ICRU RECOMMENDATIONS FOR GYNECOLOGICAL BRACHYTHERAPY

41st ICRO PG TEACHING PROGRAM

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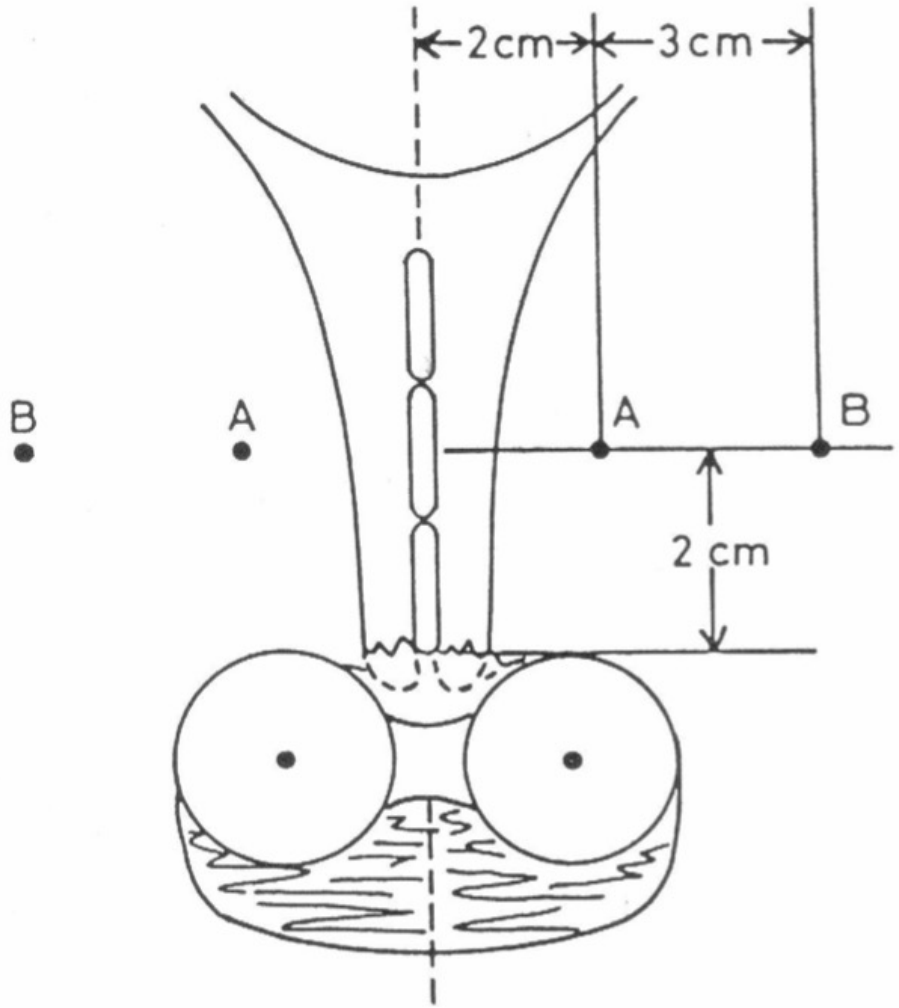
Conventionally, dose prescribed to point A

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

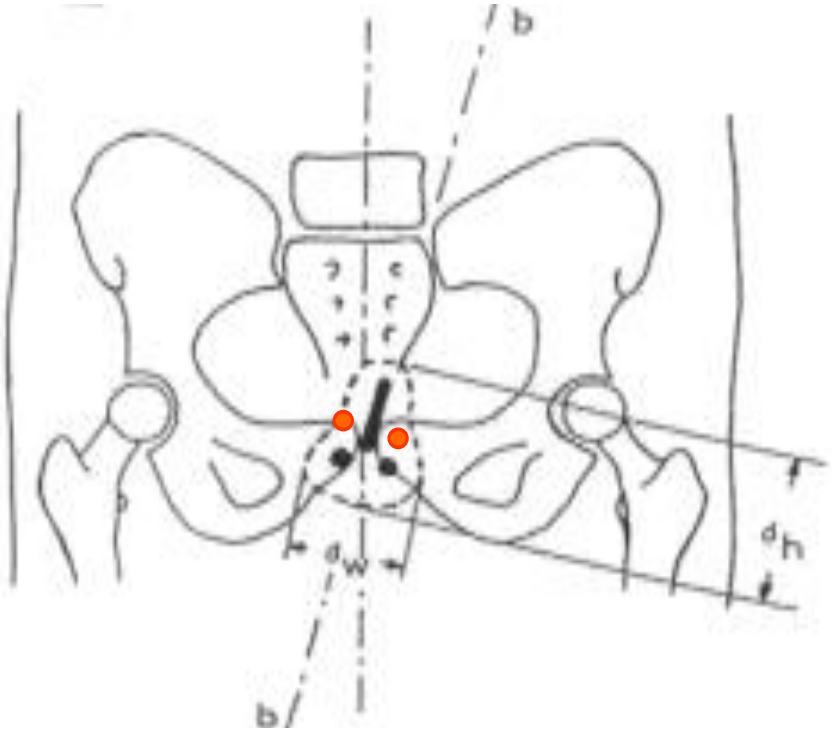
- applicator type,
- source type
- loading
- orthogonal radiographs of the application.

