ICRU 89- Time to move beyond point A

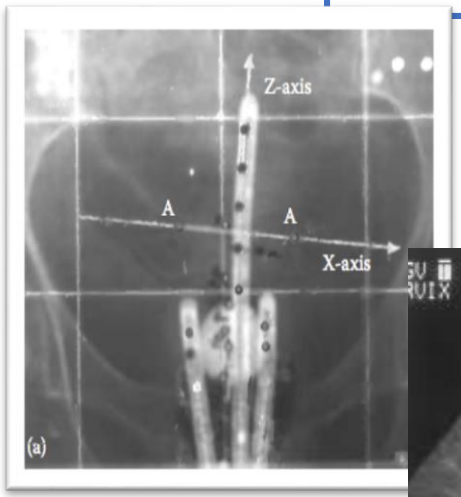
35th AROI-ICRO Sun PG TEACHING COURSE

Dr. Bhavana Rai
Department of Radiotherapy
Regional Cancer Center
Post Graduate Institute of Medical Education and Research
Chandigarh

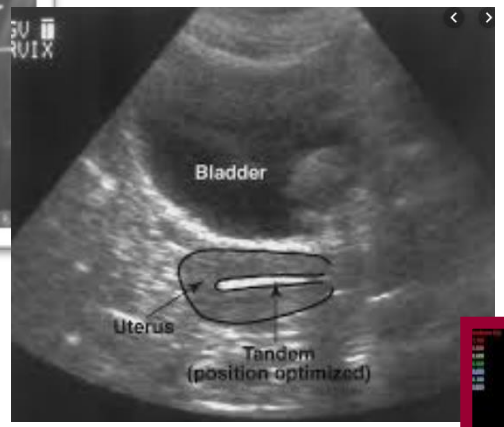
Historically, dose prescription based on « systems »:

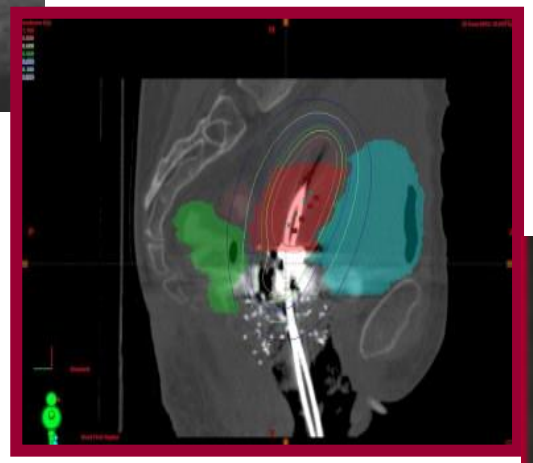
- mg/h of radium or TRAK
- mainly to point A
- or to a reference volume- ICRU-38

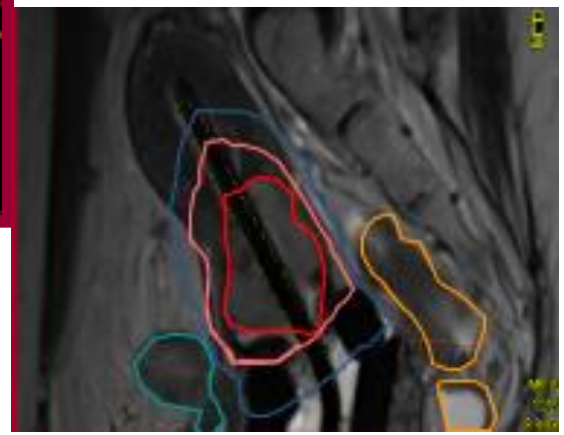
2D to 3D and 4D Brachytherapy



2D Brachytherapy







3D/4D Brachytherapy

Image based brachytherapy- GEC- ESTRO Recommendations

ELSEVIER

Radiotherapy and Oncology 74 (2005) 235–245

RADIOTHERAPY & ONCOLOGY

www.elsevier.com/locate/radonline

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 Haie-Meder[a,*], Richard Pötter[b], Erik Van Limbergen[c], Edith Briot[a], Marisol De Brabandere[c], Johannes Dimopoulos[b], Isabelle Dumas[a], Taran Paulsen Hellebust[d], Christian Kirisits[b], Stefan Lang[b], Sabine Muschitz[b], Juliana Nevinson[e], An Nulens[c], Peter Petrow[f], Natascha Wachter-Gerstner[b]

Recommendations from gynaecological (GYN) GEC ESTRO working group (II): Concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy–3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology

Richard Pötter[a,*], Christine Haie-Meder[b], Erik Van Limbergen[c], Isabelle Barillot[d], Marisol De Brabandere[c], Johannes Dimopoulos[a], Isabelle Dumas[b], Beth Erickson[e], Stefan Lang[a], An Nulens[c], Peter Petrow[f], Jason Rownd[e], Christian Kirisits[a]

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GEC-ESTRO Recommendations

Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group: Considerations and pitfalls in commissioning and applicator reconstruction in 3D image-based treatment planning of cervix cancer brachytherapy

Taran Paulsen Hellebust[a,*], Christian Kirisits[b], Daniel Berger[b], José Pérez-Calatayud[c],

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[a], Peter Petrow[b], Kari Tanderup[c], Primoz Petric[d], Daniel Berger[e], Christian Kirisits[e], Erik M. Pedersen[c], Erik van Limbergen[f], Christine Haie-Meder[g], Richard Pötter[e,*]

[a] Metropolitan Hospital, Athens, Greece; [b] Institut Curie, Paris, France; [c] Aarhus University Hospital, Denmark; [d] Institute of Oncology Ljubljana, Slovenia; [e] Comprehensive Cancer Center, Medical University of Vienna, Austria; [f] Universitaire Ziekenhuis Gasthuisberg Leuven, Belgium; [g] 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_{init} (the GTV at diagnosis)
  - GTV_{res} (the GTV at brachytherapy)
  - CTVHR (the GTV_{res} plus residual pathologic tissue plus whole cervix)
  - CTVIR: area of GTV_{init} and/or CTVHR plus safety margin if used for prescription)

Dose reporting:

- TRAK
- Point A dose
- Recto-vaginal reference-point dose
- D 0:1cm3 and D2cm3 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

