Brachytherapy updates and the future

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Disclosures and Acknowledgements

- *Teaching Faculty for the ESTRO GYN TCs (since 2016).*
- *Certified International trainer for Gyn Brachy by Eckert and Ziegler Bebig GmBH.*
- *Co-author : IBS Guidelines for Cervical Cancer and Member Co-ordination Committee of AROI for AROI ESTRO Gyn TCs.*
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Roadmap

Learning objectives

- Brachytherapy basics.
- Brachytherapy for non gynaecological sites.
- Gynaecological brachytherapy.

Brachytherapy – *basics*

Brachytherapy – early days

- Brachy (*βραχύς* (brakhús) means “short” in Greek.
- The term was first used in 1901 by Henri-Alexandre Danlos and Eugène Bloch, who received a radioactive sample from Marie Sklodowska Curie and her husband, Pierre. Danlos and Bloch were attempting to treat lupus and used it first to treat tuberculosis.

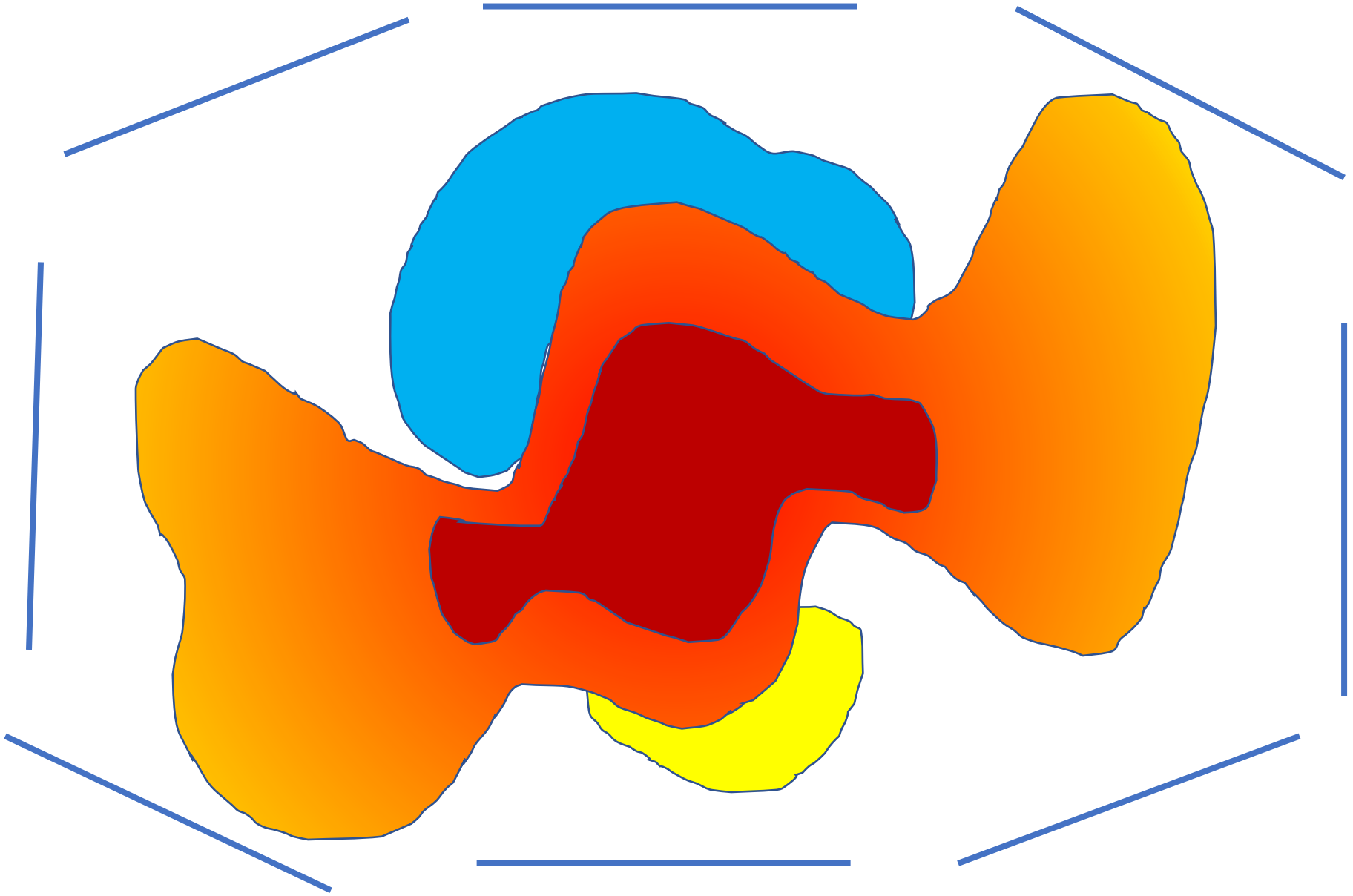
https://en.wikipedia.org/wiki/Henri-Alexandre_Danlos