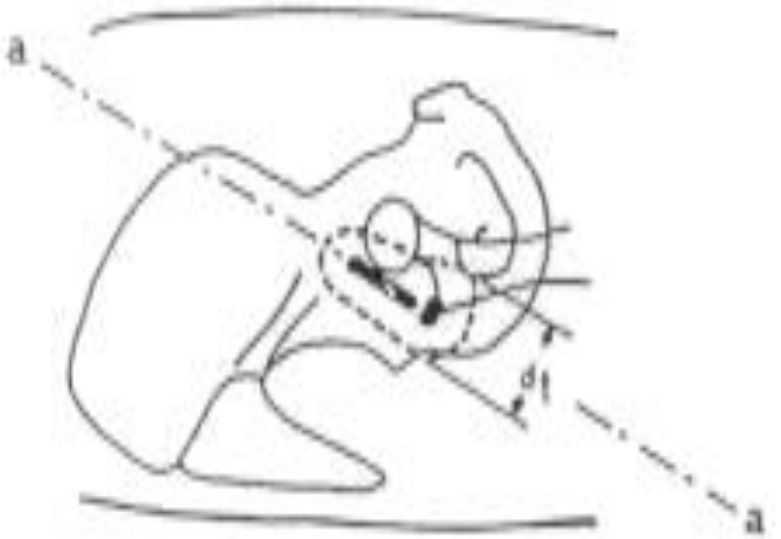
Total Reference Air Kerma

- *A*nalogous 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 x dW x dT)*



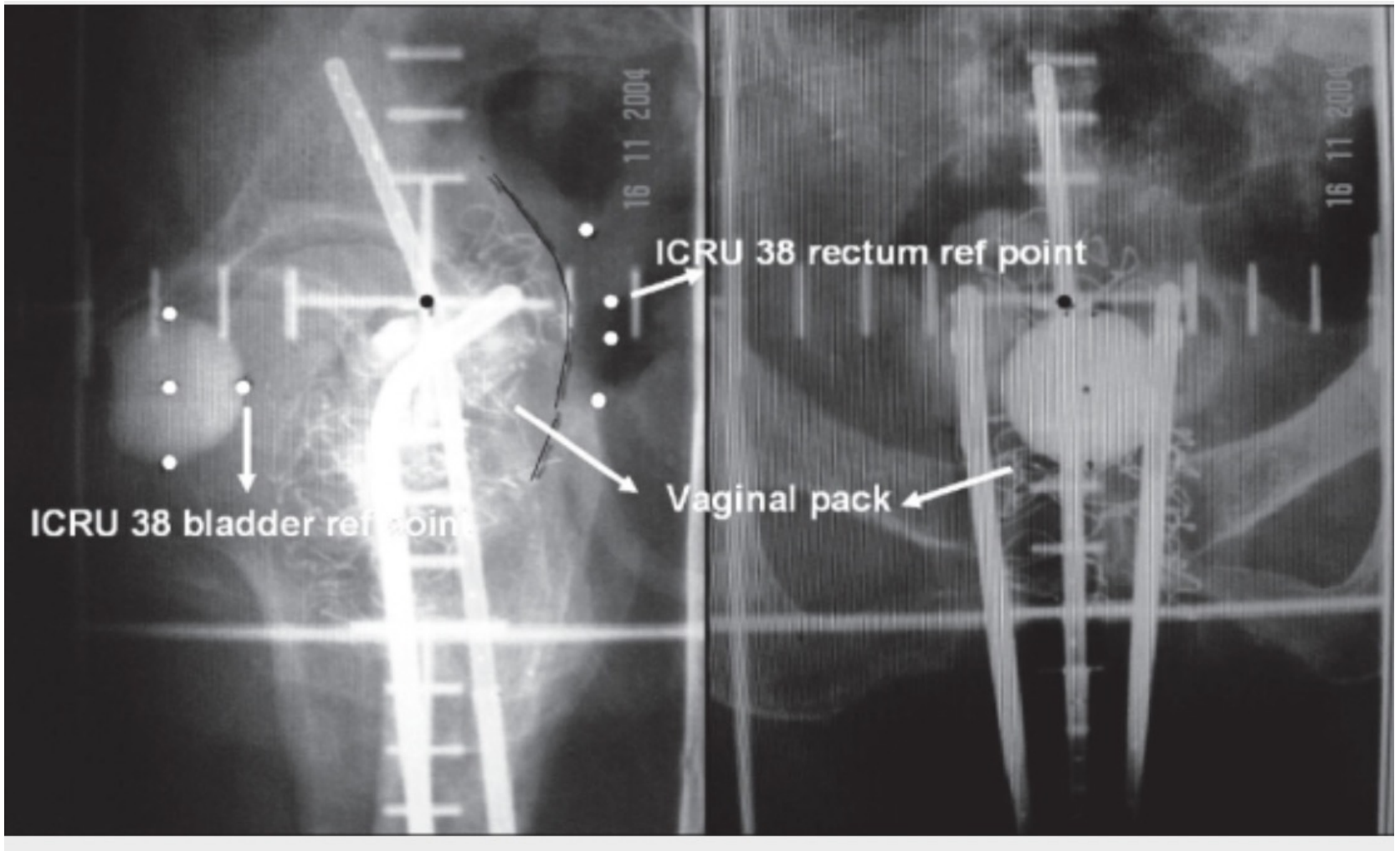


Absorbed dose at Reference points

Bladder point

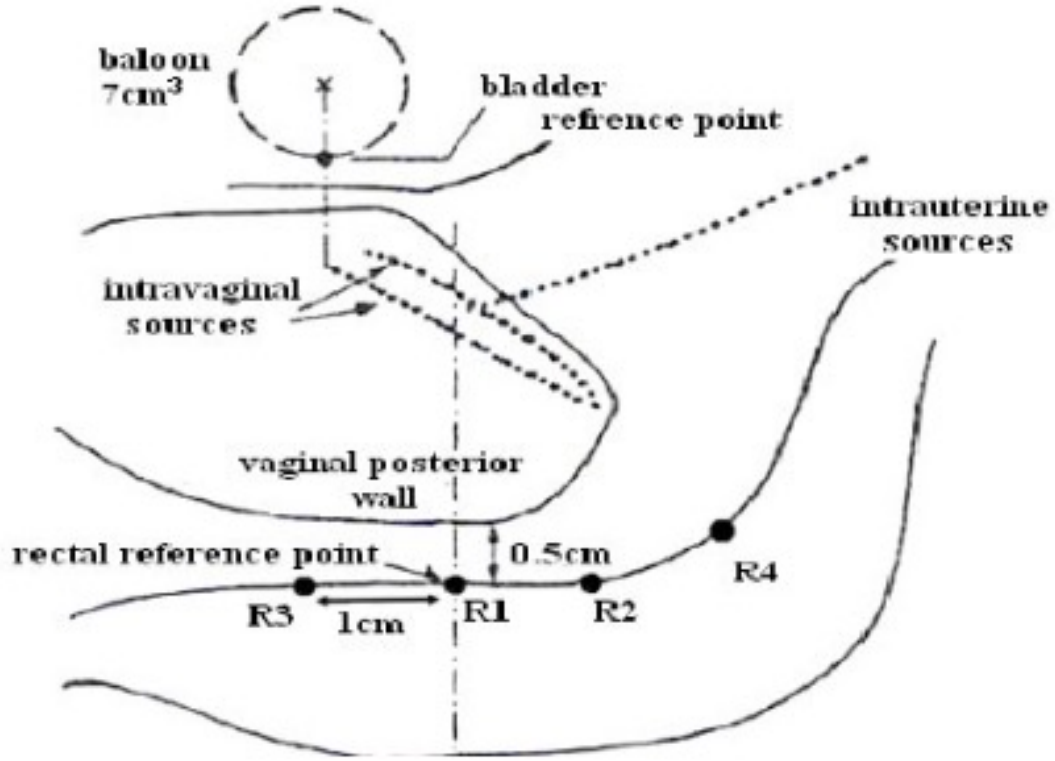
Posterior surface on lateral

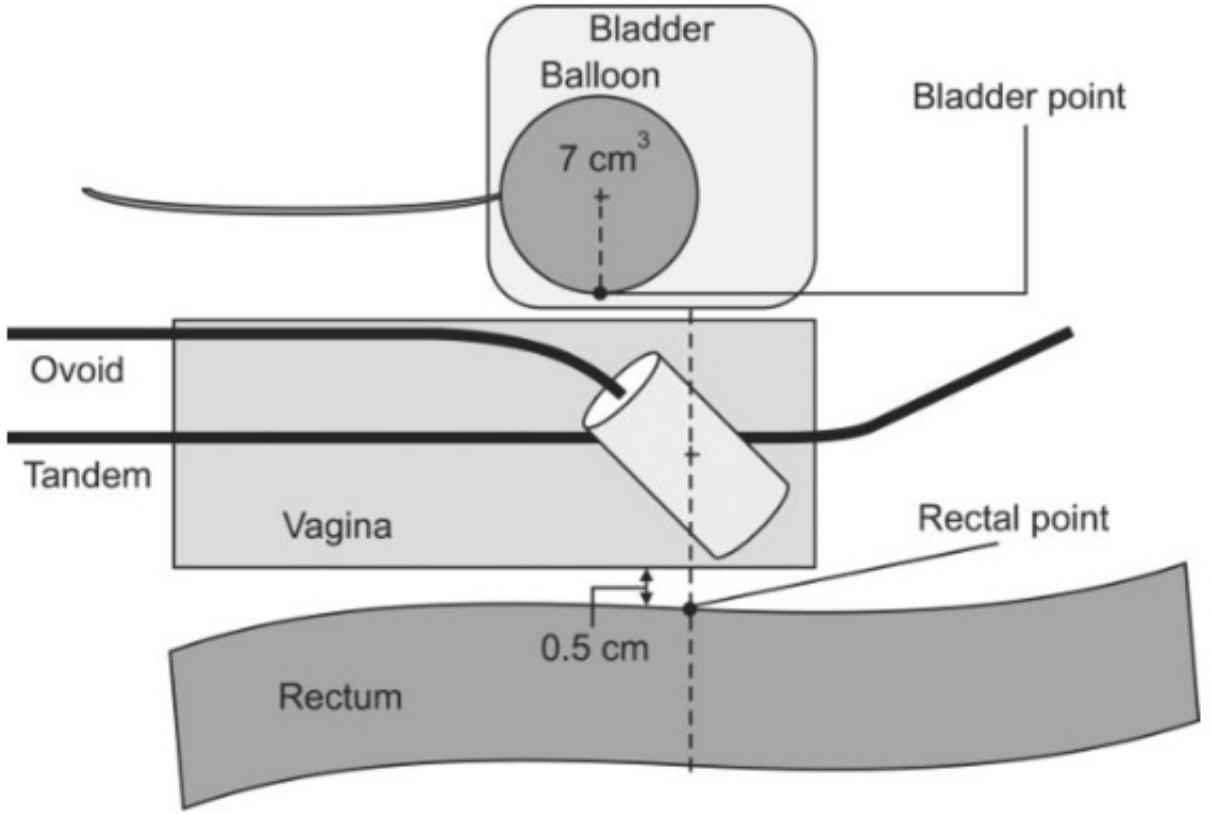
Center of AP film with foley w/ 7 cc radiopaque contrast pulled down against urethra



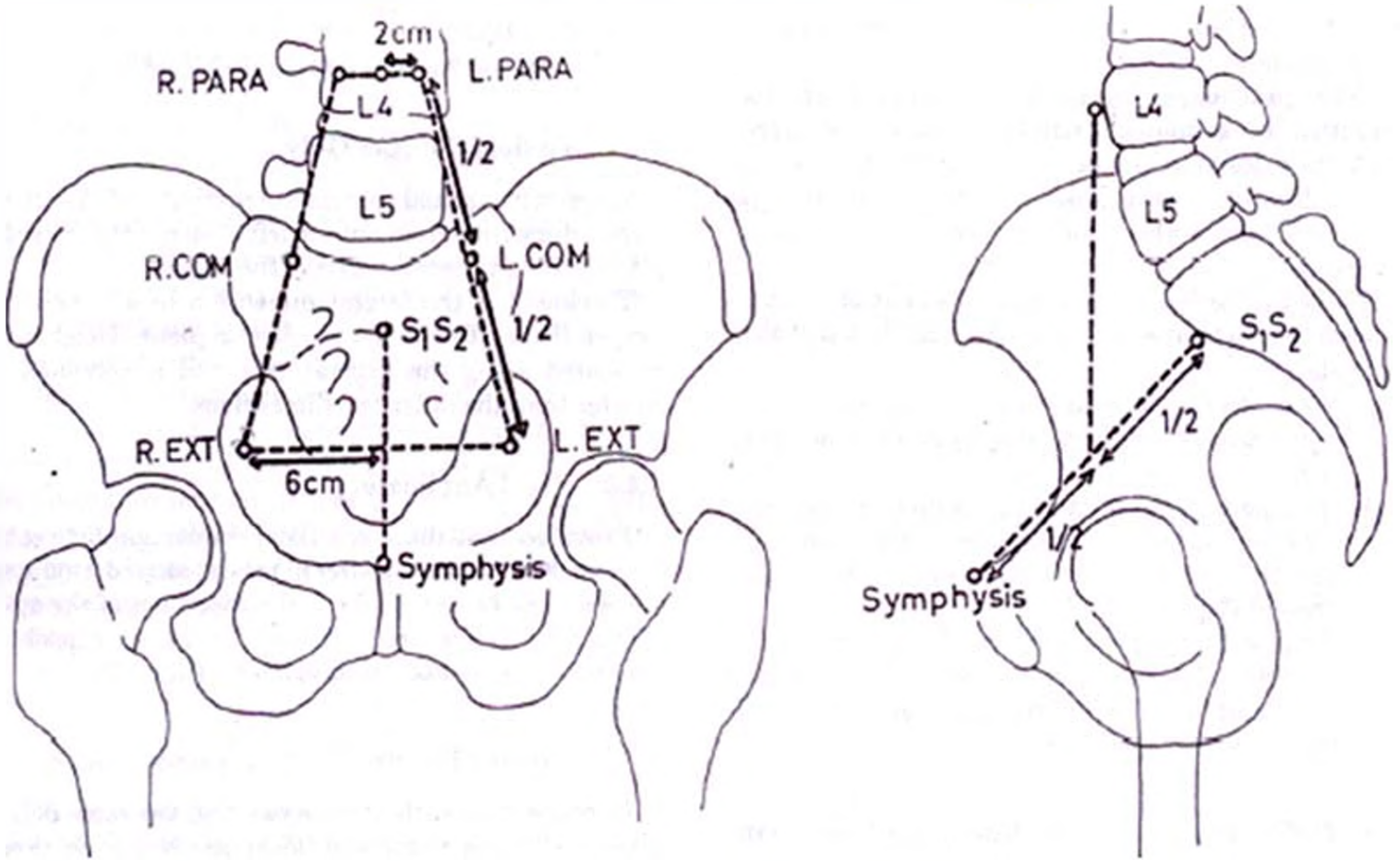
Rectal point

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



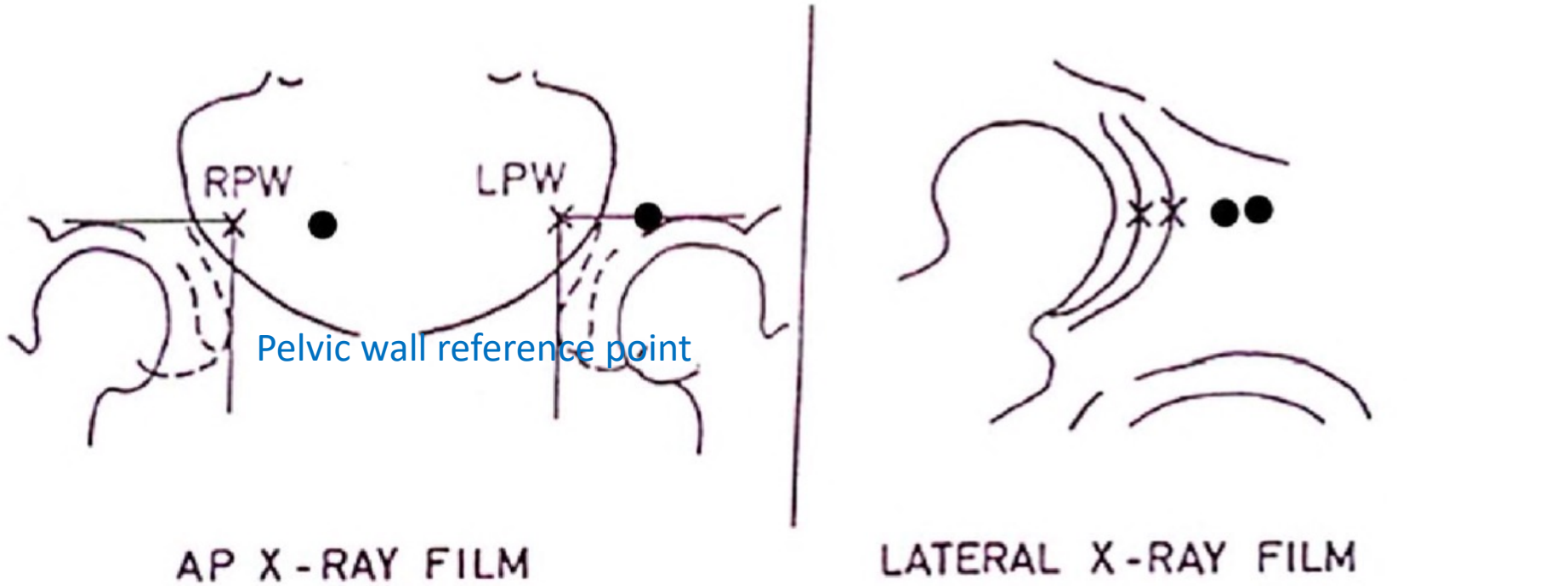


Lymphatic Trapezoid



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

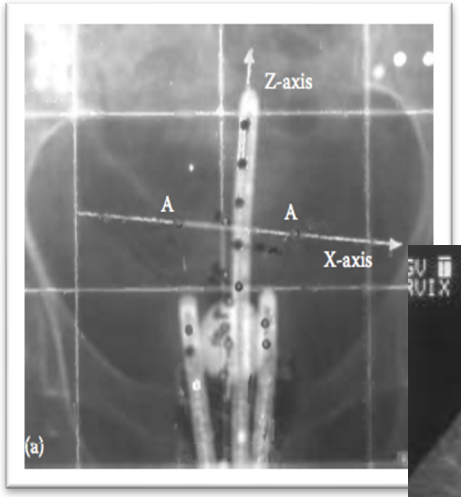
Time Dose Pattern

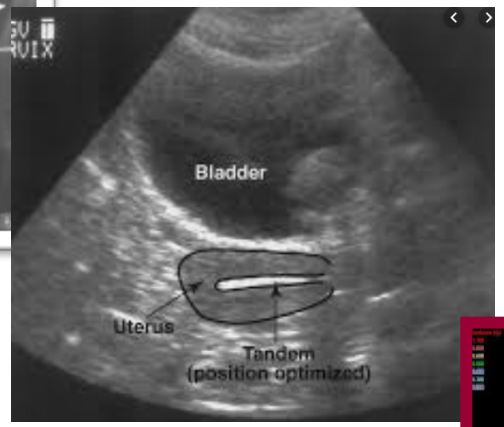
Radiobiologic effects- dose rate dependant

The duration and time sequence of the implant should be recorded

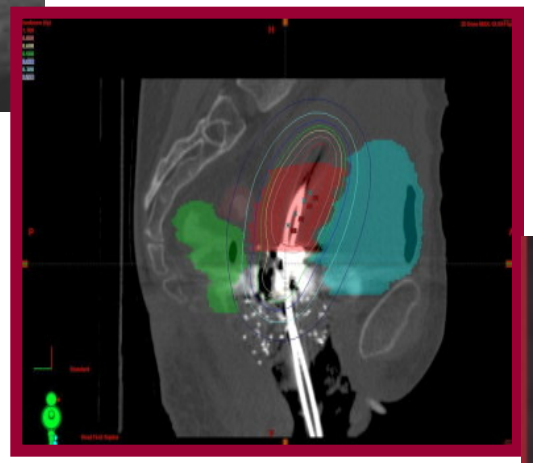
Doses for external beam treatment should be recorded.