Patient: xxx

Clinical Drawing

At Diagnosis ☒

At Brachytherapy ☐

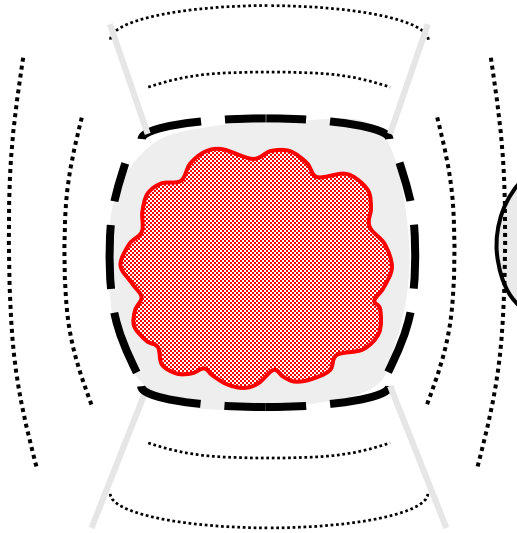
Infiltrative Exophytic

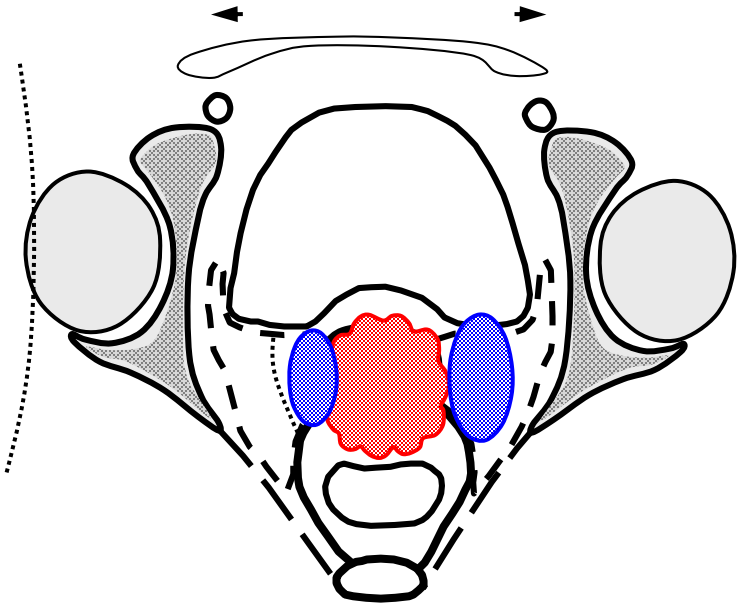
Cervix

Vagina

Parametria

Rectum or Bladder



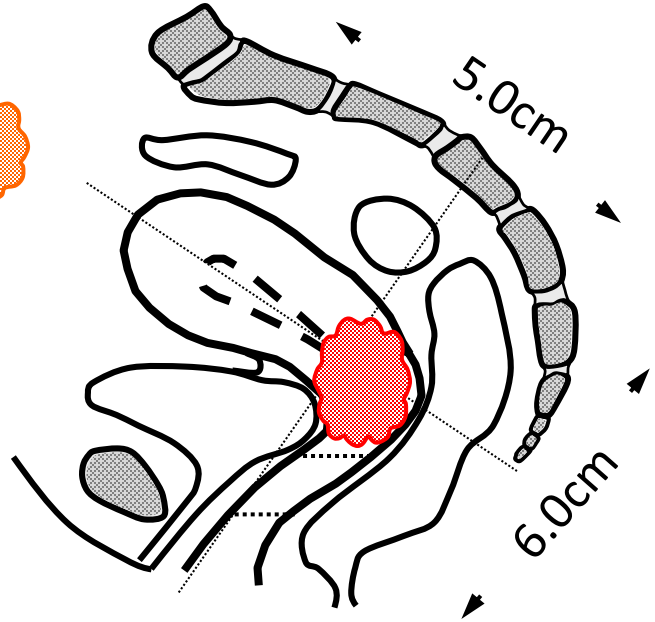


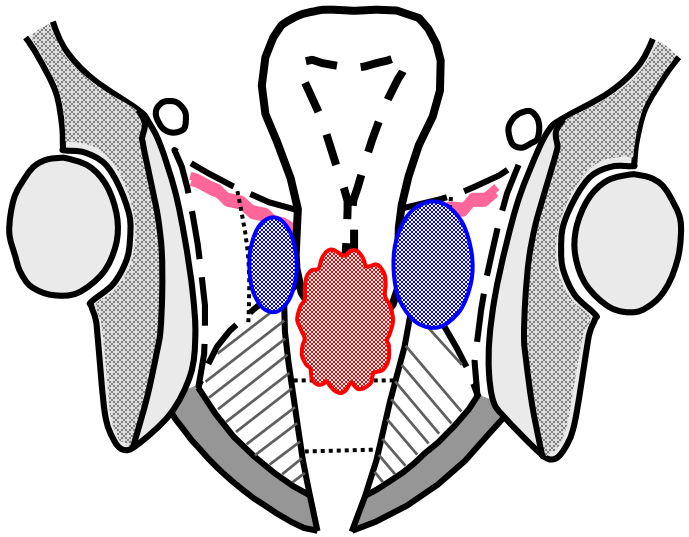
w = 6.0 cm

h =5.0. cm

t = 6.0cm

Vagina Involvement =0 cm



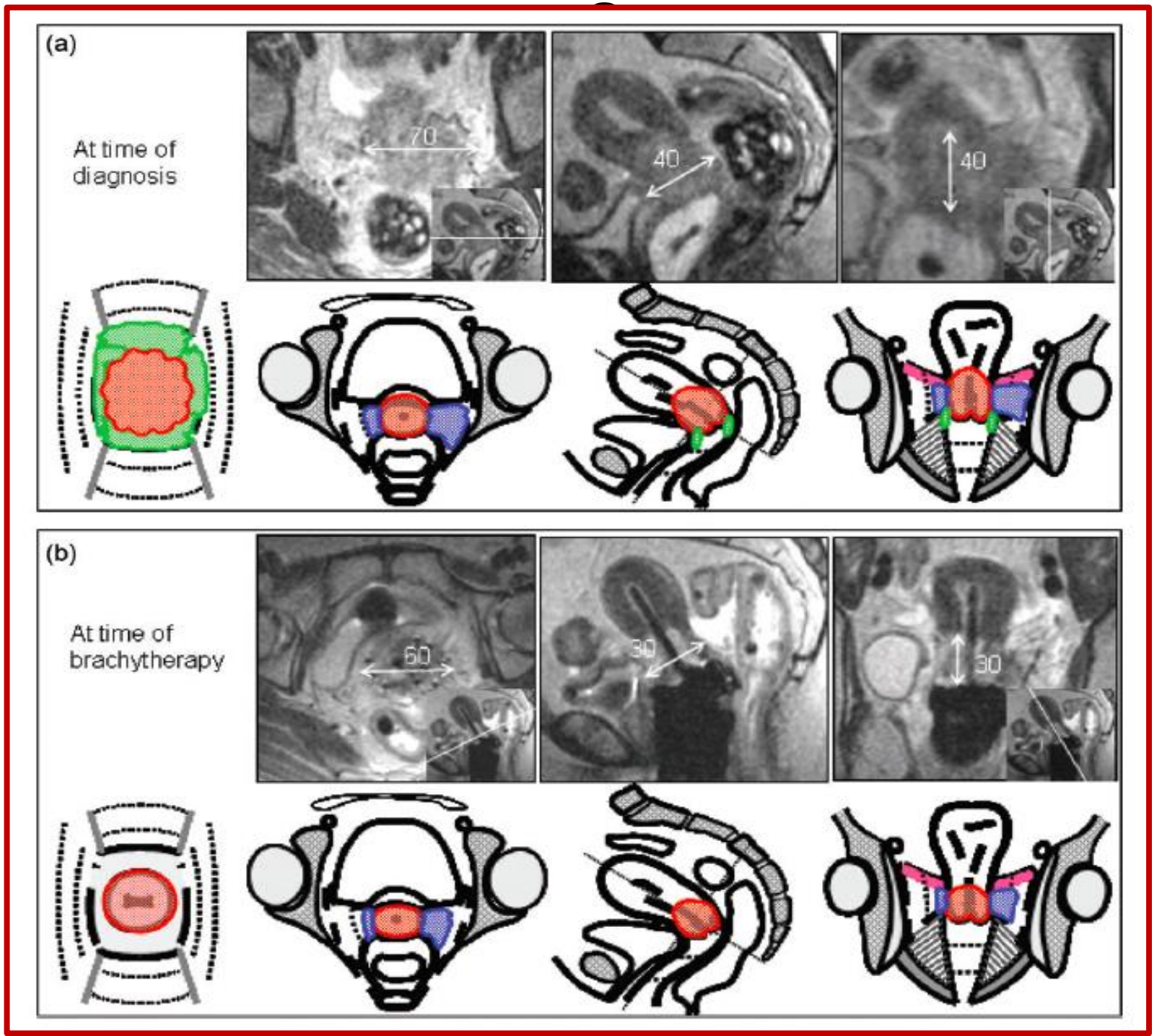


dd/mm/yy

CLINICAL DRAWINGS

Clinical examination
+
Findings at Imaging

At Diagnosis
Response assessment
Prior to brachytherapy

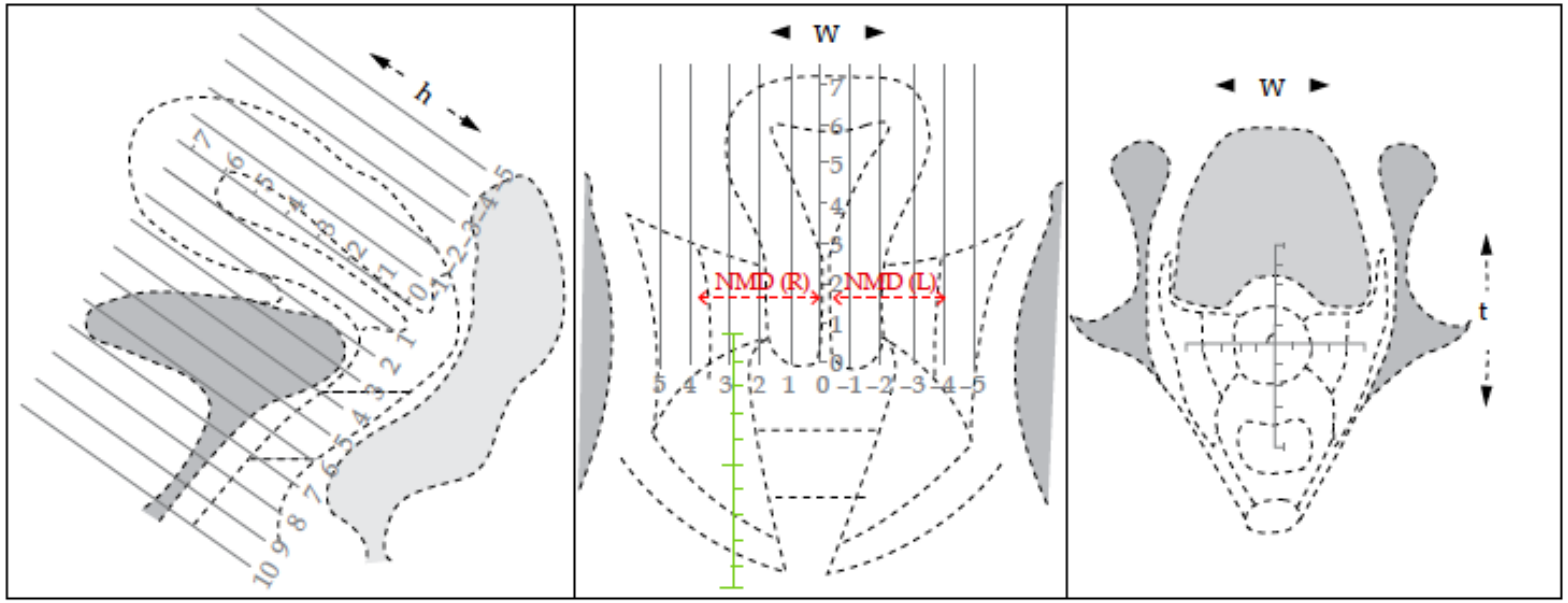


Advanced Clinical Diagram

Date:
ID:

Cervical cancer: clinical evaluation

☐ Initial evaluation
☐ At brachy (fraction no. __)

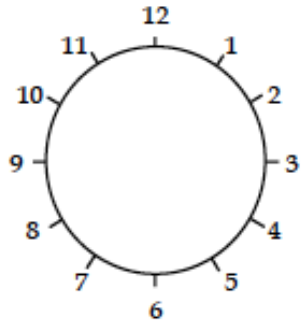


h = __ cm t = __ cm w = __ cm NMD (R) = __ cm NMD (L) = __ cm NMD – near maximum distance

Clinical examination findings:

Imaging findings:

Vaginal disease:
Ant: __ cm
Post: __ cm
Rt Lat: __ cm
Lt Lat: __ cm



FIGO stage ☐
T ☐
N ☐
M ☐

Signature

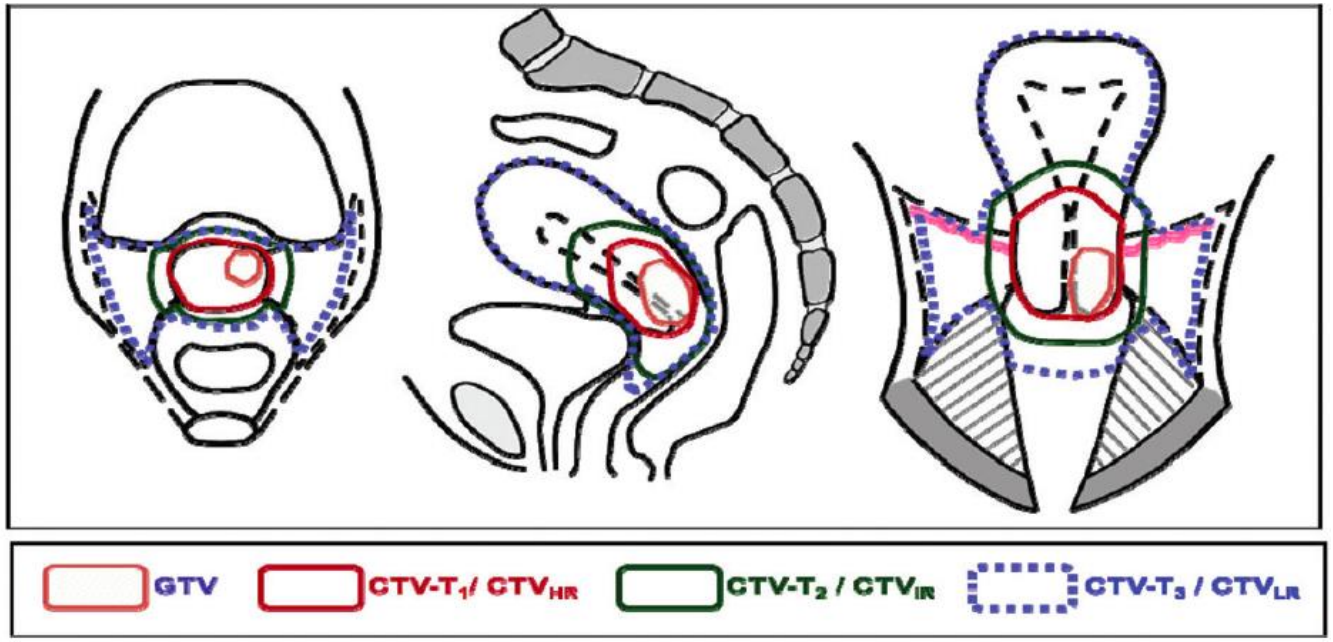
Umesh Mahantshetty, 2019

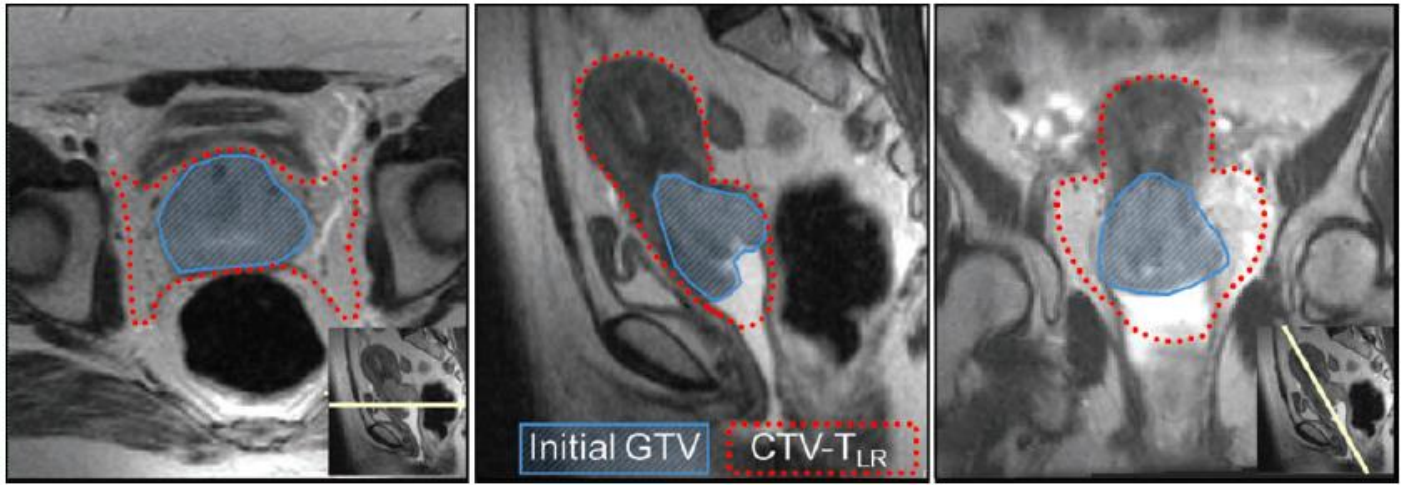
Target Concepts- Ext RT

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 incontinguous microscopic spread (initial CTV_{LR})

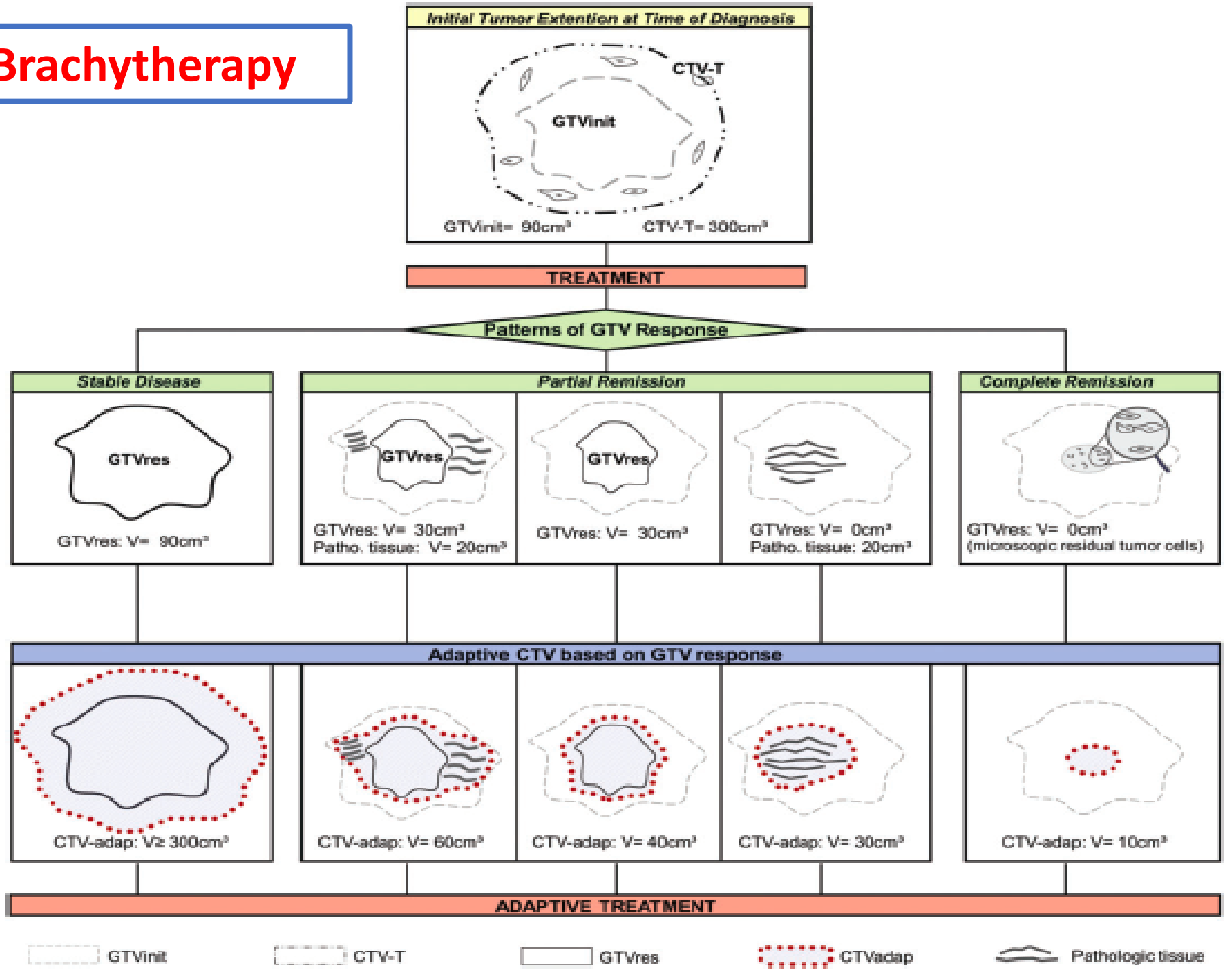




Target Concepts- Brachytherapy

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:

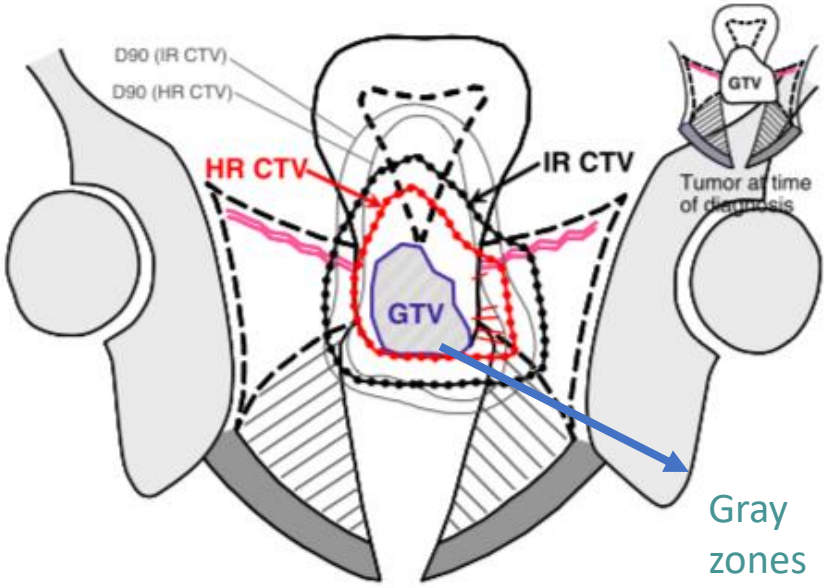
residual palpable mass;

residual visible mucosal change;

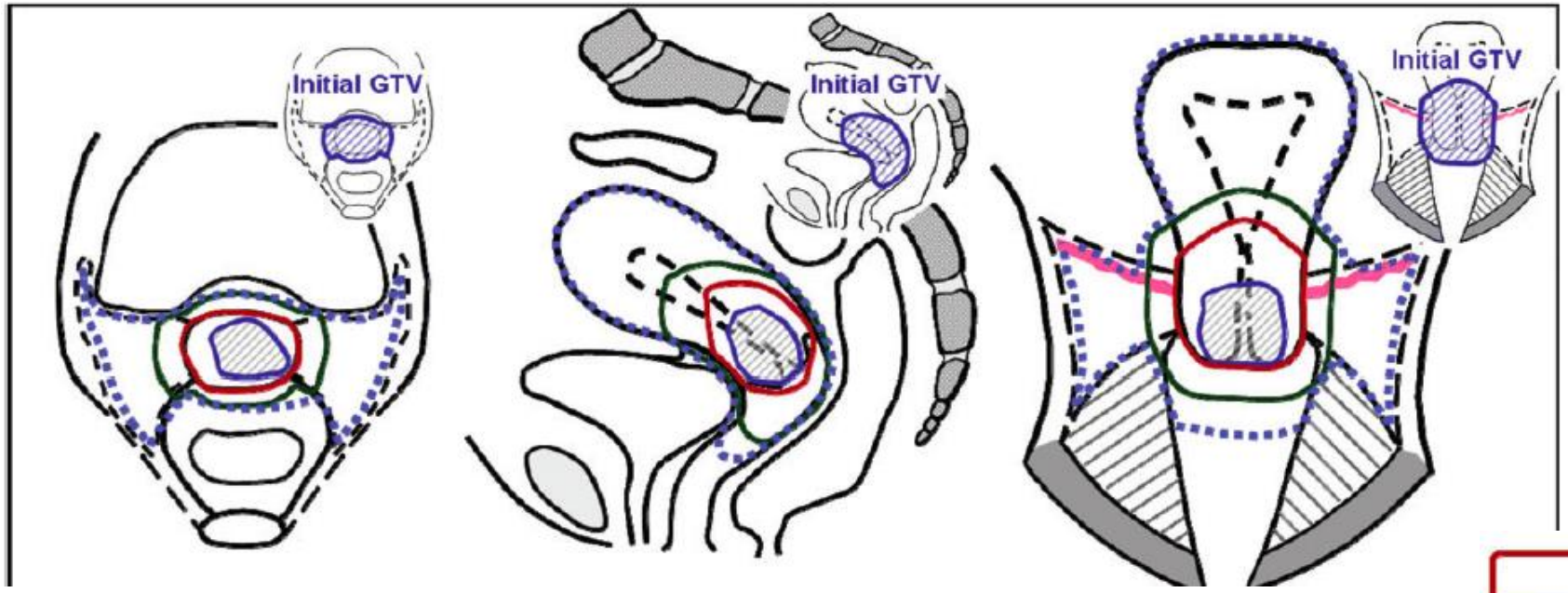
pathologic induration;

residual gray zones (MRI);