Brachytherapy – early days

- On September 15, 1903, Margaret Abigail Cleaves used Radium brachytherapy for the treatment of cervical cancer.
- In 1905, Robert Abbe from St. Luke Memorial Hospital, New York, performed the first radium implant following the excision of tumor in 1905.
- Urologist Octave Pasteau and radium therapist Paul-Marie Degrais also began treating prostate cancer with intracavitary radium in 1909.

https://en.wikipedia.org/wiki/Margaret_Cleaves
https://en.wikipedia.org/wiki/Robert_Abbe

EBRT vs BT



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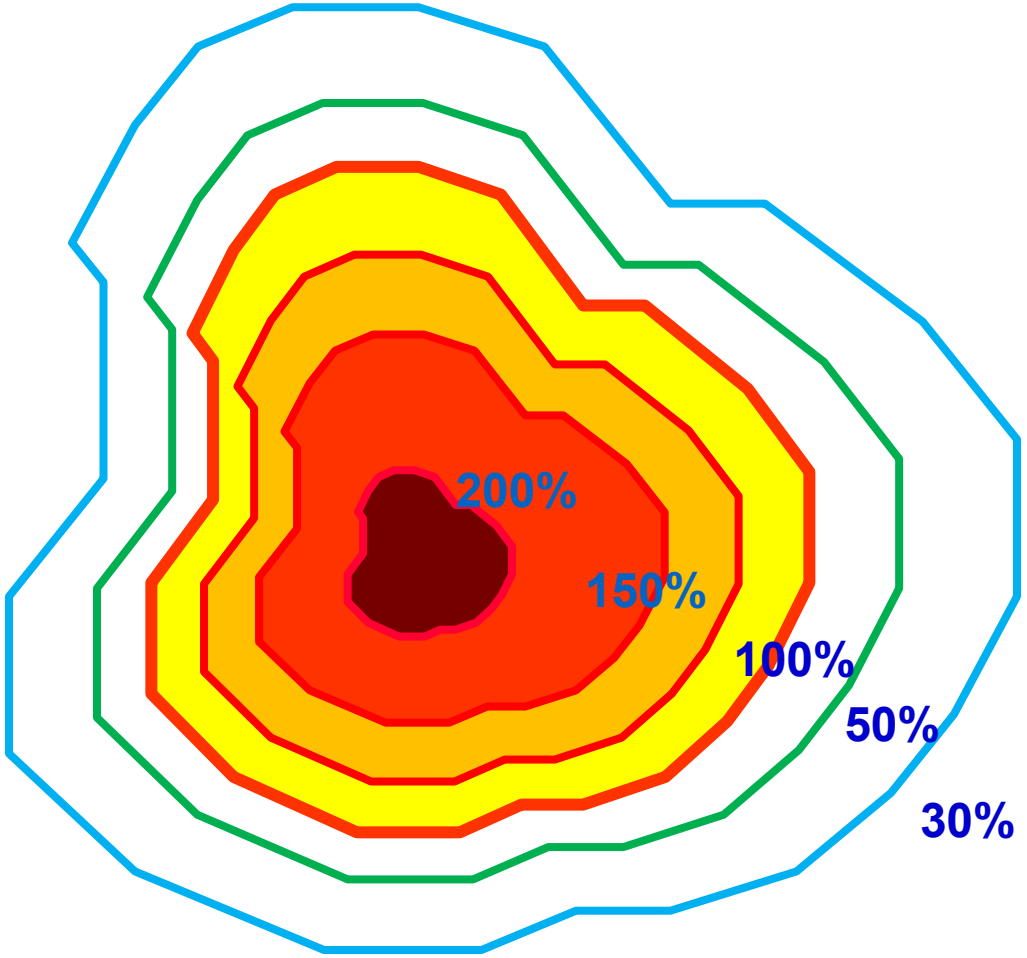
Advantages of BT : Dosimetric

- Conforms best to irregular tumor volumes.
- Avoids geographical miss - moves with the tumor.
- Rapid dose fall off – Inverse Square Law.