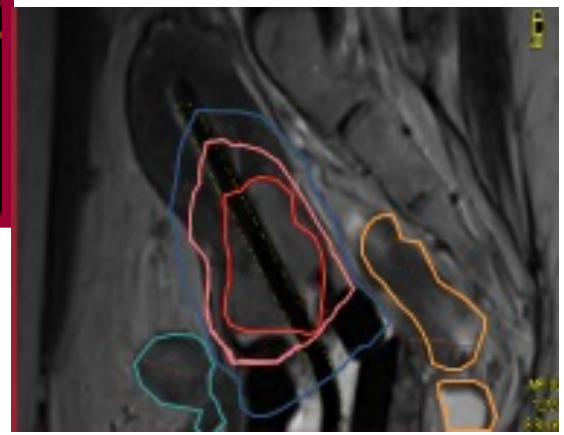
2D to 3D and 4D Brachytherapy





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]

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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],

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 (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

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**

Patient: xxx

Clinical Drawing

At Diagnosis ☒

At Brachytherapy ☐

Infiltrative Exophytic

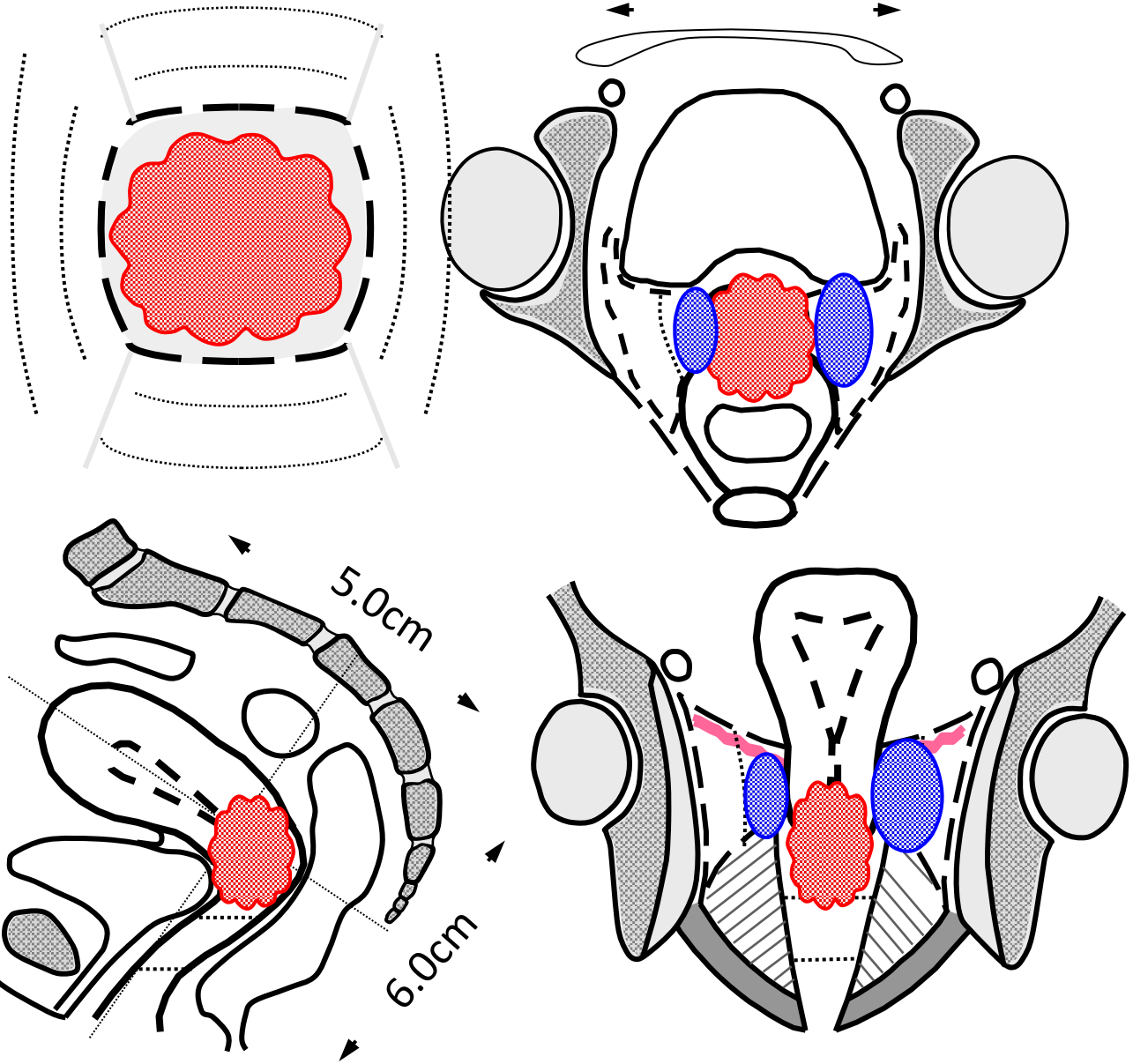
Cervix

Vagina

Parametria

Rectum or Bladder

dd/mm/yy



w = 6.0 cm

h =5.0. cm

t = 6.0cm

Vagina Involvement =0 cm

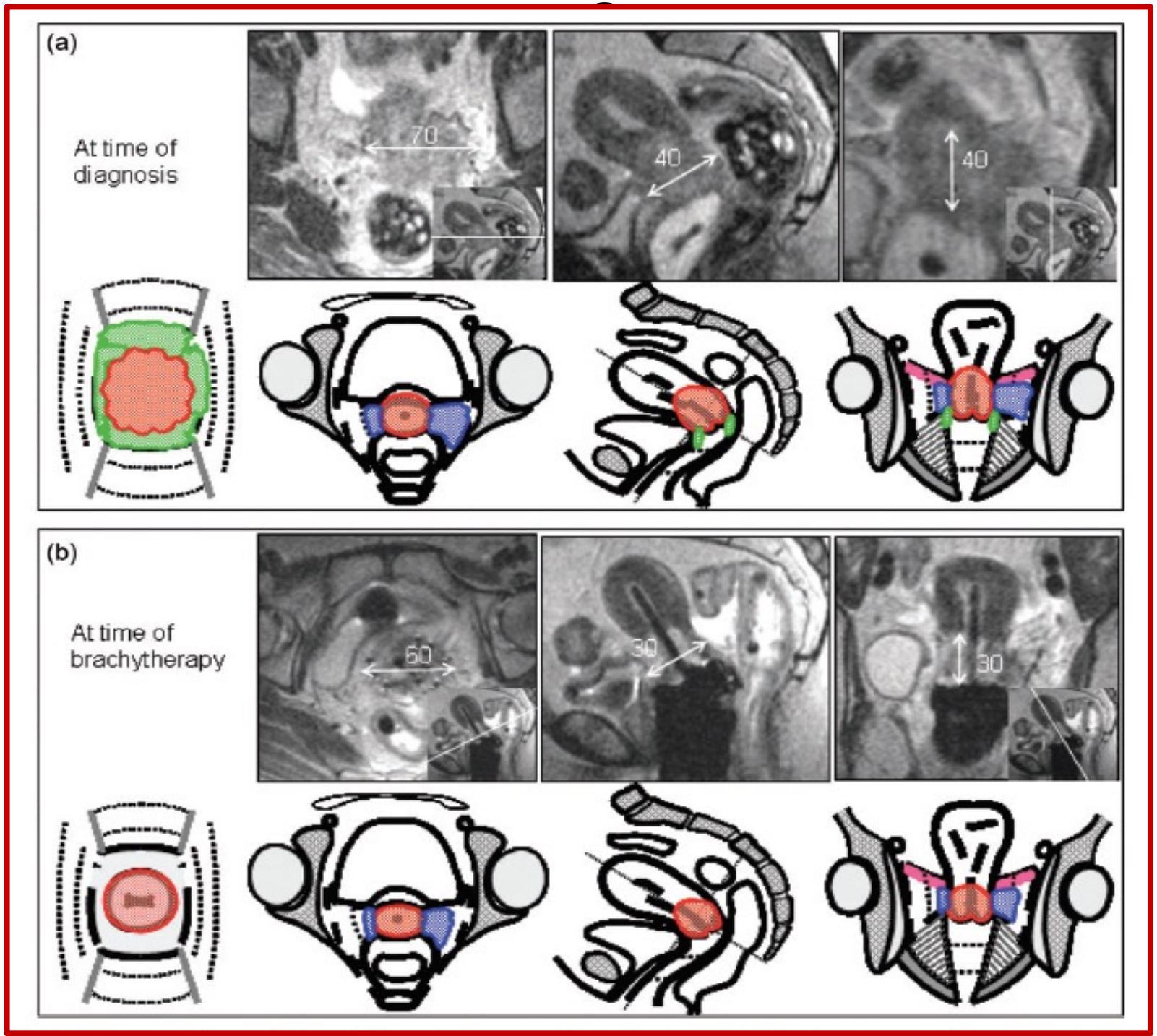
CLINICAL DRAWINGS

Clinical examination

+

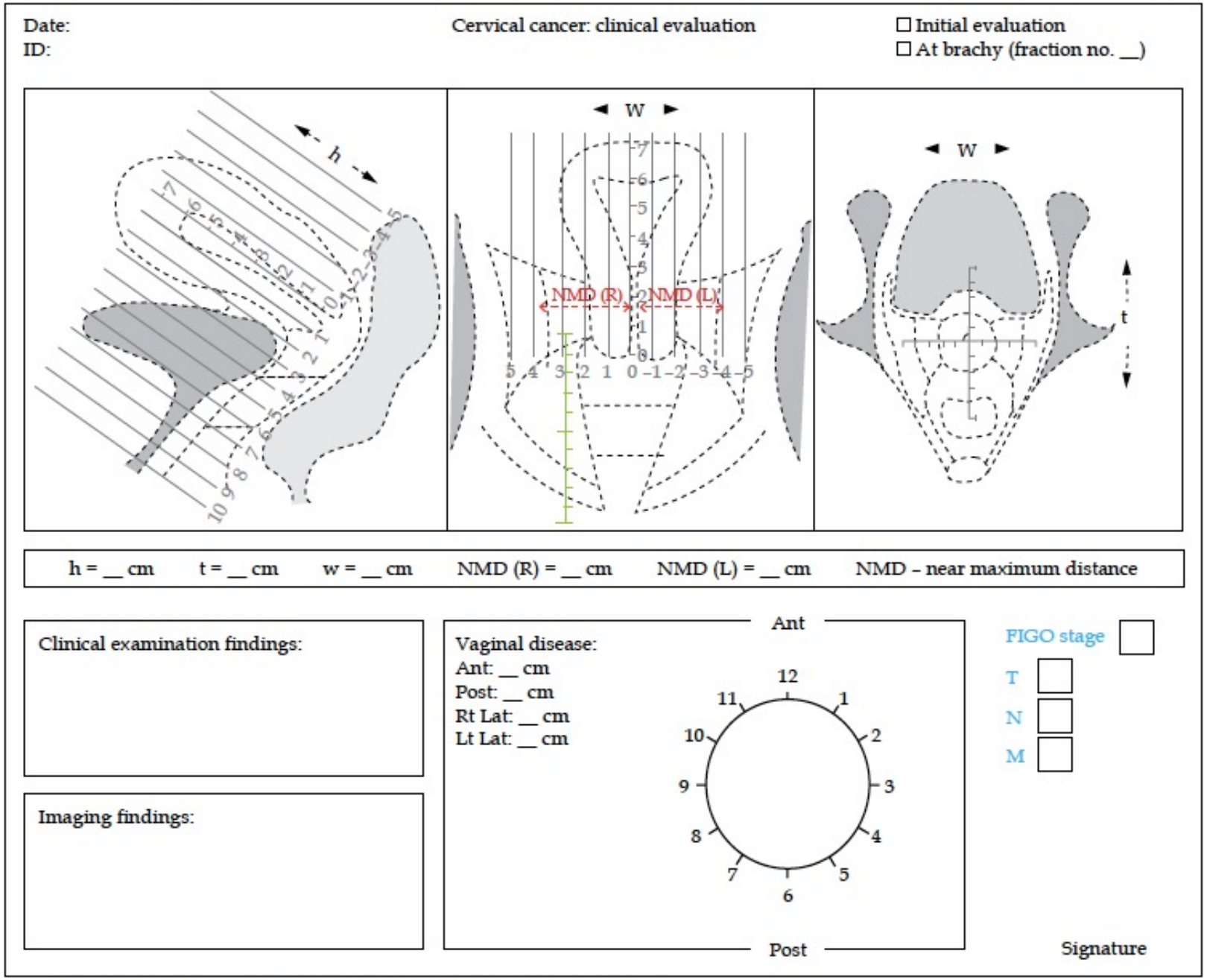
Findings at Imaging

- At Diagnosis
- Response assessment
- Prior to brachytherapy



Advanced Clinical Diagram

- NMD
