPY

41st ICRO PG TEACHING PROGRAM

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Conventionally, dose prescribed to point A

Drawbacks for point A

- No fixed relationship to anatomy, target or tolerance.
- Point A dose can be identical for applications that differ in fundamental ways and deliver different overall 3D dose distributions.
- Variation in dose prescription dependent on applicator geometry
ICRU reports in gynecological brachytherapy - ICRU 38

- Discouraged the use of point A and B
- Encourages the use of target volume for dose prescription and reporting absorbed dose prescription
- Included some dose points similar to the classical systems
- Not a brachytherapy system, nor a method of prescription
List of data needed for reporting intracavitary therapy in gynecology ICRU-38

• Description of the technique used
• Total reference air kerma (cGy at 1 meter)
• Prescription of the reference volume
  - Dose level if not 60 Gy.
  - Dimensions of the reference volume (H x W x T)
• Absorbed dose at reference points
  - Bladder reference point
  - Rectal reference point
  - Lymphatic trapezoid
  - Pelvic wall reference point
• Time dose pattern
Description of the Technique
Minimum information regarding

- applicator type,
- source type
- loading
- orthogonal radiographs of the application.

Total Reference Air Kerma

- Analogous to mgRaEq-hr
- Is the product of air kerma strength and the duration of the implant
- The total air kerma at 1 meter from the implant
- Integral dose delivered to the patient
- Does not take into account fraction size, dose rate
- Physical parameter, not a biological parameter (e.g. TRAKpdr > TRAKhdr)
**Reference Volume**

- The volume of the isodose surface that just surrounds the Target Volume.
- EBRT + BT dose
- The value of the isodose surface prescription, based on the Paris experience, is set at 60Gy.
- The reference volume is approximated by \((dH \times dW \times dT)\)
Absorbed dose at Reference points

Bladder point

Posterior surface on lateral

Center of AP film with foley w/ 7 cc radiopaque contrast pulled down against urethra
Rectal point

0.5mm behind posterior vaginal wall between ovoids at inferior point of last intrauterine tandem source, or mid vaginal source
Lymphatic Trapezoid

Represents dose at lower paraaortic, common iliac and external iliac lymph node
Pelvic wall reference point

Representative of dose at the parametrium and at obturator nodes
Time Dose Pattern

Radiobiologic effects- dose rate dependant

The duration and time sequence of the implant should be recorded

Doses for external beam treatment should be recorded.
2D to 3D and 4D Brachytherapy
Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (I): concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV


Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (IV): Basic principles and parameters for MR imaging within the frame of image based adaptive cervix cancer brachytherapy

Johannes C.A. Dimopoulos, Peter Petrov, Kari Tanderup, Primož Petrič, Daniel Berger, Christian Kirisits, Erik M. Pedersen, Erik Van Limbergen, Christine Haie-Meder, Richard Pötter
Prescribing, recording and reporting brachytherapy for cancer of the cervix

1. Introduction
2. Prevention, Diag, Prognosis, Treatment & Outcome
3. Brachytherapy Techniques and Systems
4. Brachytherapy Imaging for Treatment Planning
5. Tumor and Target Volumes & Adaptive Radiotherapy
6. Organs At Risk and Morbidity-Related Concepts & Volumes
7. Radiobiological Considerations
8. DoseVol Parameters for Prescribing, Recording & Reporting
9. Volumetric Dose Assessment
10. Radiographic Dose Assessment
11. Sources & Absorbed-Dose Calculation
12. Treatment Planning
13. Summary of the Recommendations
   • Clinical Examples
Integrated approach using dose volume parameters

Level 1: Minimum standard of treatment

Level 2: Advanced standards of dose planning and treatment

Level 3: Describes new forms of planning and treatment- largely related to research and development for which reporting criteria cannot yet be established.
Tumor Assessment and Clinical examination

