ICRU 89- Time to move beyond point A

35\textsuperscript{th} AROI-ICRO Sun PG TEACHING COURSE

Dr. Bhavana Rai
Department of Radiotherapy
Regional Cancer Center
Post Graduate Institute of Medical Education and Research
Chandigarh
Historically, dose prescription based on « systems »:

- mg/h of radium or TRAK
- mainly to point A
- or to a reference volume- ICRU-38
2D to 3D and 4D Brachytherapy

2D Brachytherapy

3D/4D Brachytherapy
Image based brachytherapy - GEC- ESTRO Recommendations

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

Christine Hate-Melder, Richard Pütter, Erik Van Limbergen, Edith Briot, Mariol De Brabantere, Johannes Dimopoulos, Isabelle Dumas, Taran Paulsen Hellebust, Christian Kirisits, Stefan Lang, Sabine Maschitz, Juliana Neymon, An Nulens, Peter Petrow, Natascha Wachter-Gerstner

GEC-ESTRO Recommendations

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 Petrow, Kari Tanderup, Primož Petrič, Daniel Berger, Christian Kirisits, Erik M. Pedersen, Erik van Limbergen, Christine Hate-Meder, Richard Pütter

*Metropolitan Hospital, Athens, Greece; †Institut Curie, Paris, France; ‡Aarhus University Hospital, Denmark; §Institute of Oncology Ljubljana, Slovenia; #Comprehensive Cancer Center, Medical University of Vienna, Austria; ^Universitätsklinikum Cottbus-Senftenberg, Germany; ×Institut Gustave Roussy, Villejuif, France
PRESCRIBING, RECORDING, AND REPORTING BRACHYTHERAPY FOR CANCER OF THE CERVIX

- Appendix
- Prevention, Diagnosis, Prognosis, Treatment, and Outcome
- Brachytherapy Techniques and Systems
- Brachytherapy Imaging for Treatment Planning
- Tumor and Target Volumes and Adaptive Radiotherapy
- Organs At Risk and Morbidity-Related Concepts and Volumes
- Radiobiological Considerations
- Dose and Volume Parameters for Prescribing, Recording, and Reporting
- Volumetric Dose Assessment
- Radiographic Dose Assessment
- Sources and Absorbed-Dose Calculation
- Treatment Planning
- 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.
LEVEL-1 MINIMAL STANDARD OF REPORTING

- Volumetric imaging (MR, CT, US, PET–CT) at the time of diagnosis and brachytherapy
- 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\textsubscript{init} (the GTV at diagnosis)
  - GTV\textsubscript{res} (the GTV at brachytherapy)
  - CTVHR (the GTV\textsubscript{res} plus residual pathologic tissue plus whole cervix)
  - CTVIR: area of GTV\textsubscript{init} and/or CTVHR plus safety margin if used for prescription

Dose reporting:
- TRAK
- Point A dose
- Recto-vaginal reference-point dose
- D 0:1cm\textsuperscript{3} and D2cm\textsuperscript{3} for the bladder and rectum

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

Patient: xxx

- Infiltrative
- Exophytic

- Cervix
- Vagina
- Parametria
- Rectum or Bladder

dd/mm/yy

At Diagnosis

At Brachytherapy

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

Vagina Involvement = 0 cm
Clinical examination + Findings at Imaging

At Diagnosis
Response assessment
Prior to brachytherapy
Advanced Clinical Diagram
Target Concepts- Ext RT

**GTV-T** (GTV-$T_{\text{init}}$): 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 $CTV_{\text{HR}}$)
- **CTV-T2**: CTV-T1 plus margins (initial $CTV_{\text{IR}}$)
- **CTV-T3**: CTV-T2 plus areas in adjacent compartments at risk for potential contiguous or incontiguous microscopic spread (initial $CTV_{\text{LR}}$)
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-T (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-THR)** form of the adaptive CTV-T for “cervix cancer radiotherapy”

CTV-THR includes the $GTV_{T_{res}}$ and the whole cervix and adjacent residual pathologic tissue, if present. It is the volume bearing the highest risk. The CTV-THR for cervix cancer 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 examin

**Intermediate-risk CTV-T (CTV-TIR)** 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-THR) in areas without an initial GTV. The CTV-TIR therefore always includes the CTV-THR 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
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.
ICRU 89 - Is it time to move beyond point A?

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- Is point A still relevant?

• 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
Do ICRU bladder and rectum points represent the maximum doses?

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.

GYN GEC ESTRO Rec.(II), 2006
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 D2cm3 in the individual patient

• ICRU rectal absorbed dose is, on average, 20% larger than the rectumD2cm

• ICRU bladder absorbed dose on approximately 20% smaller than the bladder D2cm3
ICRU Recto vaginal point

Correlation with Post vaginal wall dose – vaginal stenosis

Kirchheiner et al., 2016
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, V45 Gy 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 ≥ 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

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

[Westerveld et al. 2013]
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 CTVIR 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≥2 20%; >75Gy) *Spampinato et a, 2020 (in press)*

• Bladder D2cm3- superior part of bladder wall

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

• Vaginal Reference Length (VRL)- Bladder base dose

Ureteral dose ≥77 Gy to D0.1cm3 correlates with development of late grade ≥3 US.
*Rodríguez-López et al,2020 (in press)*
Conclusion

• ICRU-89 provides comprehensive recommendations on prescribing, recording, and reporting brachytherapy focusing 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.