- Better depiction of vaginal extension
- Staging- Clinical & Imaging



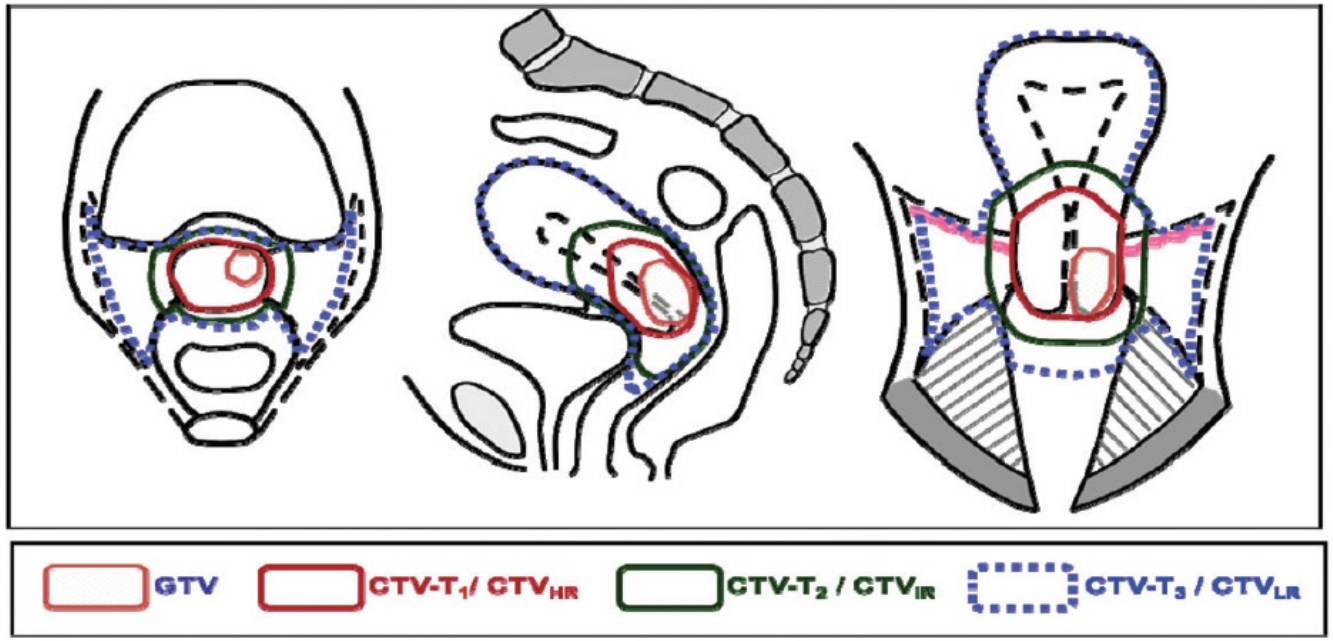
Umesh Mahantshetty, 2019

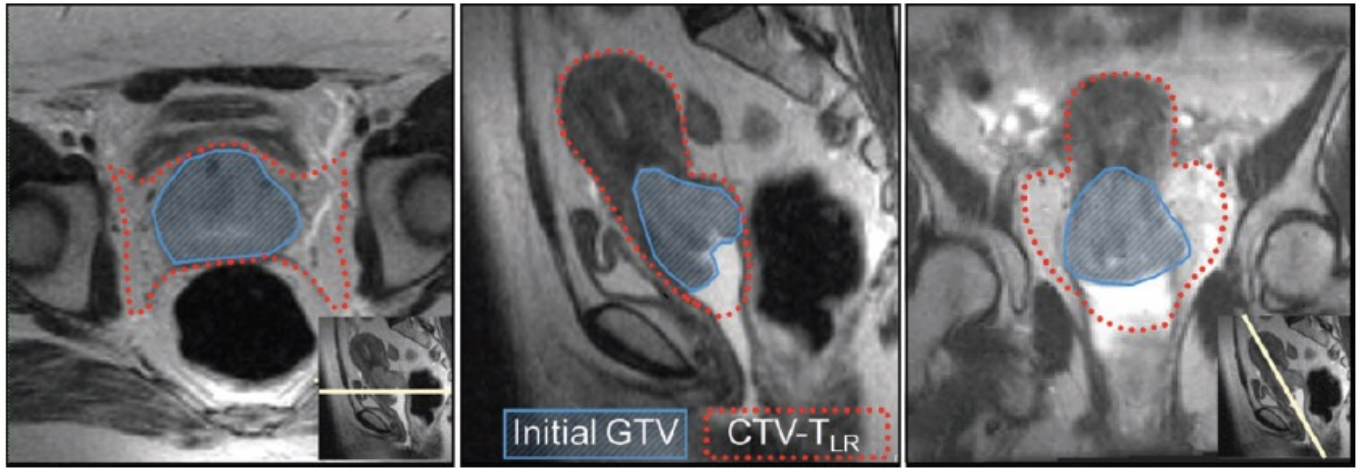
Target Concepts- Ext RT

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})

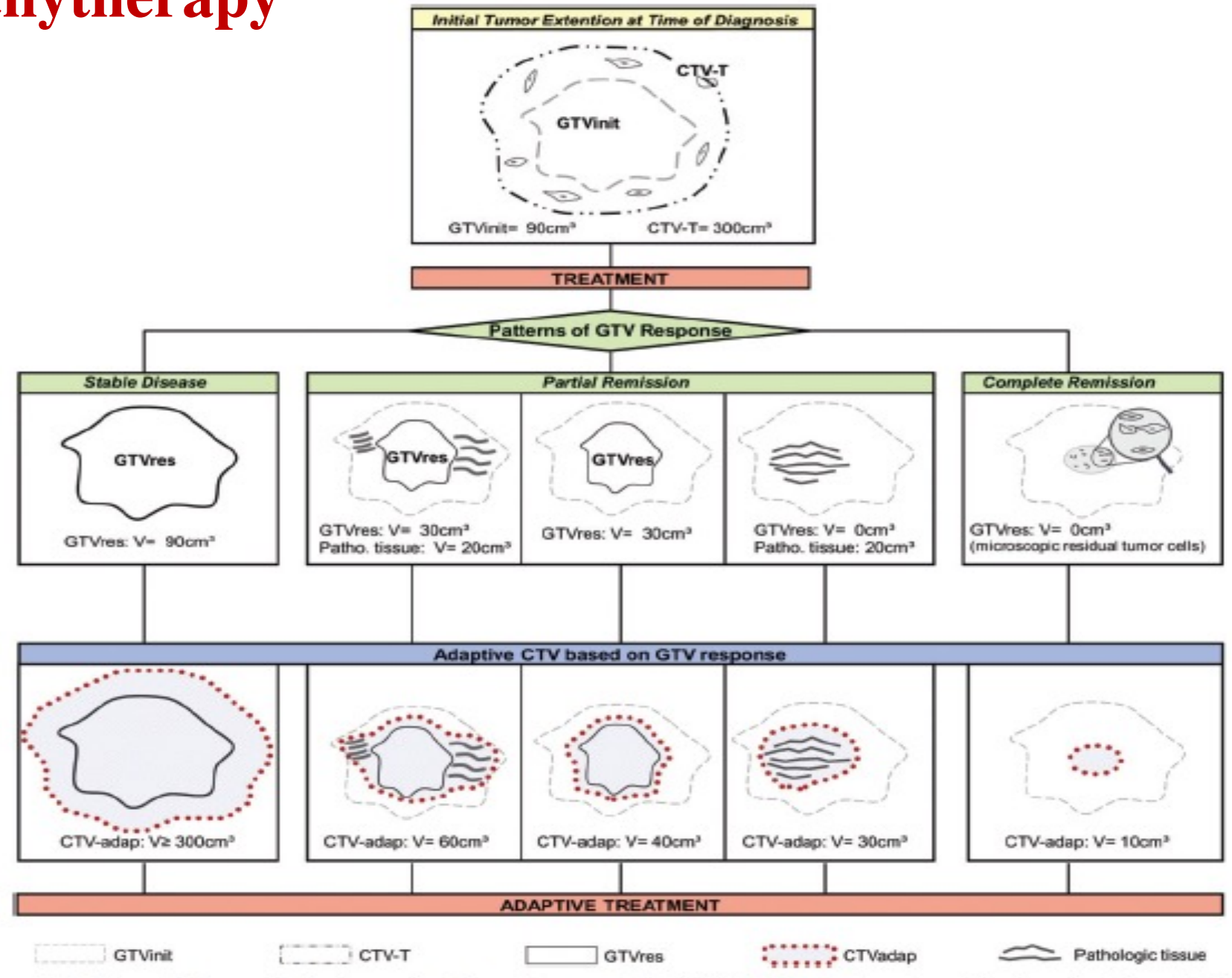




Target Concepts- Brachytherapy

Residual GTV-T ($GTV\text{-}T_{res}$) residual macroscopic tumor at the time of (brachytherapy) boost after treatment assumed sufficient to control microscopic disease.

Adaptive CTV- ($CTV\text{-}T_{adapt}$) $GTV\text{-}T_{res}$ 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:

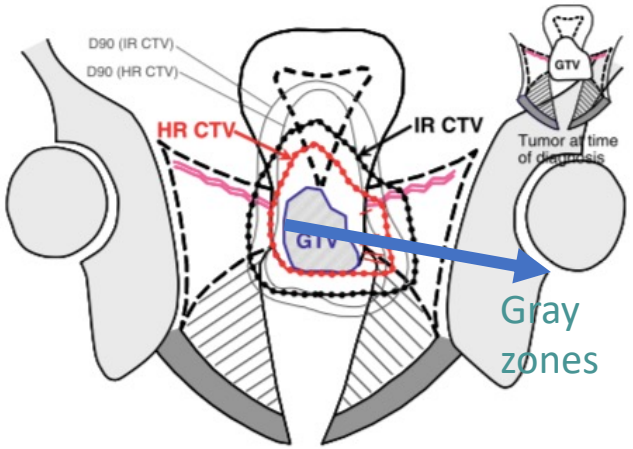
-residual palpable mass;

-residual visible mucosal change;

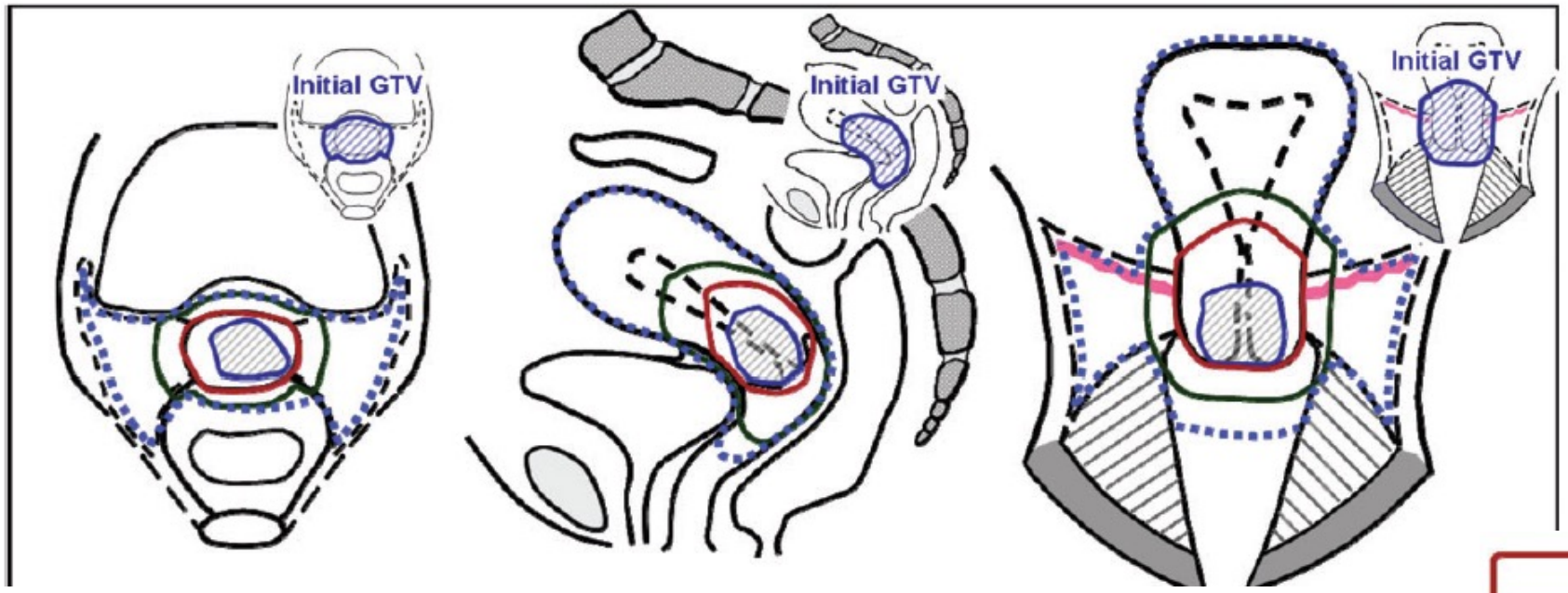
-pathologic induration;

-residual gray zones (MRI);

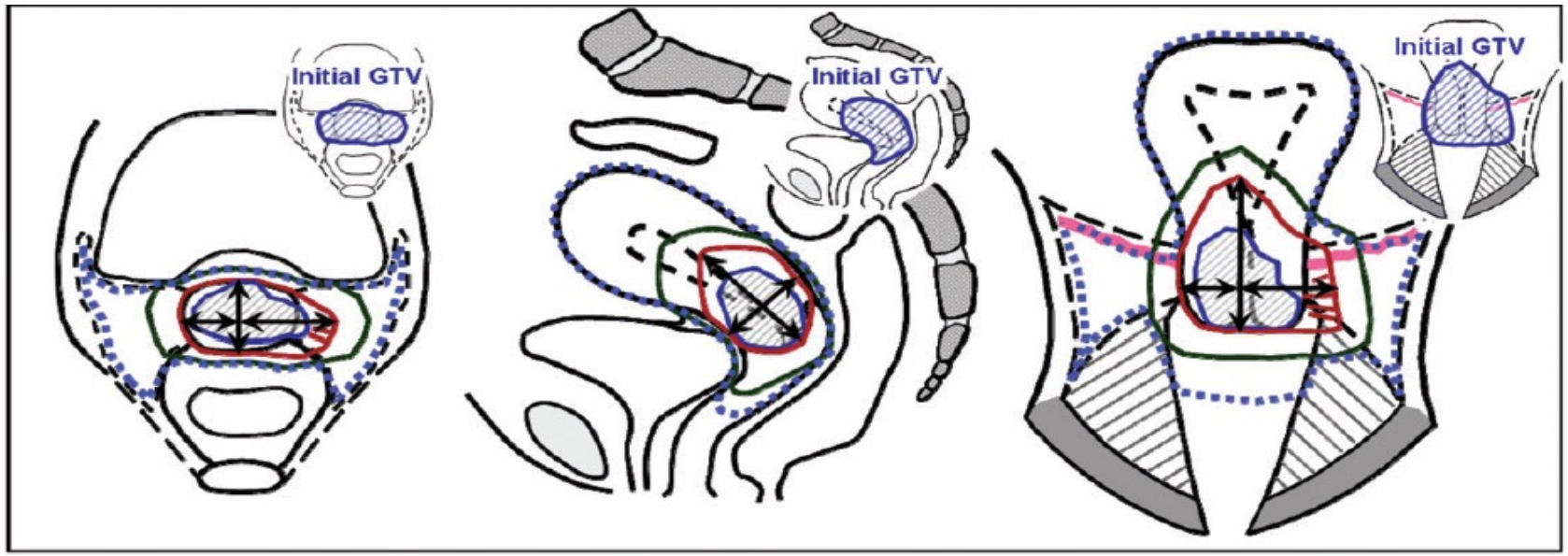
-any other residual pathologic tissue on MRI or clinic exam