- Volumetric imaging (MR, CT, US, PET–CT) at the time of diag. & brachy (or radiographic approximation based on clin exam + 3D imaging, if available)

- FIGO/TNM stage

- Baseline morbidity and QoL assessment

- Comprehensive clinical gynecologic examination

- Schematic 3D clinical diagram indicating dimensions
Clinical Drawing

Patient: xxx

At Brachytherapy

At Diagnosis

Infiltrative Exophytic

Cervix

Vagina

Parametria

Rectum or Bladder

dd/mm/yy

6.0 cm

w = 6.0 cm
h = 5.0 cm
t = 6.0 cm

Vagina Involvement = 0 cm
Clinical drawings

Clinical examination + Findings at Imaging

- At Diagnosis
- Response assessment
- Prior to brachytherapy
Advanced Clinical Diagram

- NMD

- Better depiction of vaginal extension

- Staging - Clinical & Imaging
Target Concepts- Ext RT

**GTV-T (GTV-T_{init}):** Defined at diagnosis as macroscopic demonstrable disease assessed through various clinical, imaging, and/or pathologic investigations.

**CTV-T:** The GTV-T and an area of surrounding tissue with potential contiguous and/or incontiguous microscopic disease.

- **CTV-T1:** GTV-T and adjacent tissue, always including the whole cervix (initial CTV_{HR})
- **CTV-T2:** CTV-T1 plus margins (initial CTV_{IR})
- **CTV-T3:** CTV-T2 plus areas in adjacent compartments at risk for potential contiguous or incontiguous microscopic spread (initial CTV_{LR})
Residual GTV-T (GTV-T_{res}) residual macroscopic tumor at the time of (brachytherapy) boost after treatment assumed sufficient to control microscopic disease.

Adaptive CTV- (CTV-T_{adapt}) GTV-T_{res} and the residual surrounding pathologic tissue, if present. Is a sub-volume of the initial CTV-T, except in the case of tumor progression.
High risk & Intermediate risk CTV

**High-Risk CTV-T (CTV-T_{HR})** form of the adaptive CTV-T for “cervix cancer radiotherapy”

CTV-T_{HR} includes the GTV-T_{res} + the whole cervix + adjacent residual pathologic tissue, if present. It is the volume bearing the highest risk.

The residual (extra-cervical) pathologic tissue is defined as one or more of the following:

- residual palpable mass;
- residual visible mucosal change;
- pathologic induration;
- residual gray zones (MRI);
- any other residual pathologic tissue on MRI or clinic exam

**Intermediate-risk CTV-T (CTV-T_{IR})** represents the area of the GTV_{init} as superimposed on the topography at the time of brachytherapy and a margin surrounding the anatomical cervix borders (CTV-T_{HR}) in areas without an initial GTV. *The CTV-T_{IR} therefore always includes the CTV-T_{HR} and margins as appropriate.*
Stage IB2 (bulky disease), good response after chemo-radiotherapy

Stage IIB bulky disease, good response after chemo-radiotherapy
Cervical cancer, IIIB, extensive disease, poor response after chemo-radiotherapy

Cervical cancer, with bladder infiltration, Stage IVA, and good response after chemo-radiotherapy
LEVEL-1 MIN. STANDARD OF REPORTING

- Volumetric imaging (MR, CT, US, PET–CT) at the time of diag. & brachy (or radiographic approximation based on clin exam + 3D imaging, if available)
- FIGO/TNM stage
- Baseline morbidity and QoL assessment
- Comprehensive clinical gynecologic examination

- **Schematic 3D clinical diagram indicating dimensions** (width, thickness, height) and volumes for:
  - $GTV_{\text{init}}$ (the GTV at diagnosis)
  - $GTV_{\text{res}}$ (the GTV at brachytherapy)
  - $CTV_{\text{HR}}$ (the $GTV_{\text{res}}$ plus residual pathologic tissue plus whole cervix)
  - $CTV_{\text{IR}}$: area of $GTV_{\text{init}}$ and/or $CTV_{\text{HR}}$ plus safety margin if used for prescription)