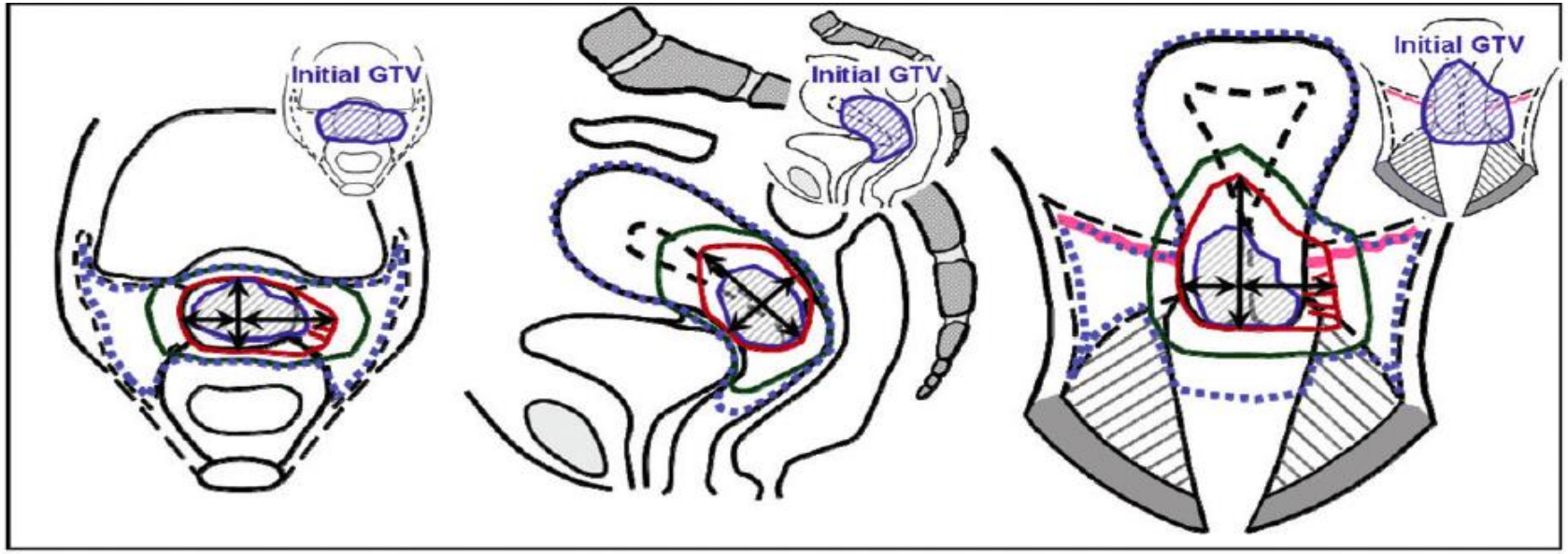
any other residual pathologic tissue on MRI or clinic examin



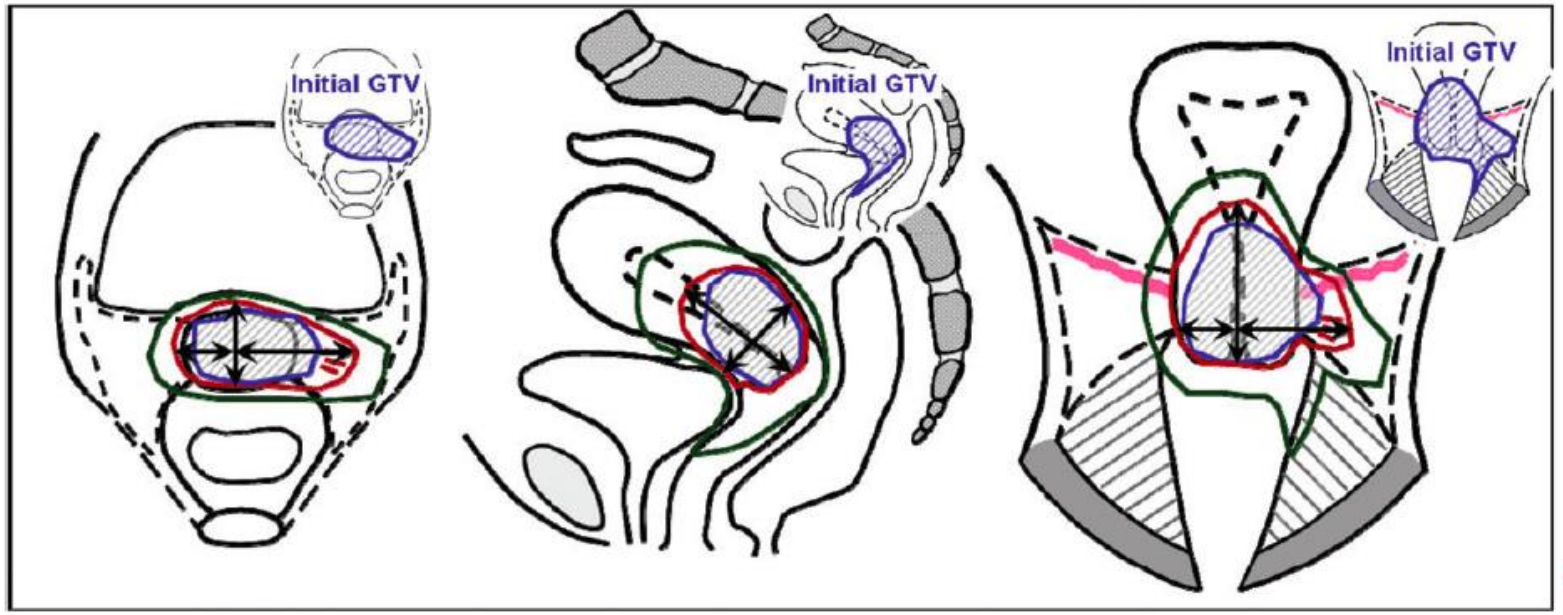
Intermediate-risk CTV-T (CTV-TIR) represents the area of the GTV$_{init}$ as superimposed on the topography at the time of brachytherapy and a margin surrounding the anatomical cervix borders (CTV-THR) in areas without an initial GTV. The CTV-TIR therefore always includes the CTV-THR and margins as appropriate.



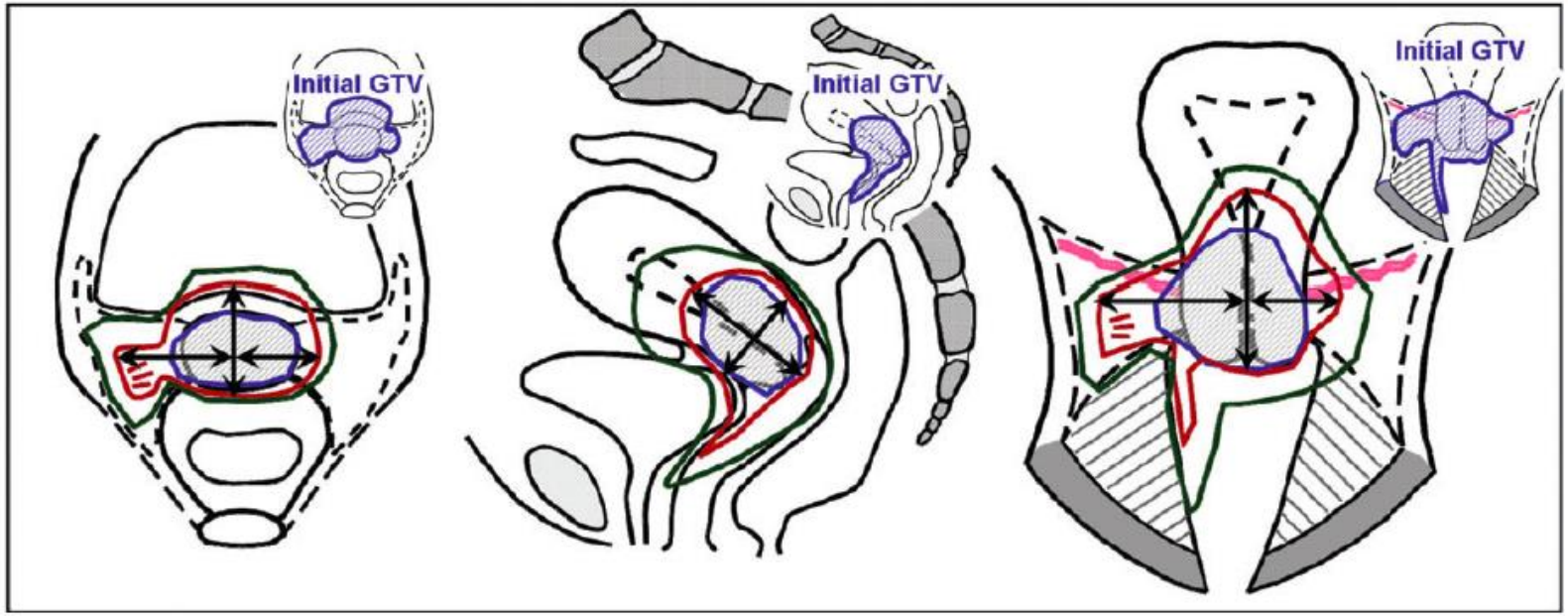
Stage IB2 (bulky disease), good response after chemo-radiotherapy



Stage IIB bulky disease, good response after chemo-radiotherapy



Cervical cancer, IIIB, extensive disease, poor response after chemo-radiotherapy



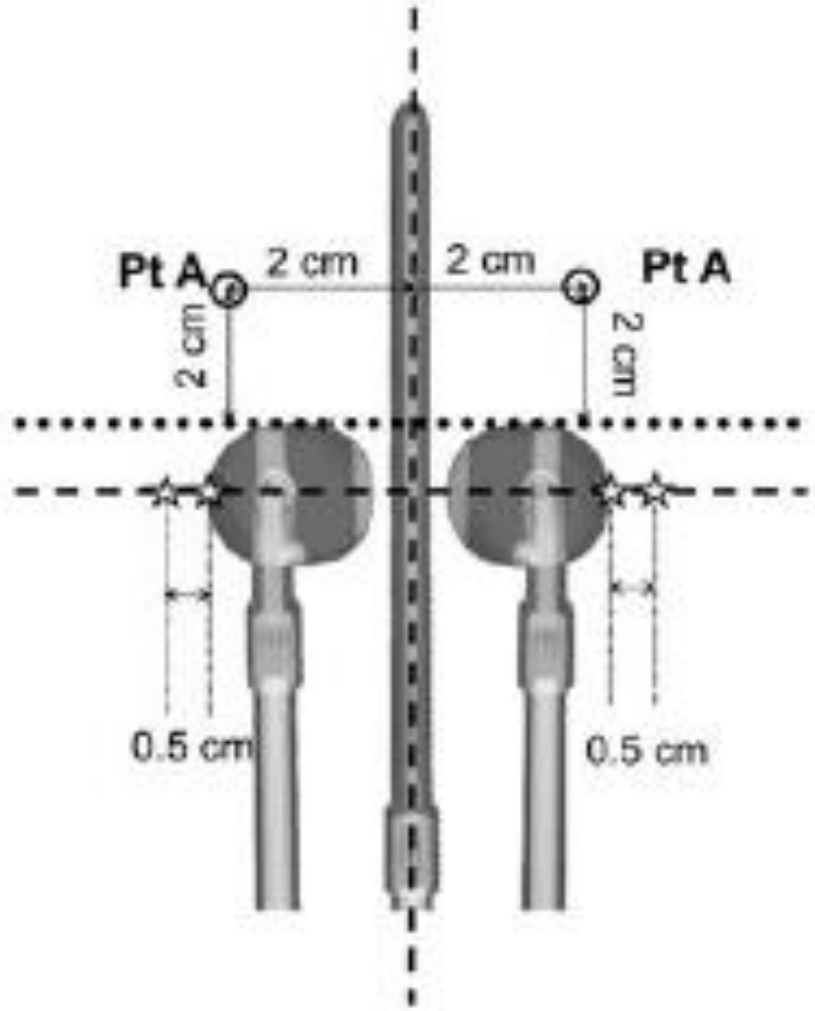
Cervical cancer, with bladder infiltration, Stage IVA, and good response after chemo-radiotherapy