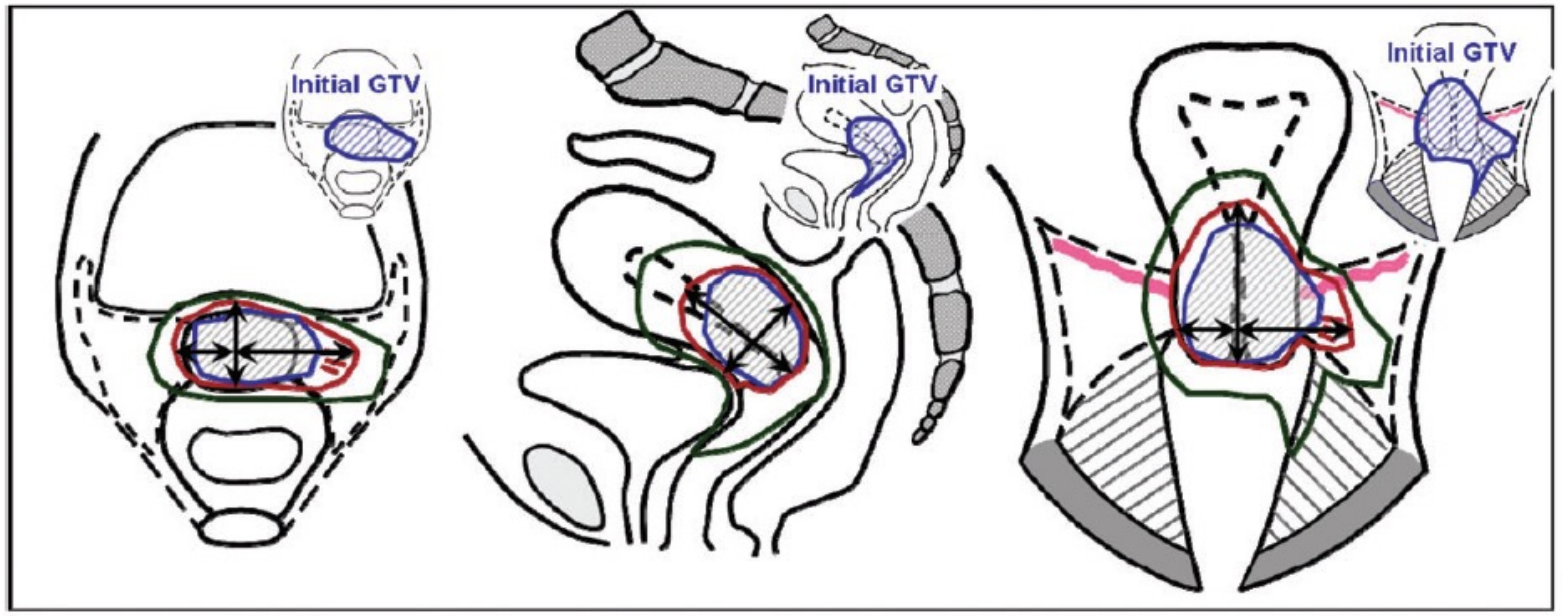
Intermediate-risk CTV-T (CTV-T_{IR}) represents the area of the **GTV_{init}** as superimposed on the topography at the time of brachytherapy and a margin surrounding the anatomical cervix borders (CTV-T_{HR}) in areas without an initial GTV. *The CTV-T_{IR} therefore always includes the CTV-T_{HR} and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



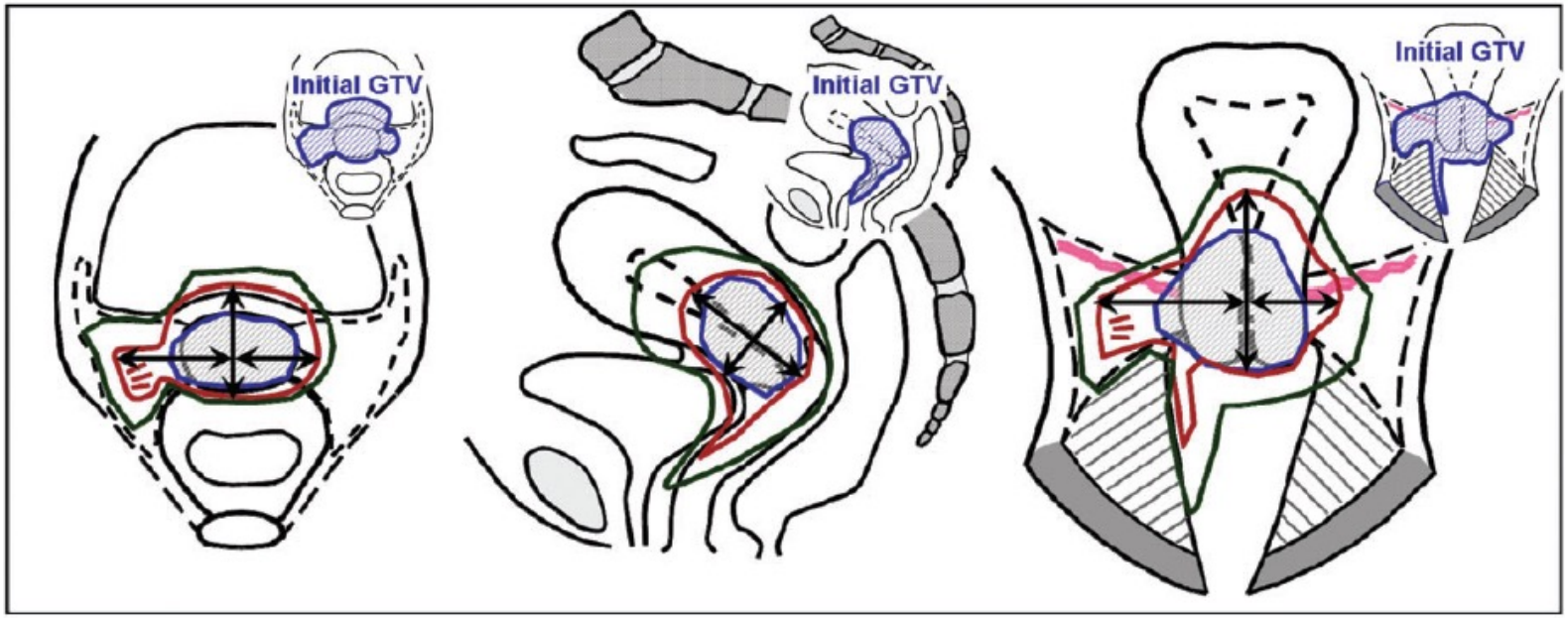
Stage IB2 (bulky disease), good response after chemo-radiotherapy



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_{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 safetymargin 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:

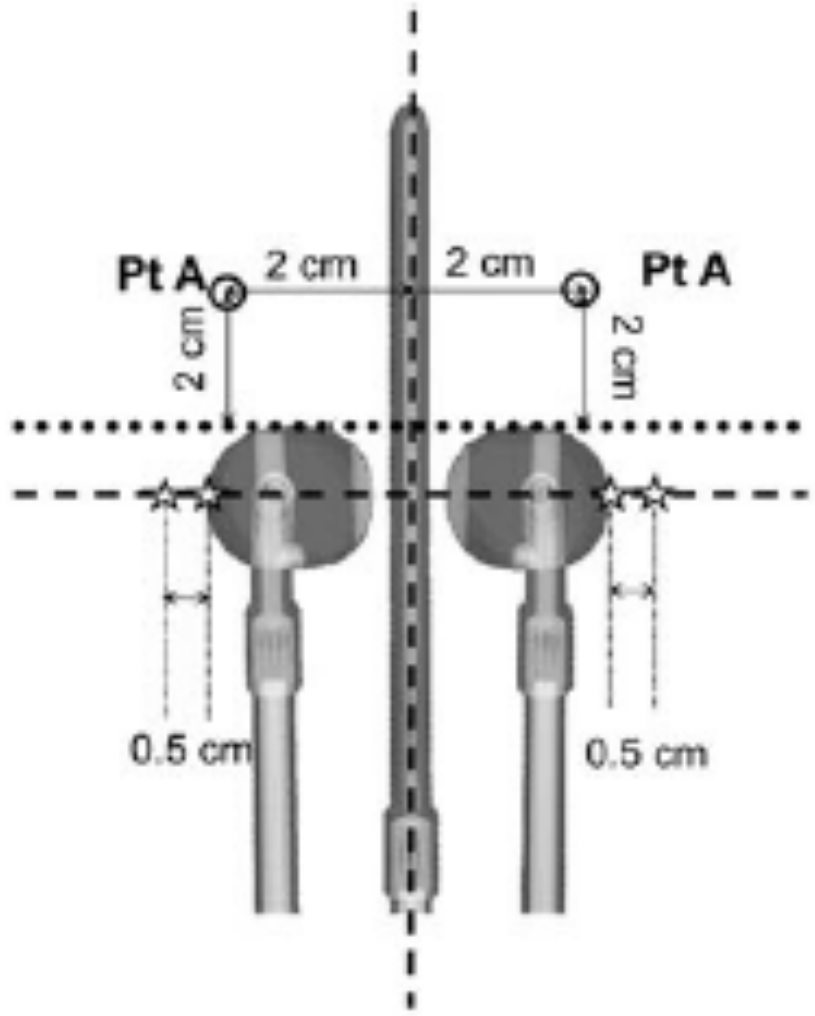
- Absorbed-dose rate/dose per frac.
- Number of fractions
- Time between fractions
- Overall treatment time
- Total EQD2 dose
- Radionuclide and source model
- Source strength
- Dose-calculation algorithm

Dose Reporting

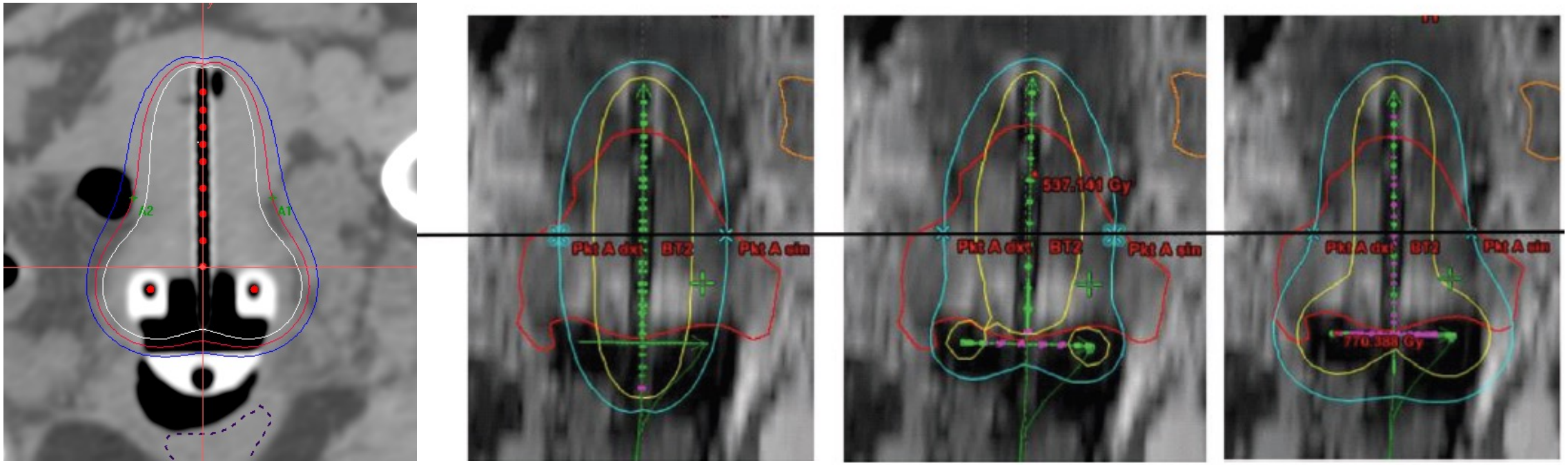
- TRAK

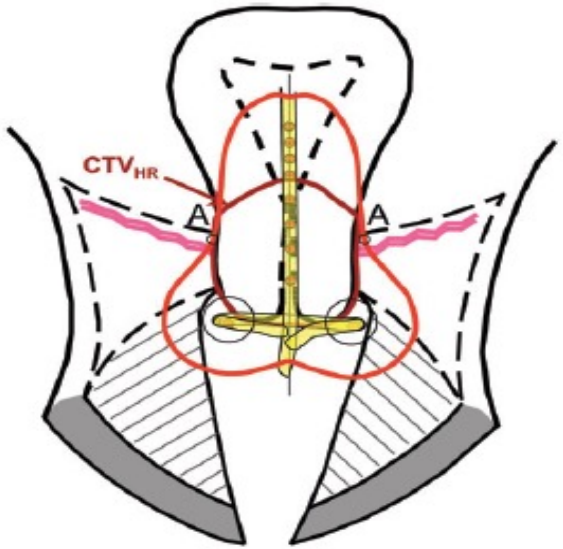
- Adoption of Point A as a major reference point with a definition related to the applicator for absorbed-dose specification:

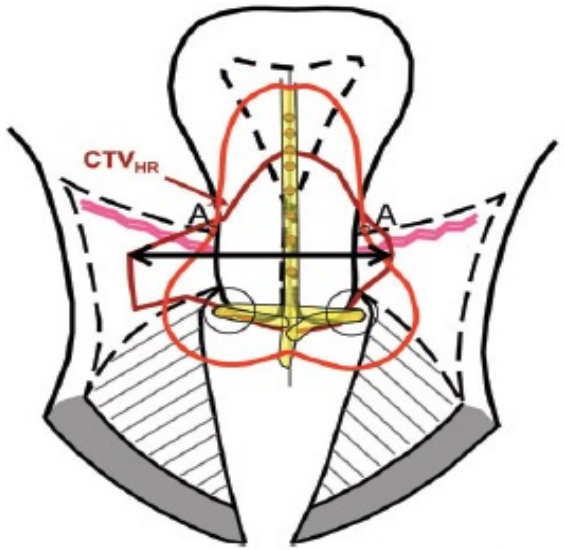
  - **Optional**- for the planning aim and for prescribing
  - **Mandatory**- for reporting the volumetric image-based approach as well.
  - Represents the most widely used parameter in gynecologic brachytherapy worldwide.