Dose reporting:
- TRAK
- Point A dose
- Recto-vaginal ref-point dose
- D 0:1cm3 and D2cm3 for the bladder and rectum (bladder ref point)

Dose delivery pattern:
- Absorbed-dose rate/dose per frac.
- Number of fractions
- Time between fractions
- Overall treatment time
- Total EQD2 dose
- Radionuclide and source model
- Source strength
- Dose-calculation algorithm
Dose Reporting

- TRAK

- Adoption of Point A as a major reference point with a definition related to the applicator for absorbed-dose specification:

  • **Optional** - for the planning aim and for prescribing
  • **Mandatory** - for reporting the volumetric image-based approach as well.
  • Represents the most widely used parameter in gynecologic brachytherapy worldwide.
Is it time to move beyond point A based dose prescription?

Point A-based standard loading patterns delivering the same absorbed dose to Point A, but using widely different vaginal and tandem loading
Relationship between point A dose and the CTV-HR

- Good representation of “an average position” of the tumor
- Smaller tumors receive higher dose
- Large tumors receive suboptimal doses

Tanderup, 2010
ICRU 89- Relevance of point A

- Allows comparison of different approaches
- Point A dose is a surrogate of the irradiated volume
- Starting point for planning
- Helps in check for major dose escalation and reduction

Thresholds for Point A dose for volume treated to 85Gy

- 2D X-Ray based >75Gy
- CT based >70Gy
- MRI Based (EMBRACE) >65Gy
ICRU Bladder and Rectum points

1-5 times underestimation of rectum (mean diff. 0.21 Gy) and bladder doses (mean diff 6.8 Gy) with Orthogonal X-ray ICRU point doses compared to CT based volumetric calculation.
Dose reporting OAR: 3-D based DVH parameters

The minimum dose in the most irradiated tissue volume adjacent to the applicator (0.1, 1, 2, 5 cm³) is recommended for recording & reporting.

*Reference Points*
3D based dose volume constraints

OAR

Classic Maximum dose (2D): No clinical relevant point in 3D

Fixed Volume: “Minimum dose to the most irradiated tissue

0.1 cc: 3D “maximum dose” ulceration (fistula)
1 cc/2 cc: Telangiectasia
(20 mm x 20 mm x 5 mm)
>5 cc: fibrosis endpoint

*GYN GEC ESTRO Recommendations (II)
Radioth. Oncol. 2006
ICRU and Volume based OAR doses

- Significant linear correlation between the ICRU rectal point and D2cc rectal doses
- ICRU point doses not a good predictor of D2cc in the individual patient
- ICRU rectal absorbed dose is, on average, 20\% larger than the rectum D2cc
- ICRU bladder absorbed dose on approximately 20\% smaller than the bladder D2cc

Tanderup, et al
Dose Delivery pattern

- Absorbed-dose rate/dose per fraction/no. of fractions
- Time between fractions
- Overall treatment time- 50 days
- Total EQD2 dose-The current standard for reporting equieffective dose in cervix BT is equivalent dose in 2 Gy fractions (EQD2) using $\alpha/\beta$ ratios of 10 Gy for tumor volumes and 3 Gy for OARs.
Level 2: Advanced standard for reporting
All that is reported in Level 1 plus:

Volumetric-imaging approximation based on: 3D delineation of volumes (on volumetric images with applicator):
• GTVres
• CTVHR
• (CTVIR if used for prescription)
With maximum width, height, thickness, and with volume

Dose reporting for defined volumes:
• D98 %, D90 %, D50 % for the CTVHR
• (D98 %, D90 % for the CTVIR if used for prescription)
• D98 % for GTVres
• D98 % for pathological lymph nodes