Dose Reporting

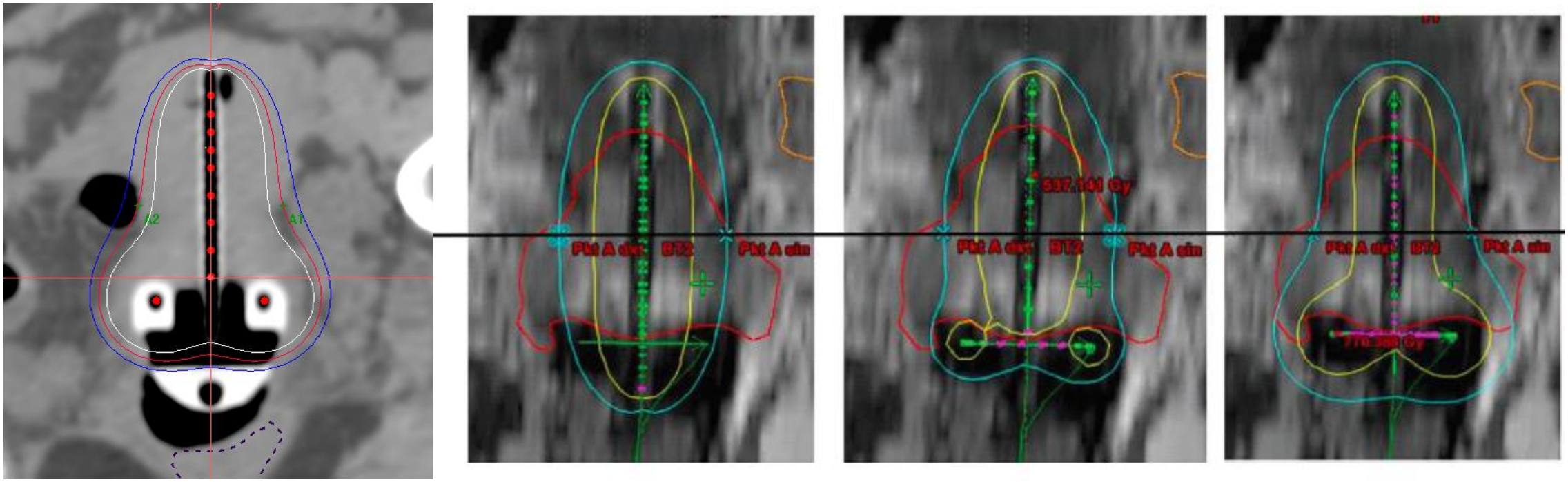
- TRAK

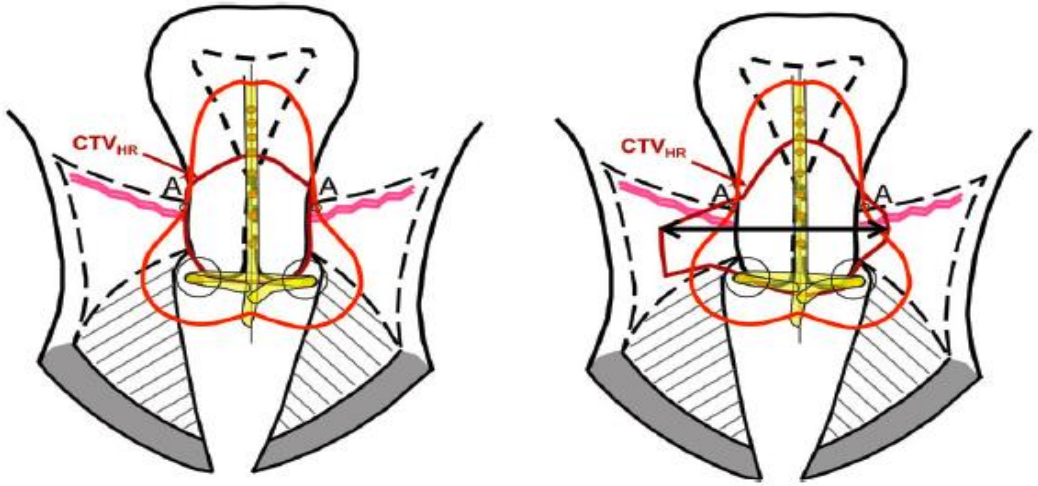
- Adoption of Point A as a major reference point with a definition related to the applicator for absorbed-dose specification:

- **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?

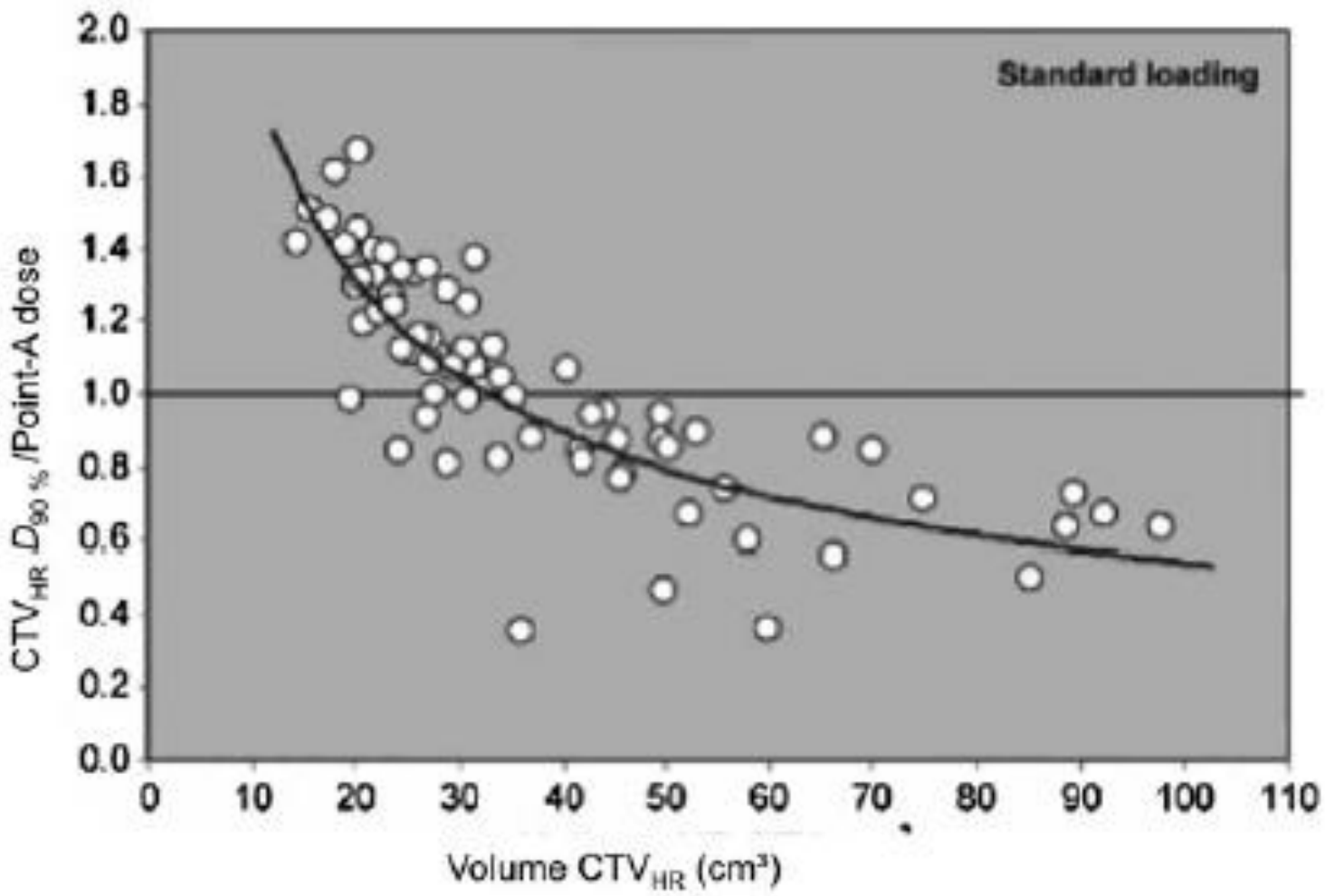




Point A-based standard loading patterns delivering the same absorbed dose to Point A, but using widely different vaginal and tandem loading

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?

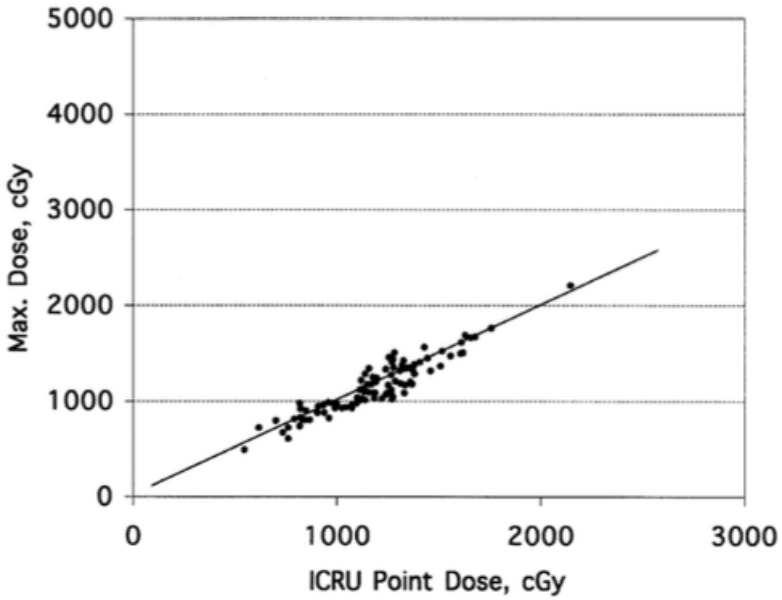
- Allows comparison of different approaches
- Point A dose is a surrogate of the irradiated volume
- Starting point for planning
- Helps in check for major dose escalation and reduction

    Thresholds for Point A dose for volume treated to 85Gy

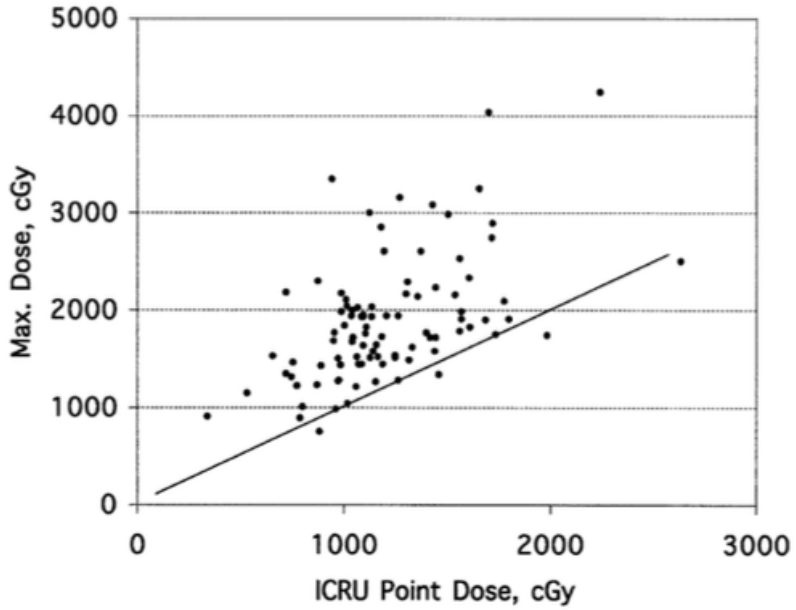
    2D X-Ray based >75Gy

    CT based >70Gy

Do ICRU bladder and rectum points represent the maximum doses ?