Is it time to move beyond point A based dose prescription?



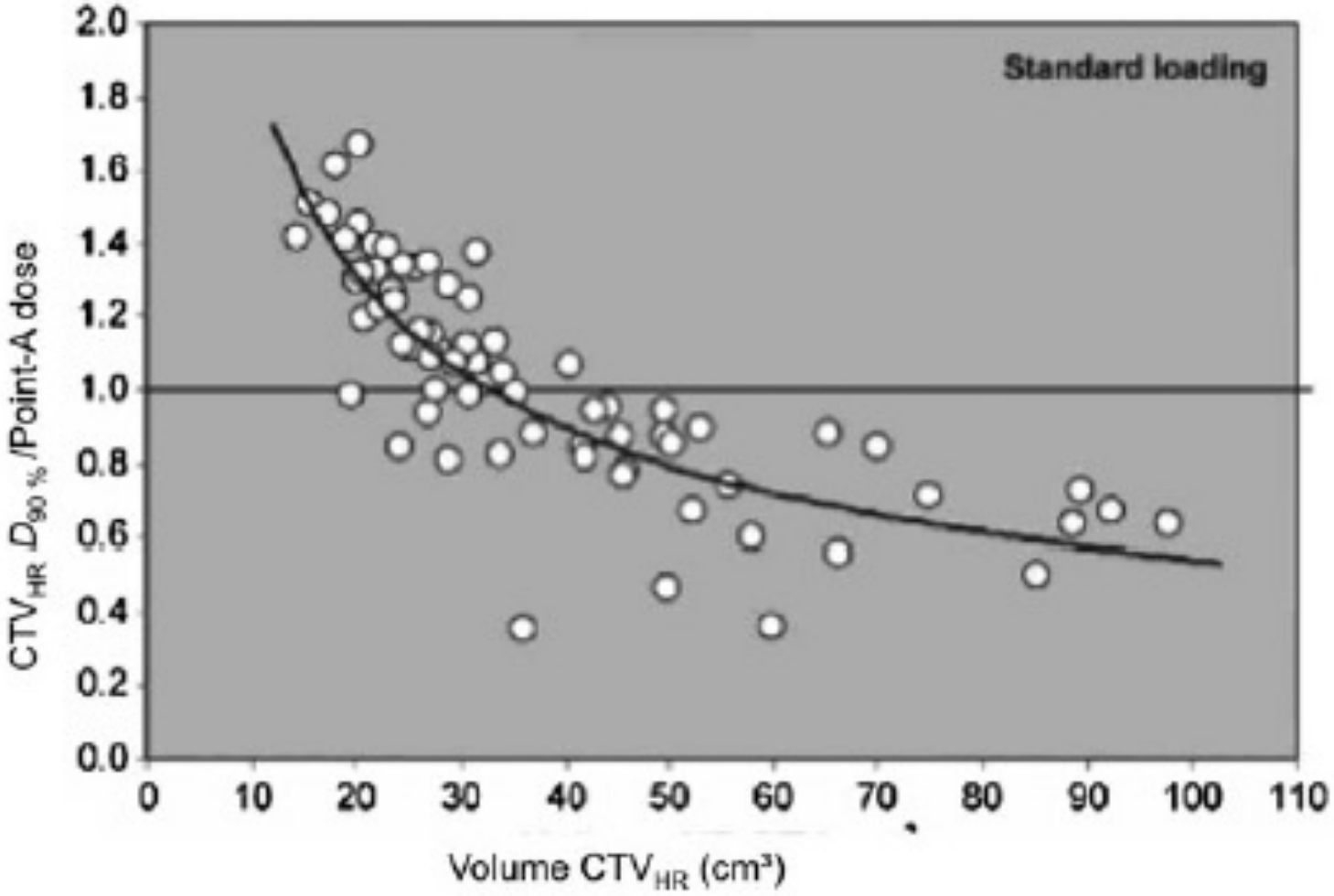




Point A-based standard loading patterns delivering the same absorbed dose to Point A, but using widely different vaginal and tandem loading

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

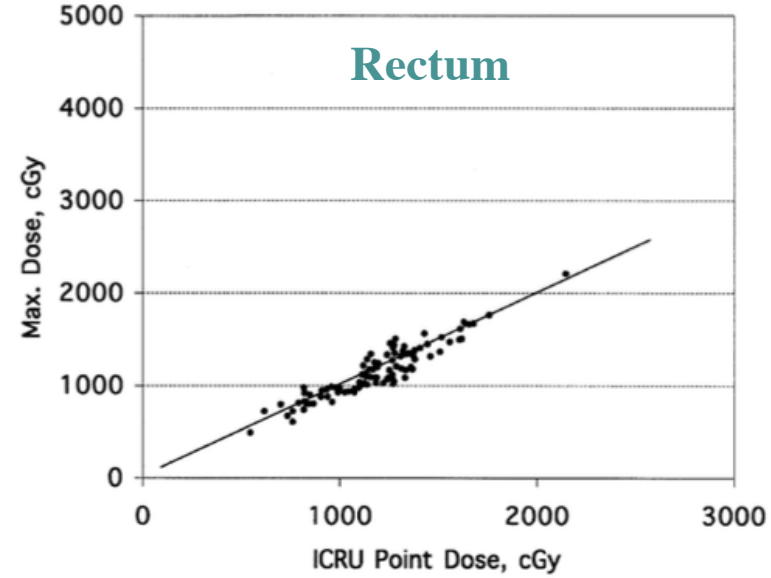
  2D X-Ray based >75Gy

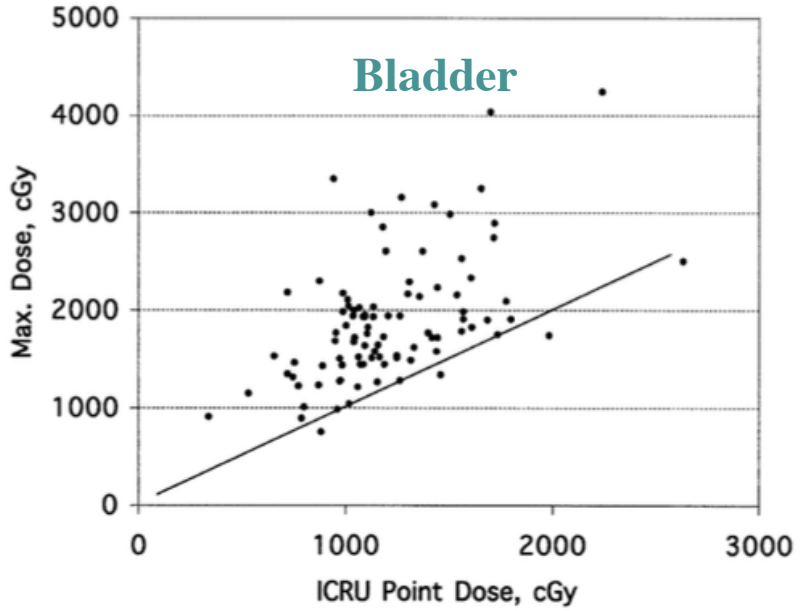
  CT based >70Gy

  MRI Based (EMBRACE) >65Gy

ICRU Bladder and Rectum points

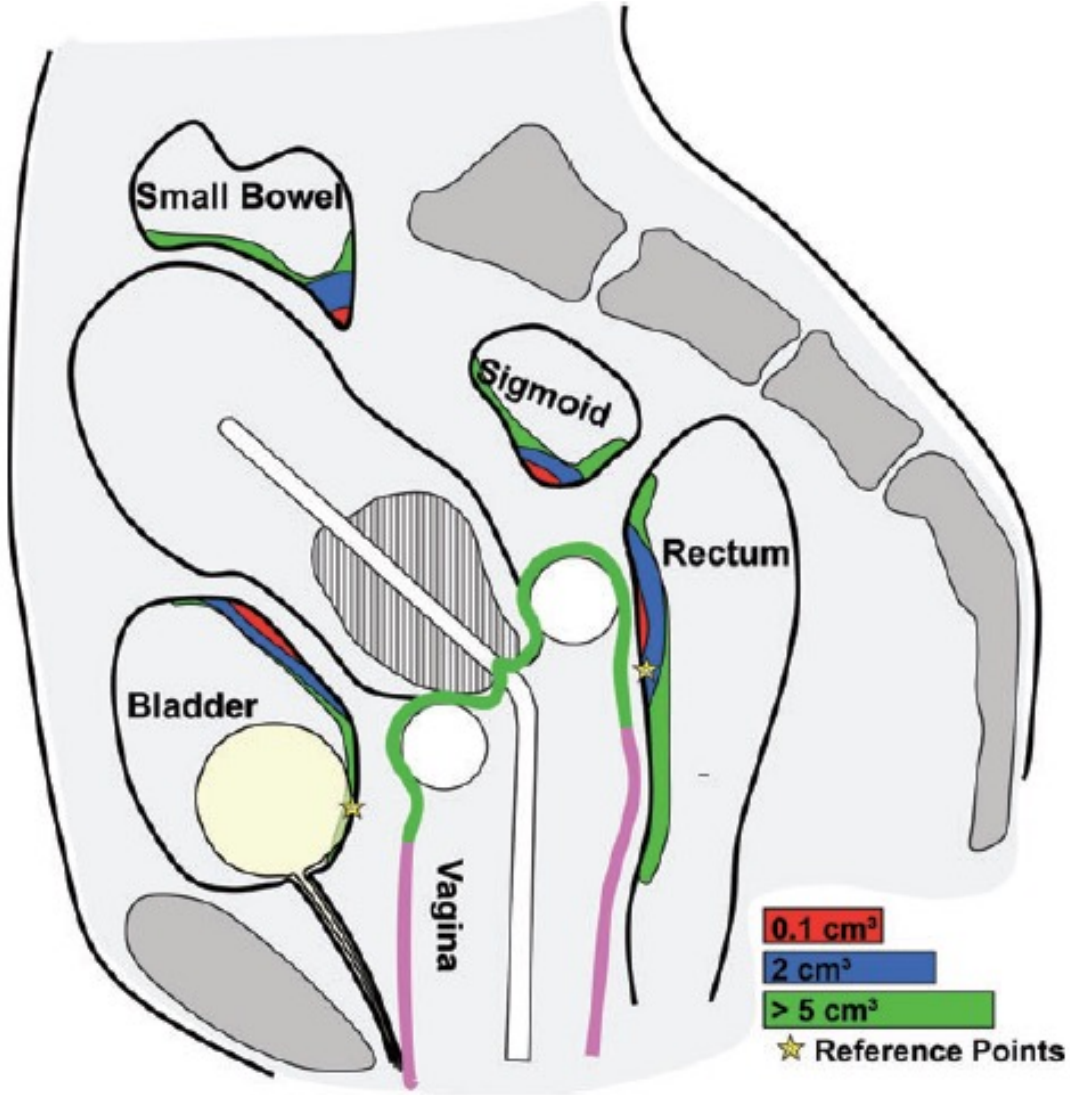
1-5 times underestimation of rectum (mean diff. 0.21 Gy) and bladder doses (mean diff 6.8 Gy) with Orthogonal X-ray ICRU point doses compared to CT based volumetric calculation