Adapted from Nag, S.

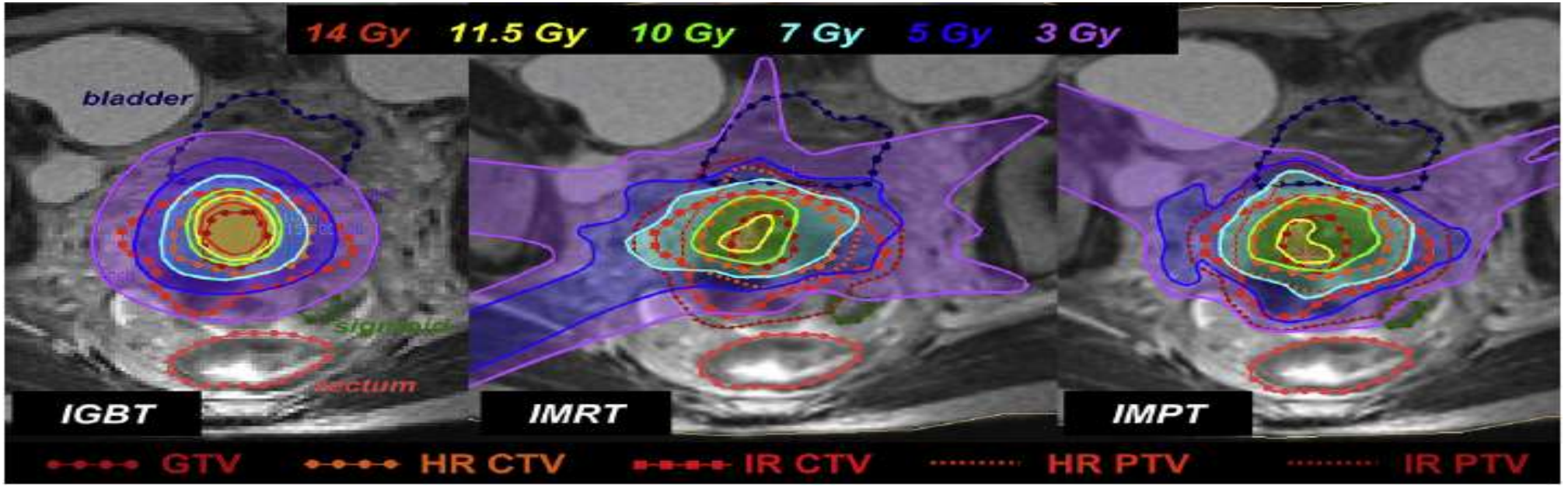
Advantages of BT : Radiobiologic

- Moderate to extremely hypofractionated RT.
- Center of tumor (hypoxic / radio-resistant area) actually receives much higher biological dose.
- Significantly shortens overall treatment time – mitigating accelerated population.
- *HDR is better than LDR.*

To determine the total physical dose, when both EBRT and HDR BT are administered, it is imperative that we convert HDR and EBRT doses to EQD2 (equivalent dose in 2 Gy per fraction) and summate.

IMAGE-GUIDED RADIOTHERAPY FOR CERVIX CANCER: HIGH-TECH EXTERNAL BEAM THERAPY VERSUS HIGH-TECH BRACHYTHERAPY

DIETMAR GEORG, PH.D., CHRISTIAN KIRISITS, PH.D., MARTIN HILLBRAND, M.SC., JOHANNES DIMOPOULOS, M.D., AND RICHARD PÖTTER, M.D., PH.D.



Conclusions

For image-guided cervix cancer treatments, both IMRT and IMPT seem to be inferior to BT.