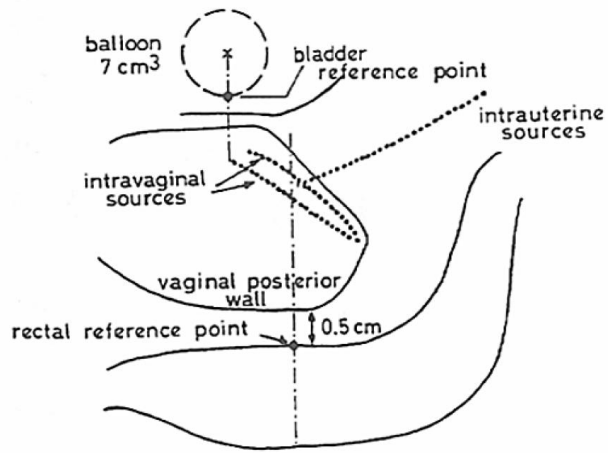


Rectum

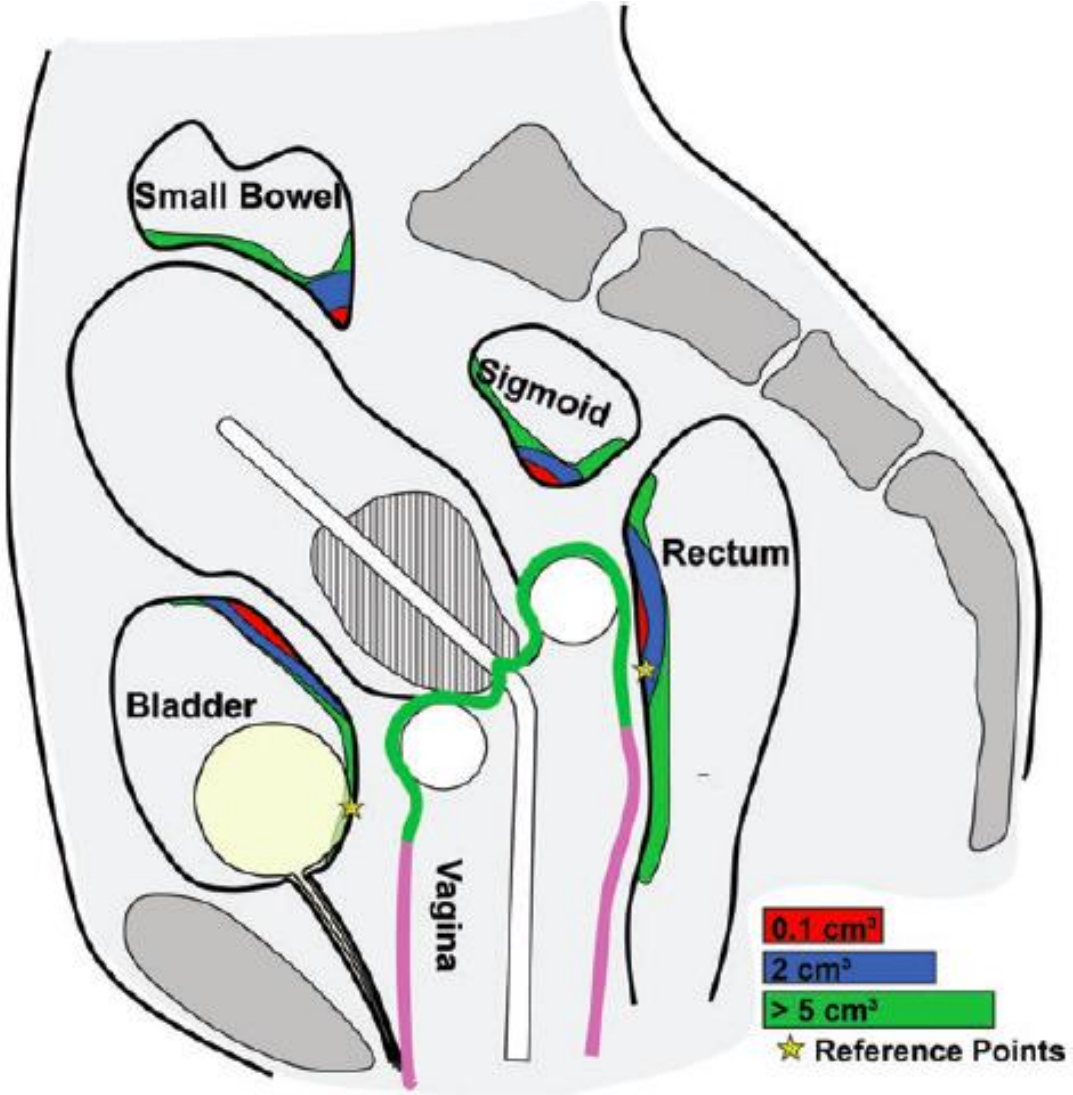


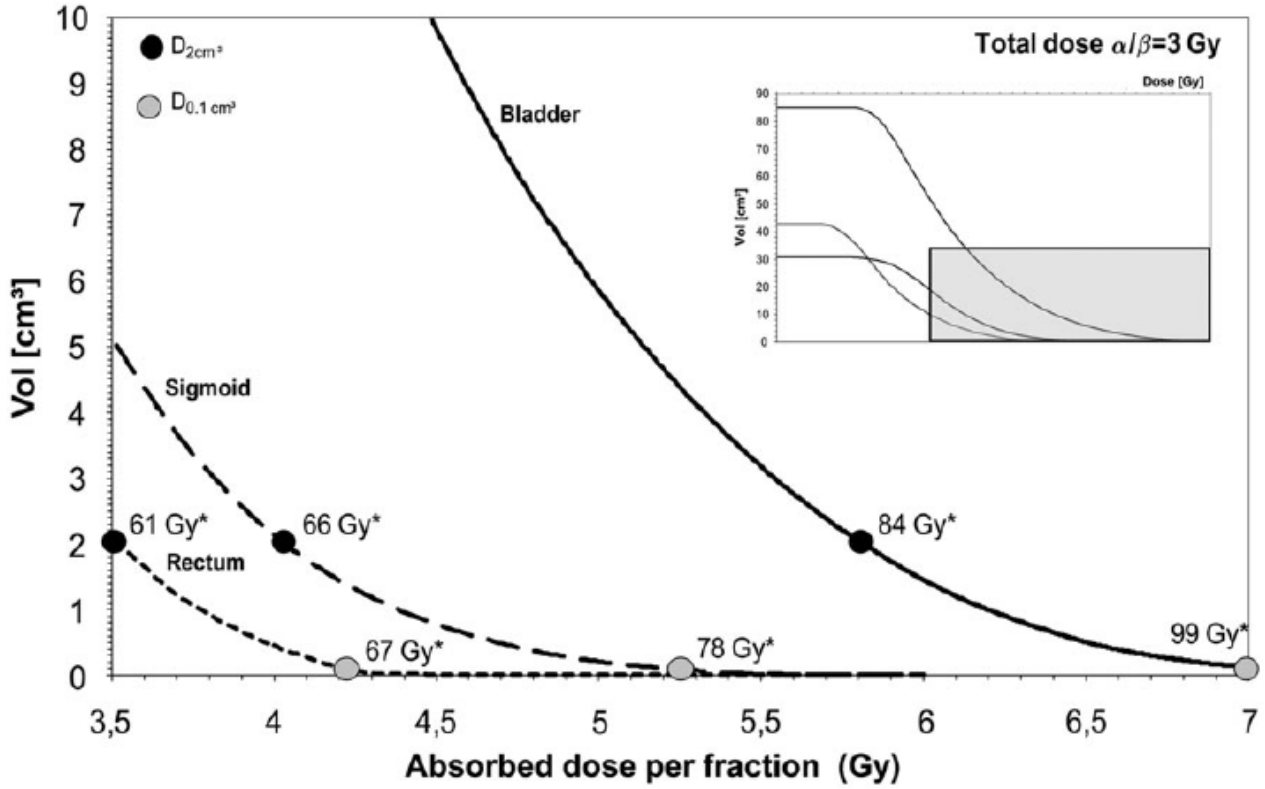
Bladder

Pelloski, et al. IJROBP 2005;62:131



Dose reporting OAR: 3-D based DVH parameters





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

GYN GEC ESTRO Rec.(II), 2006

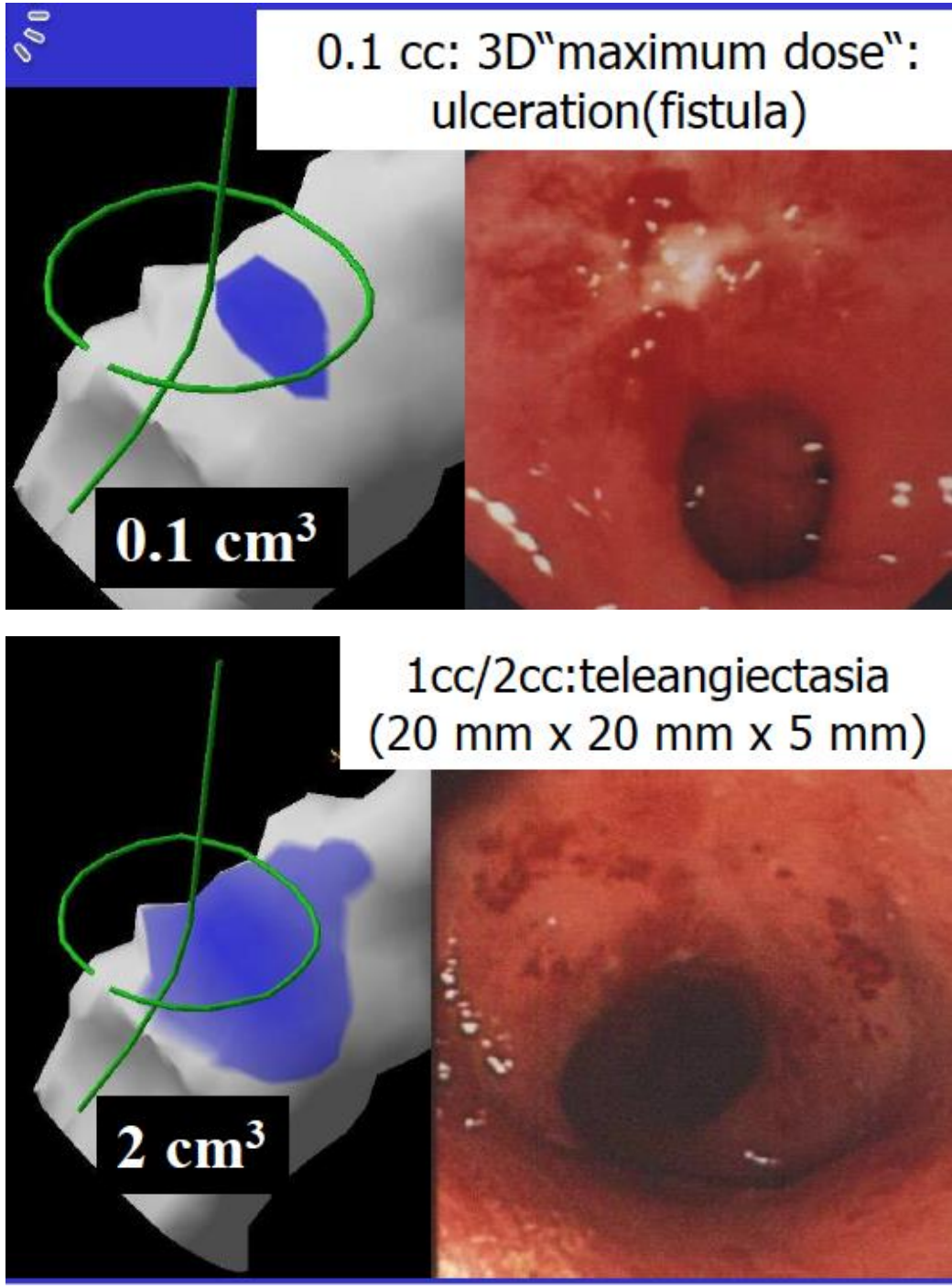
3D based dose volume constraints OAR

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

Fixed Volume : “ Minimum dose to the most irradiated tissue

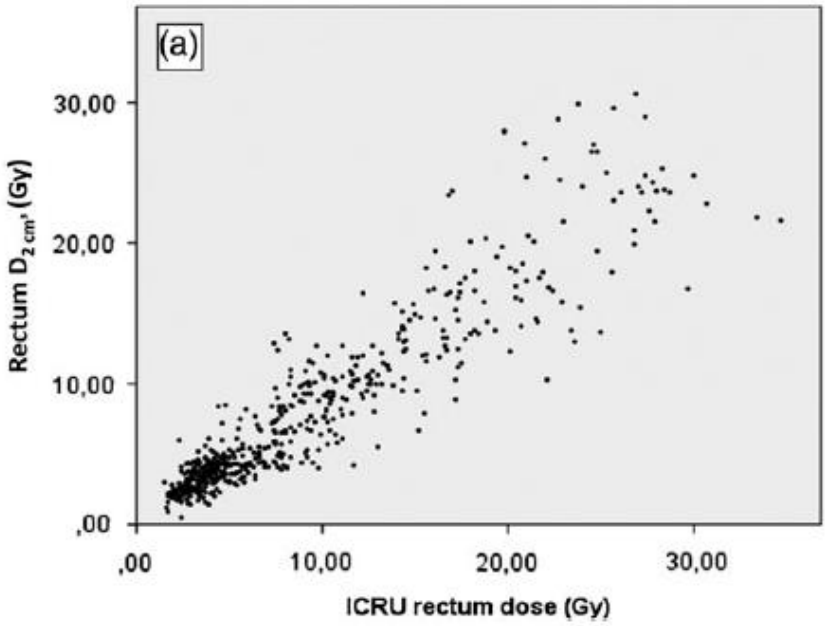