Dose reporting OARs:
• Bladder reference point dose
• D 0:1cm3 , D2cm3 for sigmoid
• D2cm3 bowel
• Intermediate- and low-dose parameters in bladder, rectum, sigmoid, bowel (e.g., V15 Gy, V25 Gy, V35 Gy, V45Gy or D98%, D50%, D2%)
• Vaginal point doses at level of sources (lateral at 5 mm)
• Lower- and mid-vagina doses (PIBS, PIBS+/-2 cm)
Dose Volume Parameters - Target

- **D100, D98 & D90** – minimum dose delivered to 100, 98 & 90% of the volume of interest respectively
- **D100** is extremely dependent on target delineation. Due to steep dose gradients, small spikes in the contour cause large deviations in D100
- **D98** reflects the dose in the outermost periphery of the target - more reliable
- **D90** is less sensitive to these influences & is therefore considered a more ‘stable’ parameter
- **D50** reflects the high dose delivered to the central part of the CTV-THR, (importance for local control)

- **V 100** – Volume receiving \( \geq 100\% \) of PD
- **V150/200** – Volume receiving 150%/200% of PD - relevant within a specific dose rate and fractionation schedule
DVHs for the GTV and the CTV in intracavitary brachytherapy have a plateau, which indicates 100% dose coverage of the volume of interest. This plateau goes down smoothly indicating decreasing percentage of dose coverage with increasing dose.
Vaginal Reference Points

PIBS vaginal-dose point – mid & lower

[Westerveld et al. 2013]

Upper Vagina- 0 mm and 5 mm from the applicator surface

[Westerveld et al. 2013]
ICRU Recto vaginal point

Correlation with Post vaginal wall dose – vaginal shortening

Kirchheiner et al., 2016
Level 3: Research-oriented reporting
All that is reported in Level 1 and 2 plus:

**Volumetric-imaging approximation based on:**
**Tumor-related volumes:**

- GTV, CTVHR sub-volumes based on functional imaging (diagnosis, during treatment, and at brachy)
- PTV
- Isodose surface volumes: eg, 85 Gy EQD2, 60Gy EQD2 volume

**Dose reporting for tumor:**

- D98 % and D90 % for the CTV-IR even if not used for prescription; D90 % for the GTVres
- DVH parameters for the PTV
- D50 % for pathological lymph nodes
- DVH parameters for non-involved nodes (ext/int iliac, common iliac)

**OAR volumes and points:**

- Additional bladder and rectum reference points
- OAR sub-volumes (e.g., trigone or bladder neck, sphincter muscles)
- Vagina (upper, middle, lower)
- Anal canal (sphincter)
- Vulva (labia, clitoris)
- Other volumes/sub-volumes of interest (e.g., ureter)

**Dose–volume reporting for OAR:**

- Dose–volume and dose–surface histogram parameters for additional OARs and sub-volumes
- Vaginal dose profiles, dose–volume, and dose–surface histograms
- Length of treated vagina
Advanced Research - level-3

Sub-structures (bladder wall, trigone, bladder neck, urethra)

• ICRU-BP dose related to the trigone region incontinence ($G \geq 20\% ; >75\text{Gy} )$ *Spampinato et al, 2020*

• Internal-Urethral-Ostium (IUO) and PIBS-Urethra (PIBS-U) points -urethral dose surrogates.

• Vaginal Reference Length (VRL)- Bladder base dose

**Ureteral dose** $\geq 77\text{ Gy to } D_{0.1\text{cm}^3}$ correlates with development of late grade $\geq 3$ US. *Rodríguez-López et al, 2020*
Conclusion

- ICRU-38 and 89 provides comprehensive recommendations on prescribing, recording, and reporting of intracavitary brachytherapy.

- ICRU-89 focuses on volumetric imaging in cervix cancer using an “integrated level” approach.

- Point A is considered as major reference point for absorbed-dose specification, allows comparison of different approaches and helps in check for major dose escalation and reduction.

- OAR delineation with reporting of both ICRU point doses and volumetric doses should be done.