Brachytherapy – types

By dose rate

- HDR – >12 Gy/hr
- MDR – 2 – 12 Gy/hr
- LDR – 0.4 – 2 Gy/hr
- VLDR – 0.01 – 0.3 Gy/hr
- PDR – > 12 Gy/hr in multiple pulses

By source placement

- Intracavitary
- Interstitial
- Intraluminal
- Plesiotherapy
  - Surface mould
  - Contact
- Using electrons

By loading / control

- Manual loading
  - Preloading
  - Afterloading
- Remote loading
  - Afterloading

Brachytherapy – sources

Element	Isotope	Energy (MeV)	Half-Life	HVL-Lead (mm)	Exposure Rate Constant[a] Γ_δ	Source Form	Clinical Application
Obsolete Sealed Sources of Historical Significance							
Radium	^{226}Ra	0.83 (average)	1,626 years	16	8.25[b] 7.71[c]	Tubes and needles	LDR intracavitary and interstitial
Radon	^{222}Rn	0.83 (average)	3.83 days	16	8.25[b]	Gas encapsulated in gold tubing	Permanent interstitial Temporary molds
Currently Used Sealed Sources							
Cesium	^{137}Cs	0.662	30 years	6.5	3.26	Tubes and needles	LDR intracavitary and interstitial
Cesium	^{131}Cs	0.030	9.69 days	0.030	0.64	Seeds	LDR permanent implants
Iridium	^{192}Ir	0.397 (average)	73.8 days	6	4.69	Seeds in nylon ribbon; metal wires Encapsulated source on cable	LDR temporary interstitial Intravascular brachytherapy; cardiac HDR interstitial and intracavitary Intravascular brachytherapy: peripheral
Cobalt	^{60}Co	1.25	5.26 years	11	13.07	Encapsulated spheres	HDR intracavitary
Iodine	^{125}I	0.028	59.6 days	0.025	1.45	Seeds	Permanent interstitial
Palladium	^{103}Pd	0.020	17 days	0.013	1.48	Seeds	Permanent interstitial
Gold	^{198}Au	0.412	2.7 days	6	2.35	Seeds	Permanent interstitial
Strontium/Yttrium	^{90}Sr–^{90}Y	2.24 β_{max}	28.9 years	–	–	Plaque Seeds	Treatment of superficial ocular lesions Intravascular brachytherapy
Developmental Sealed Sources							
Americium	^{241}Am	0.060	432 years	0.12	0.12	Tubes	LDR intracavitary
Ytterbium	^{169}Yb	0.093	32 days	0.48	1.80	Seeds	HDR interstitial
Californium	^{252}Cf	2.4 (average) neutron	2.65 years	–	–	Tubes	High-LET LDR intracavitary
Samarium	^{145}Sm	0.043	340 days	0.060	0.885	Seeds	LDR temporary interstitial

HVL, half-value layer; LDR, low dose rate; HDR, high dose rate; LET, linear energy transfer.

[a]No filtration in units of $R \cdot cm^2 \cdot mCi^{-1} \cdot h^{-1}$.

[b]0.5 mm platinum filtration; units of $R \cdot cm^2 \cdot mg^{-1} \cdot h^{-1}$.

[c]1.0 mm platinum filtration; units of $R \cdot cm^2 \cdot mg^{-1} \cdot h^{-1}$.

Brachytherapy evolution

The “systems”