0.1cc: 3D „maximum dose“: ulceration (fistula)
1 cc/2 cc: telengiectasia
(20 mm x 20 mm x 5 mm)
>5 cc: fibrosis endpoint

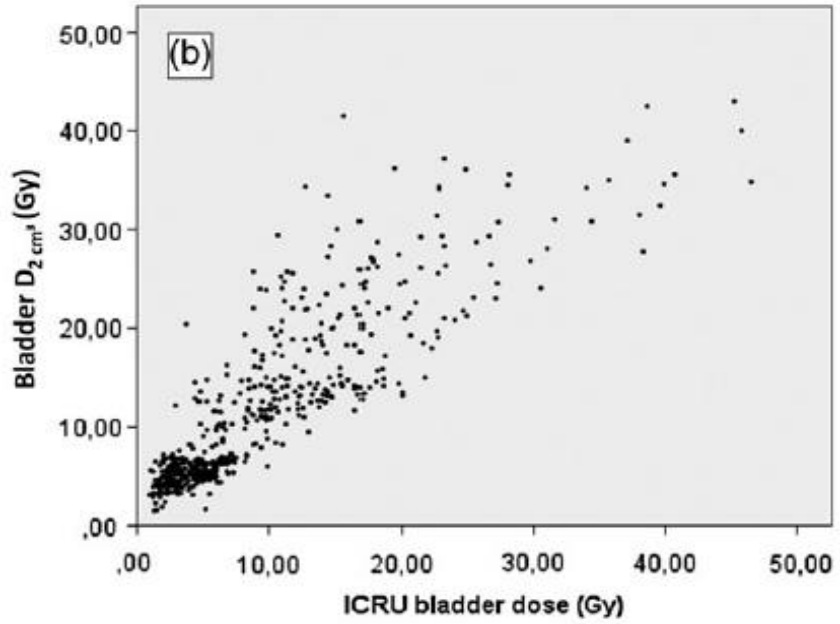
*GYN GEC ESTRO Recommendations (II)
Radioth. Oncol. 2006



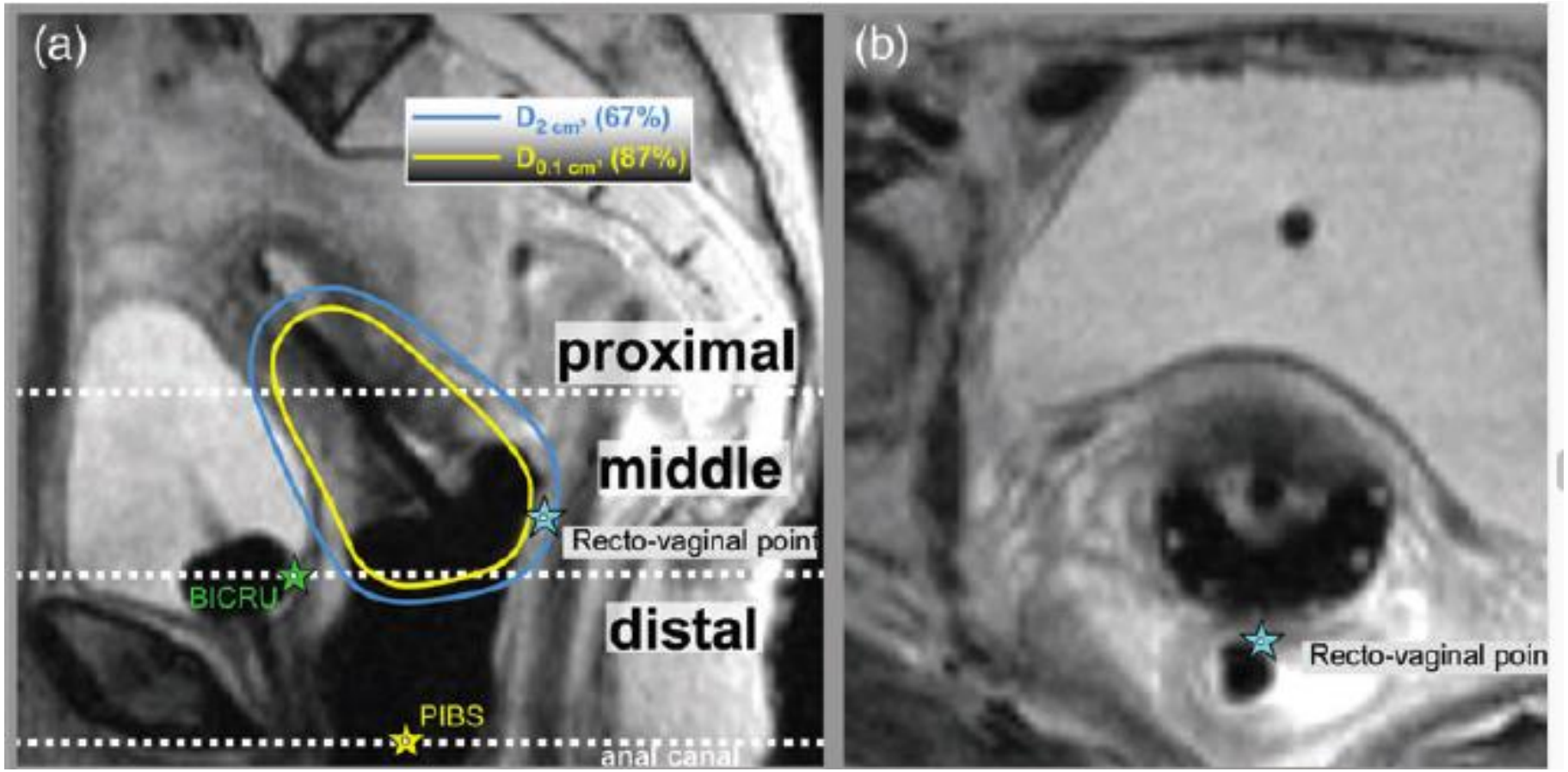
ICRU and Volume based OAR doses

- 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



Kirchheiner et al., 2016

Correlation with Post vaginal wall dose – vaginal stenosis

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 α/β 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**