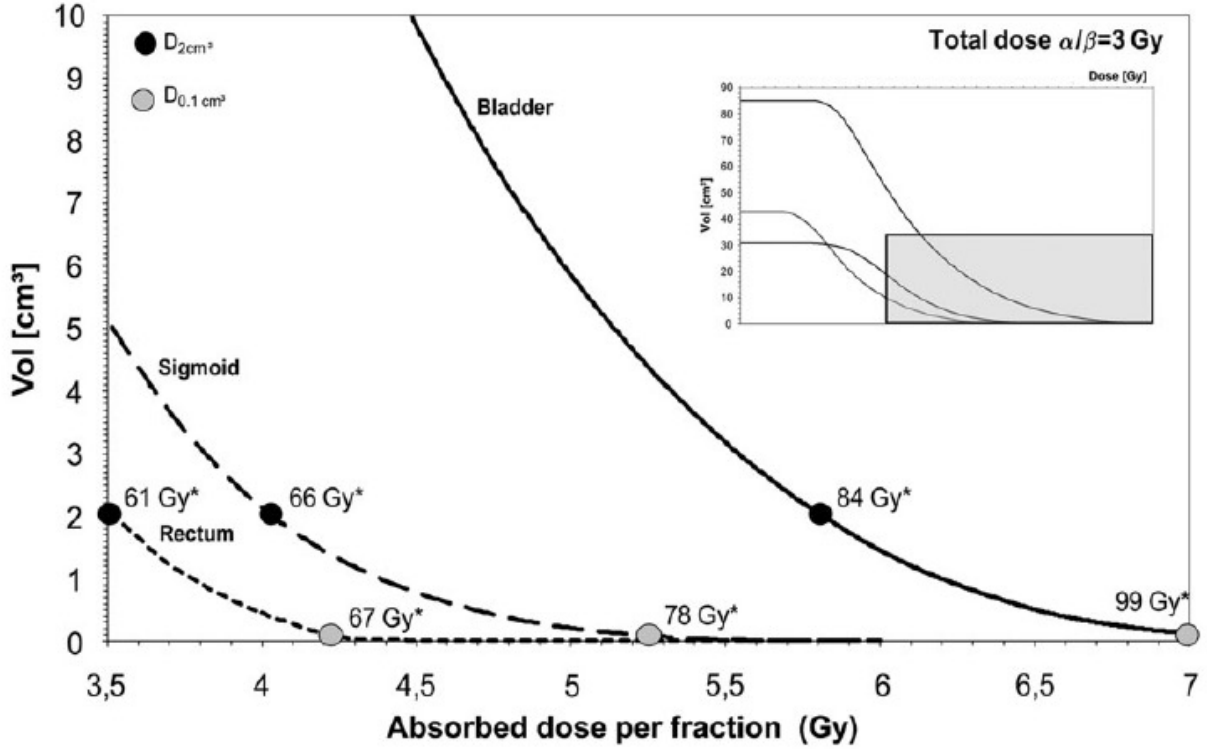




Pelloski, et al. IJROBP 2005;62:131

Dose reporting OAR: 3-D based DVH parameters





The minimum dose in the most irradiated tissue volume adjacent to the applicator ($0.1,1,2,5cm^3$)is recommended for recording & reporting

GYN GEC ESTRO Rec.(II), 2006

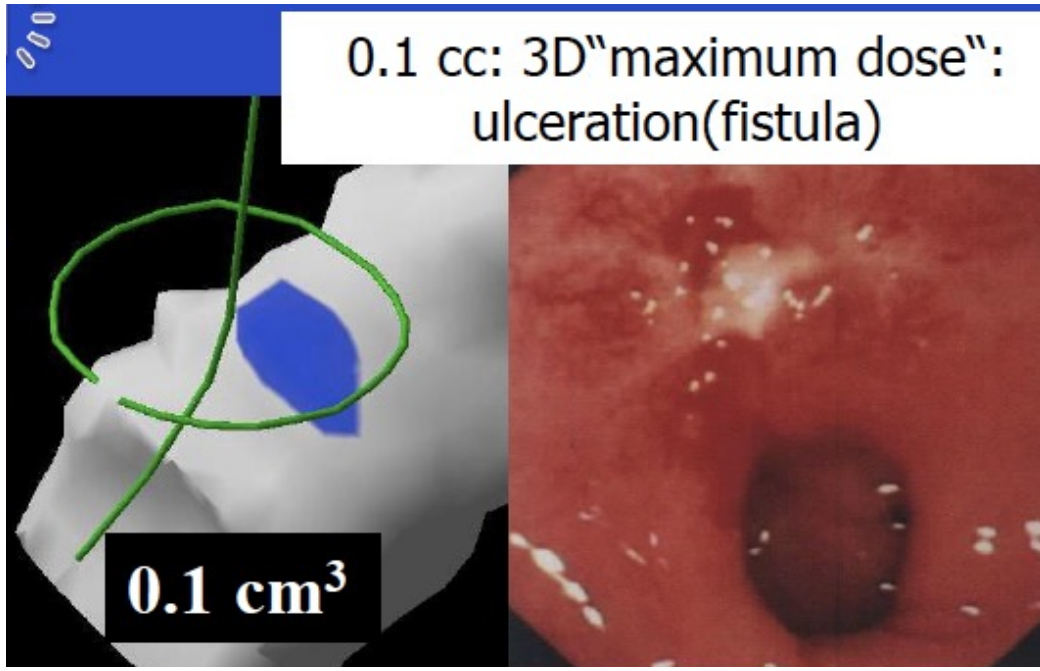
3D based dose volume constraints OAR

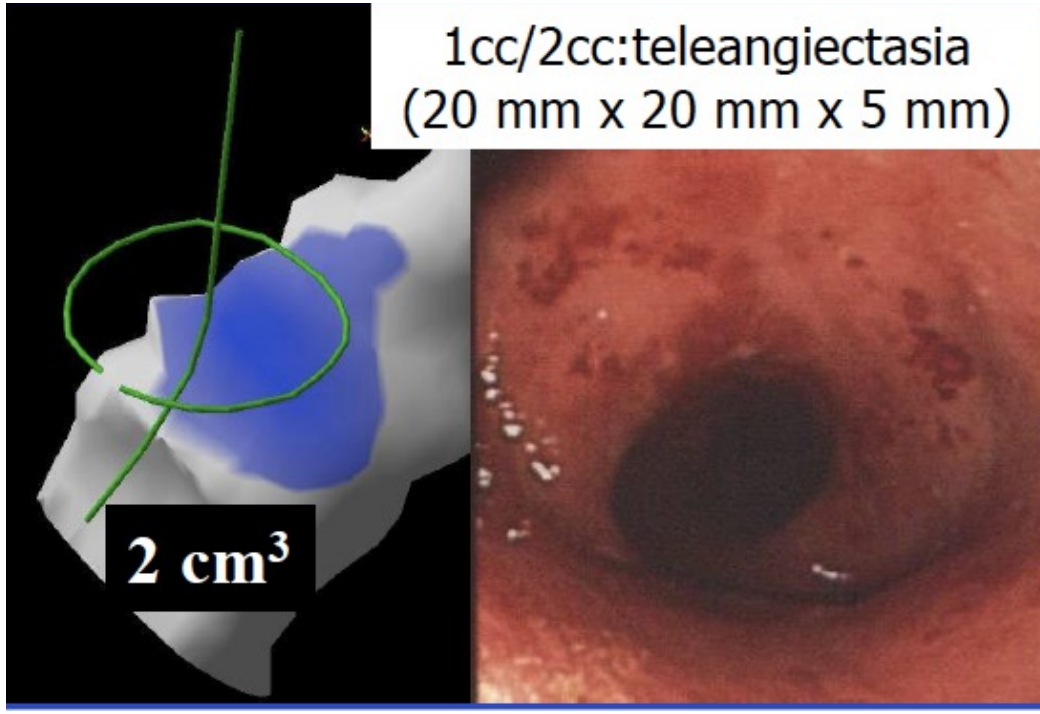
Classic Maximum dose (2D): No clinical relevant point in 3D

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

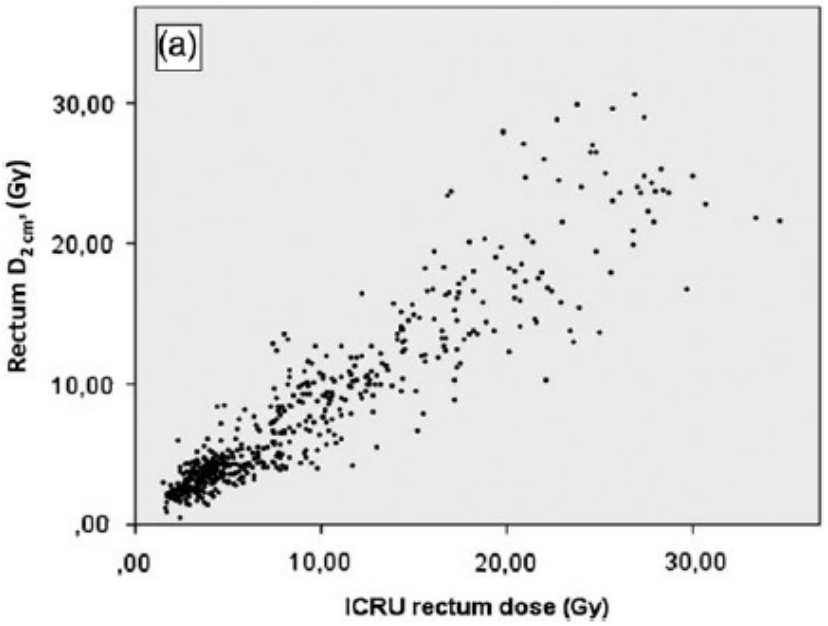
*GYN GEC ESTRO Recommendations (II)
Radioth. Oncol. 2006

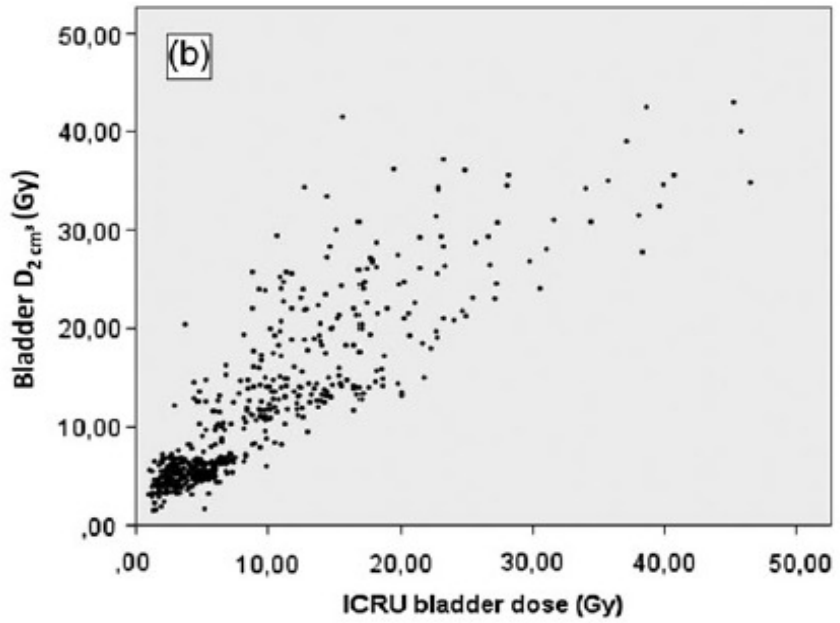




ICRU and Volume based OAR doses

- Significant linear correlation between the ICRU rectal point and D2cc rectal doses
- ICRU point doses not a good predictor of 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 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**

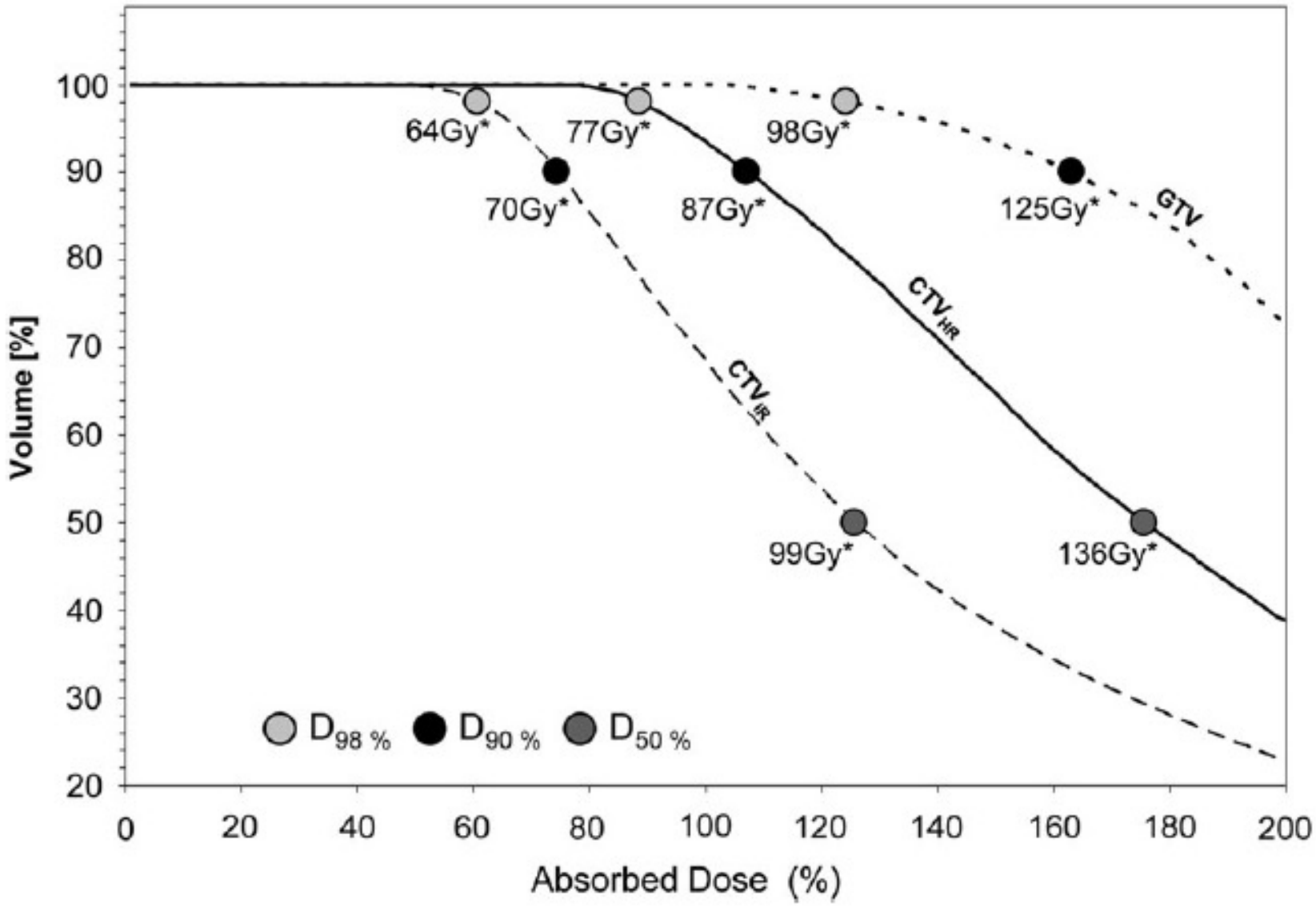
Dose reporting OARs:

- 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, 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

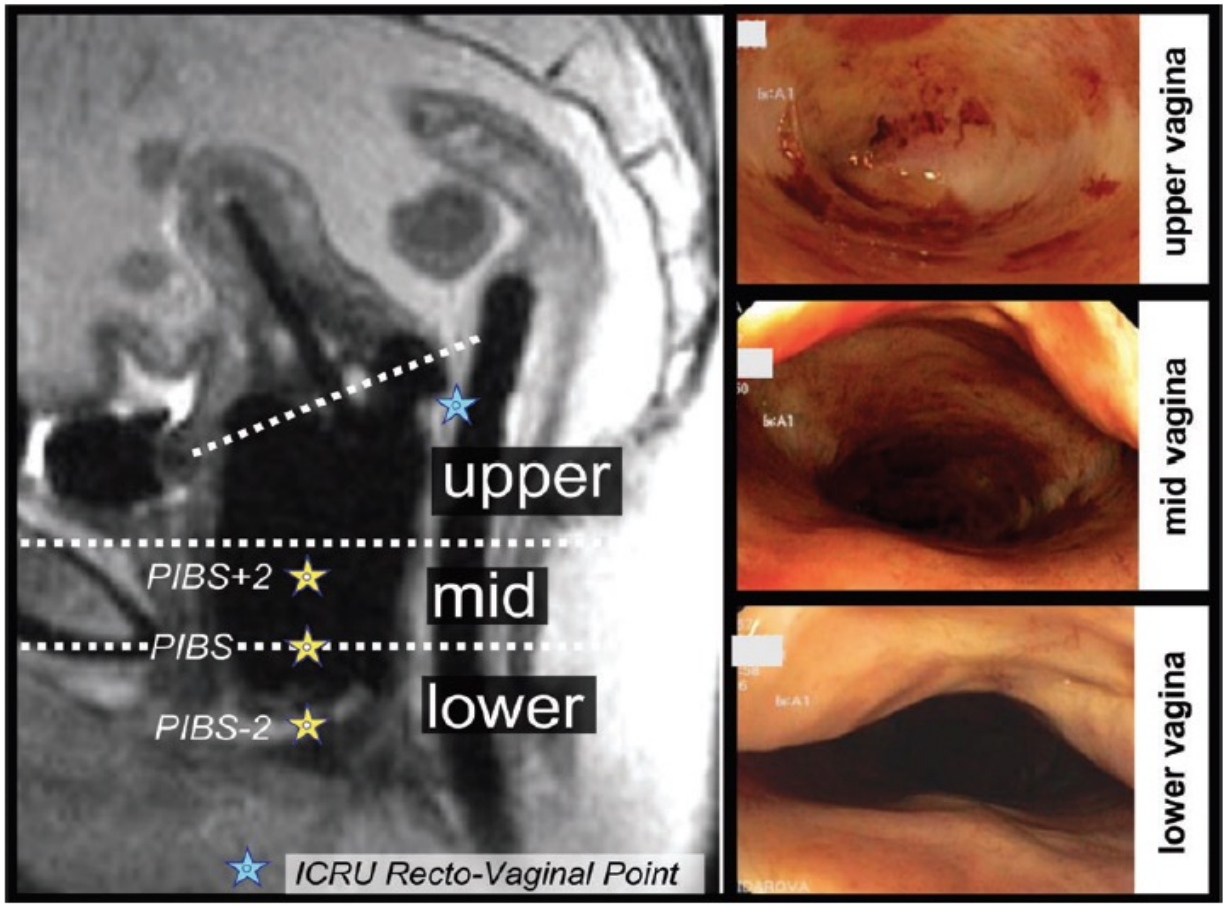
- **D100, D98 & D90** – minimum dose delivered to 100, 98 & 90% of the volume of interest respectively
- **D100** is extremely dependent on target delineation. Due to steep dose gradients, small spikes in the contour cause large deviations in D100
- **D98** reflects the dose in the outermost periphery 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 ≥ 100% of PD
- **V150/200** – Volume receiving 150%/200%of PD- relevant within a specific dose rate and fractionation schedule

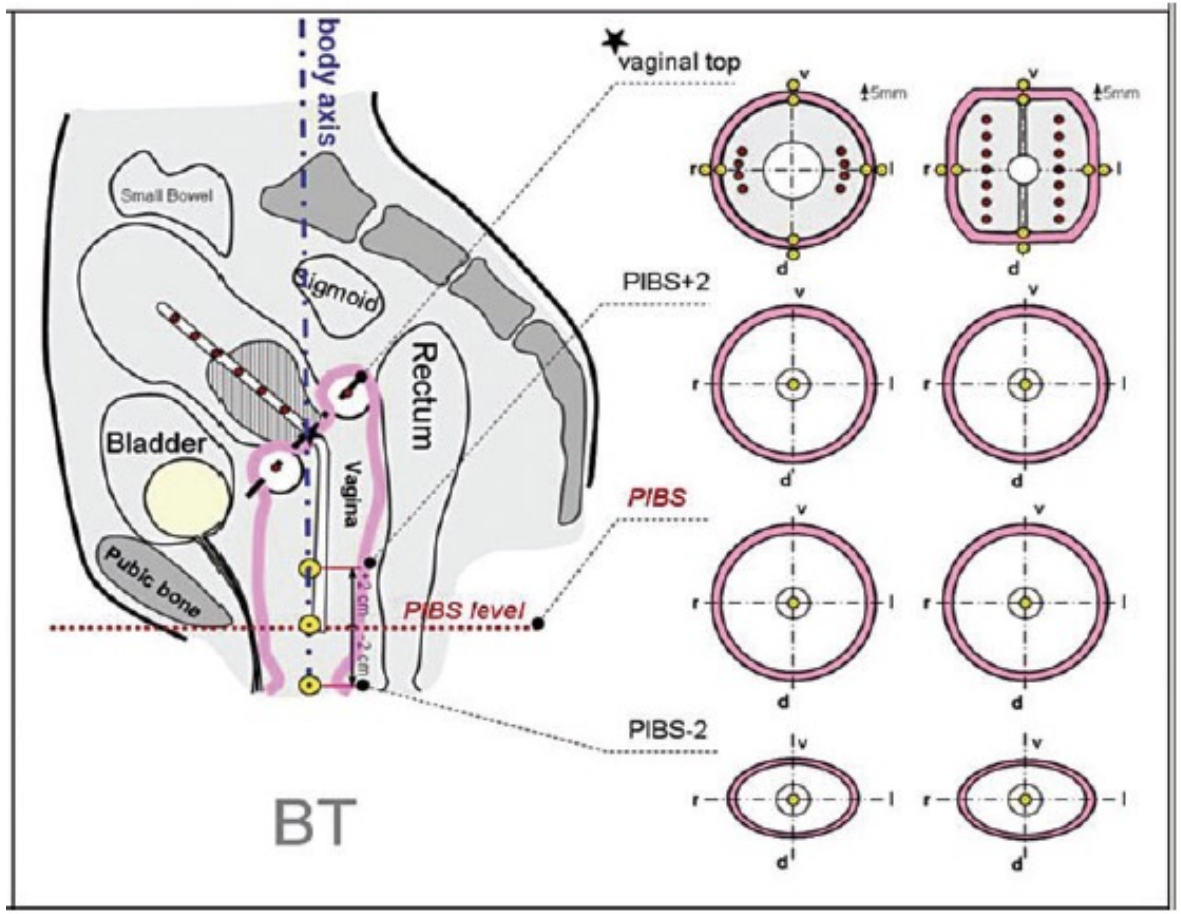


DVHs for the GTV and the CTV in intracavitary brachytherapy have a plateau, which indicates 100% dose coverage of the volume of interest. This plateau goes down smoothly indicating decreasing percentage of dose coverage with increasing dose

Vaginal Reference Points



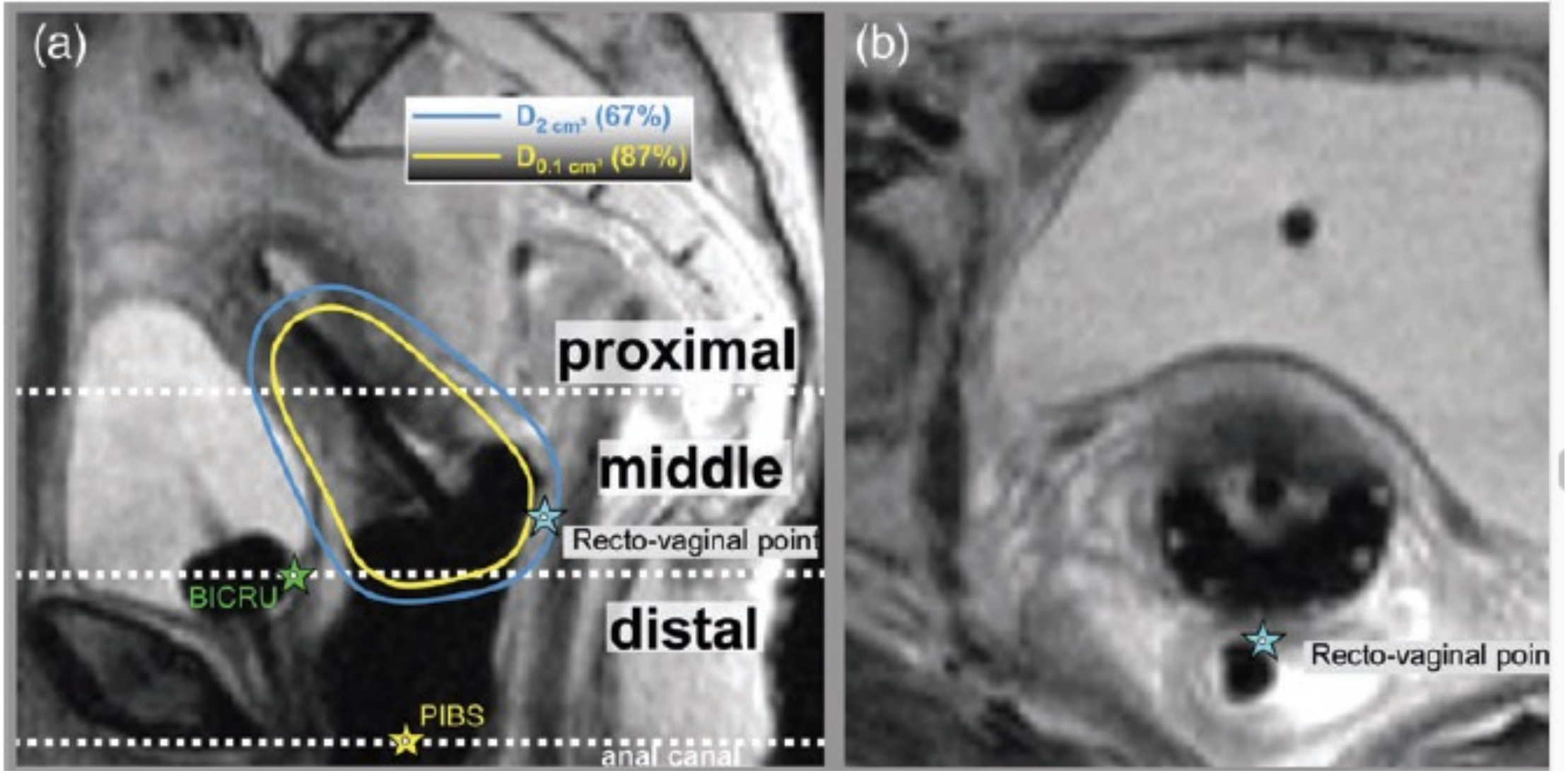
PIBS vaginal-dose point –mid & lower



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

[*Westerveld et al. 2013*]

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≥2 20%; >75Gy) ***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 ≥77 Gy to $D_{0.1cm^3}$ correlates with development of late grade ≥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