Gosta Forssell
Stockholm System

Claude Regaud
Paris System

Margaret Todd
W.J. Meredith
Manchester
System

Intracavitary systems

Edith Quimby
Quimby System

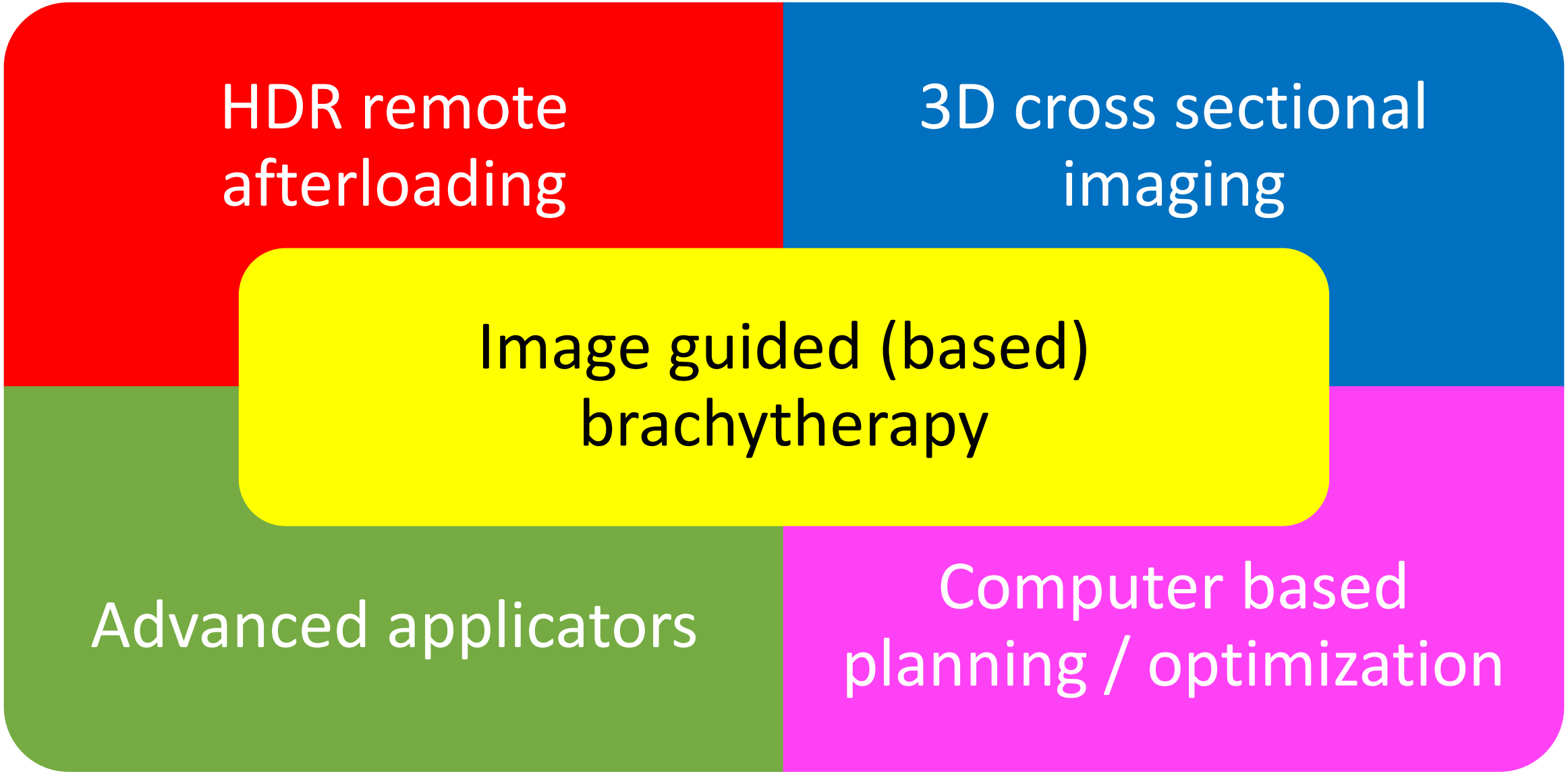
R. Paterson &
H.M. Parker
Manchester
System

B .Pierquin &
A. Dutreix
Paris System

Interstitial systems

Adapted from Joarder, R.

Modern Brachytherapy



Brachytherapy in different cancers

Summary of sites of Brachytherapy

- Brain gliomas (I-125, Ir-192 implants)
- Head and Neck cancers
  - Nasopharynx (Intraluminal, ILRT)
  - Oral / Oropharyngeal / Nodal (ISRT)
- Esophagus (ILRT)
- GI (Intra-op)
- Bronchus (ILRT)
- Breast
  - APBI or Boost (ICRT / ISRT / Electrons)
  - IMN (ILRT)
- Biliary (ILRT)
- Prostate (ISRT)
  - Permanent implant / HDR
  - Radical / Boost
- Anal canal (ISRT)
- Soft tissue sarcomas
  - Intra-op vs Post op
- Non melanoma skin cancer
- Ocular plaque

Head and Neck Cancers

Head and Neck Cancers - Guidelines

Educational Articles

Original paper

Brachytherapy in head and neck malignancies: Indian Brachytherapy Society (IBS) recommendations and guidelines

Rajendra Bhalavat, MD[1], Ashwini Budrukkar, MD, DNB[2], Sarbani Ghosh Laskar, MD[2], Dayanand Sharma, MD[3], Ashutosh Mukherji, MD[4], Manish Chandra, DNB[1], Umesh Mahantshetty, MD[2], Vibhay Pareek, DNB[5], Pratibha Bauskar, M.Pys, RSO[1], Sonali Saraf, MD[6]

Radiotherapy and Oncology 122 (2017) 248–254

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journal homepage: www.thegreenjournal.com