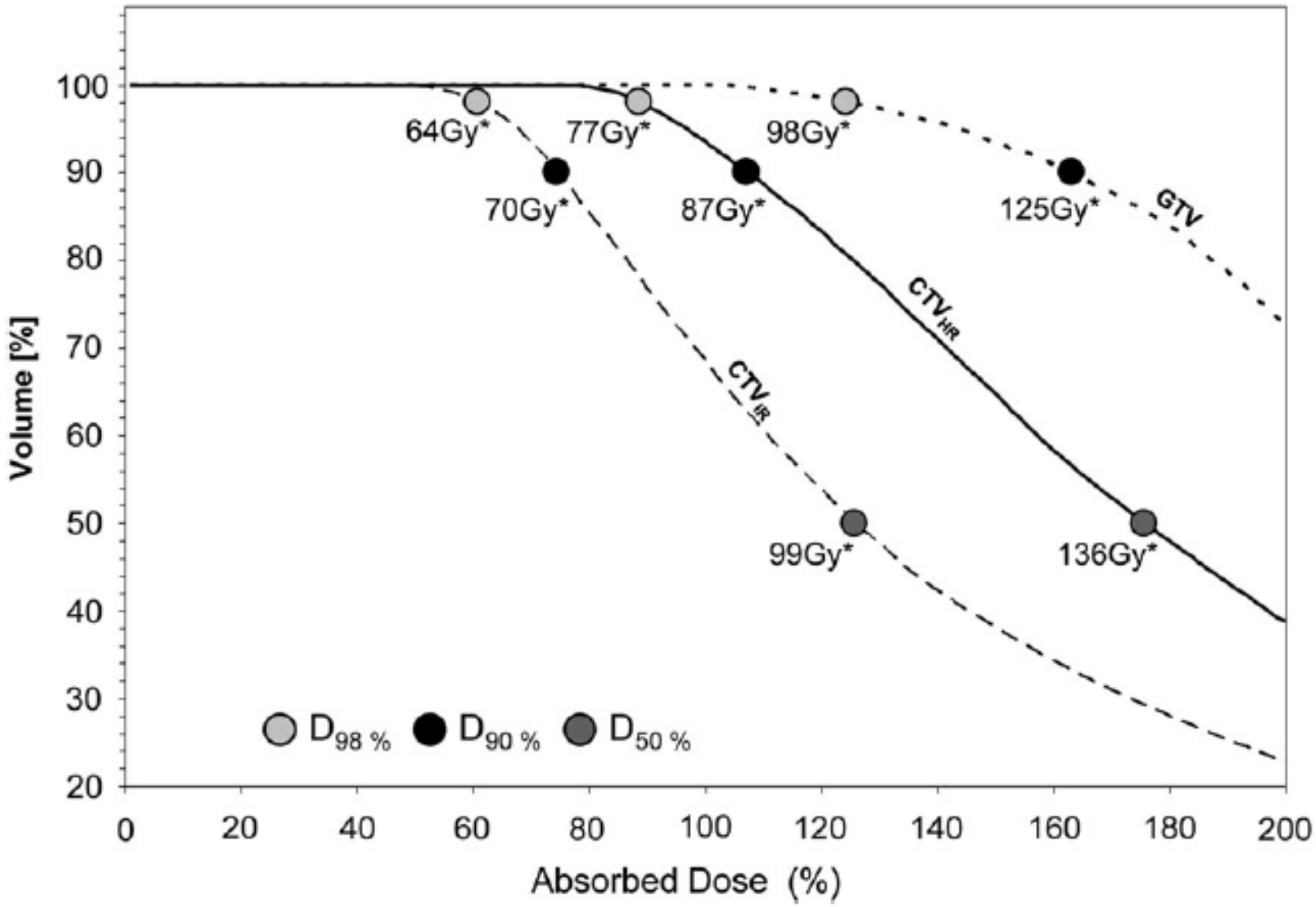
Dose reporting OARs:

- **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

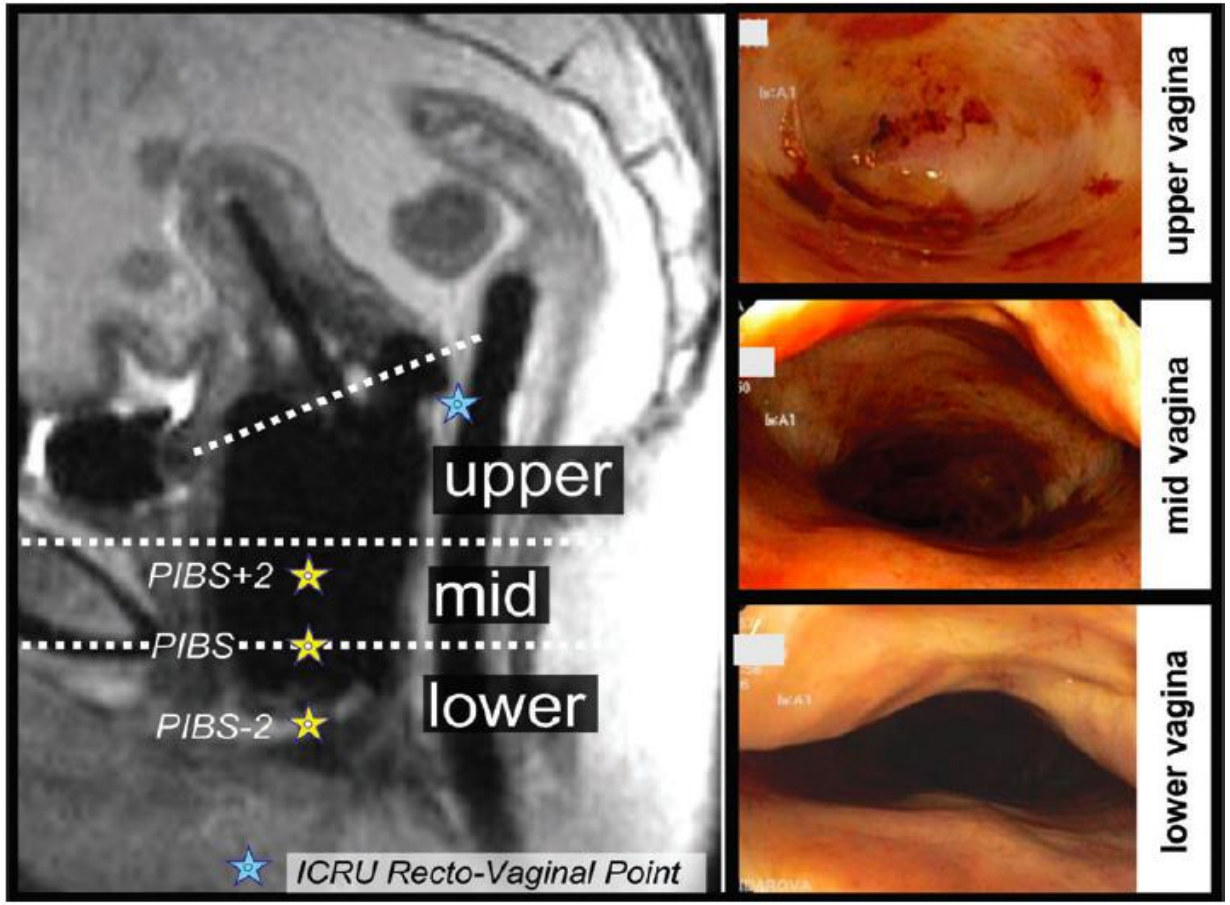
- **D100, D98 & D90** – minimum dose delivered to 100, 98 & 90% of the volume of interest respectively
- **D100** is extremely dependent on target delineation. Due to steep dose gradients, small spikes in the contour cause large deviations in D100
- **D98** reflects the dose in the outermost periphery 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



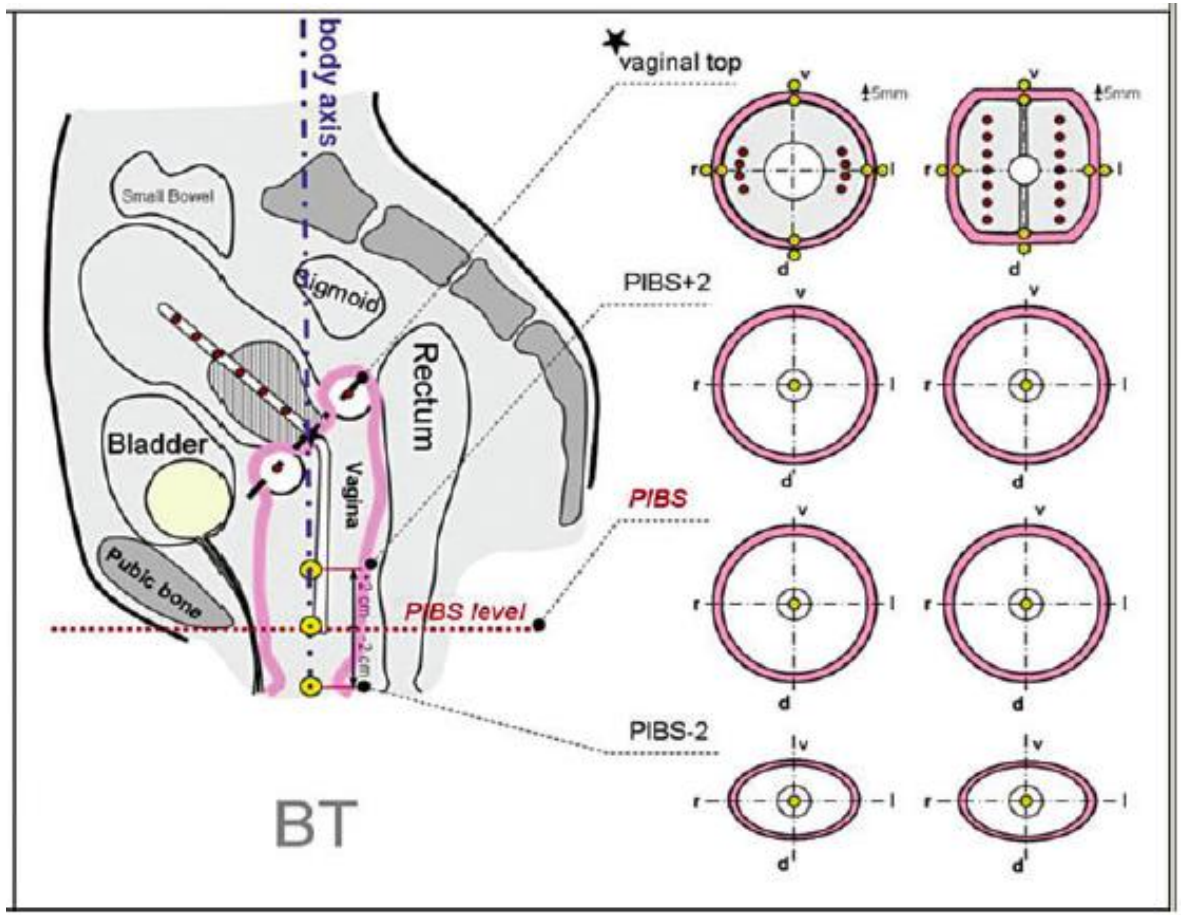
DVHs for the GTV and the CTV in intracavitary brachytherapy have a plateau, which indicates 100% dose coverage of the volume of interest. This plateau goes down smoothly indicating decreasing percentage of dose coverage with increasing dose

Vaginal Reference Points



PIBS vaginal-dose point –mid & lower

[*Westerveld et al. 2013*]



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

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 $D_{0.1cm^3}$ 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