GEC-ESTRO/ACROP recommendations

GEC-ESTRO ACROP recommendations for head & neck brachytherapy in squamous cell carcinomas: 1st update – Improvement by cross sectional imaging based treatment planning and stepping source technology

György Kovács[a,*,1], Rafael Martinez-Monge[b,1], Ashwini Budrukkar[c,1], Jose Luis Guinot[d,1], Bengt Johansson[e,1], Vratislav Strnad[f,1], Janusz Skowronek[g,h,1], Angeles Rovirosa[i,1], Frank-André Siebert[j,1], on behalf of the GEC-ESTRO Head & Neck Working Group

Patients' selection, pre-treatment workup, and patients' care

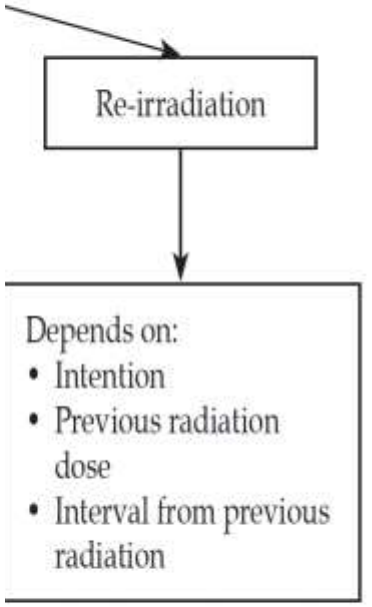
Selection of patients for brachytherapy

Table 1. Indications techniques

Technique	
Interstitial	O
	–
	–
	–
	–
	O
	–
	–
	–
	–
Intraluminal	N
	(E
Surface mould (SM)	Ex
	N
	H
	SI
SM + interstitial	H
	Tu

Selection of the patient for brachytherapy depends on following factors besides general status, type of cancer, and extent of disease:

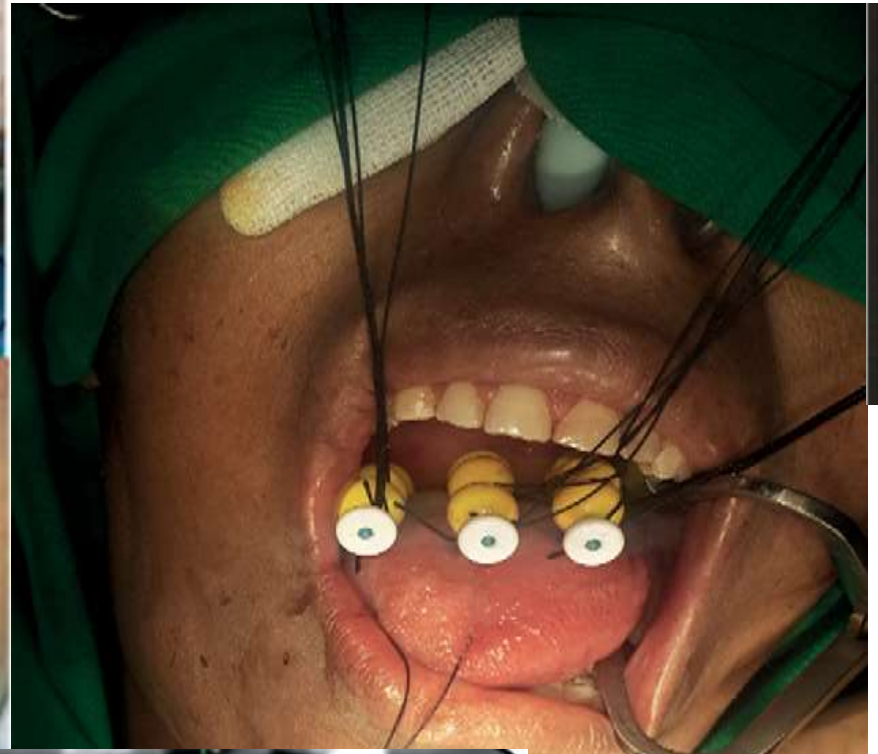
- location;
- accessibility;
- size (< 2 cm for radical curative BT);
- proximity to cartilage/bone (mandibular margin > 5 mm);
- presence or absence of trismus/submucous fibrosis (SMF);
- previous treatment;
- duration of previous treatment:
  – gap between first treatment and relapse,
  – dose details of the previous radiotherapy;
- suitability for general anesthesia for interstitial brachytherapy.

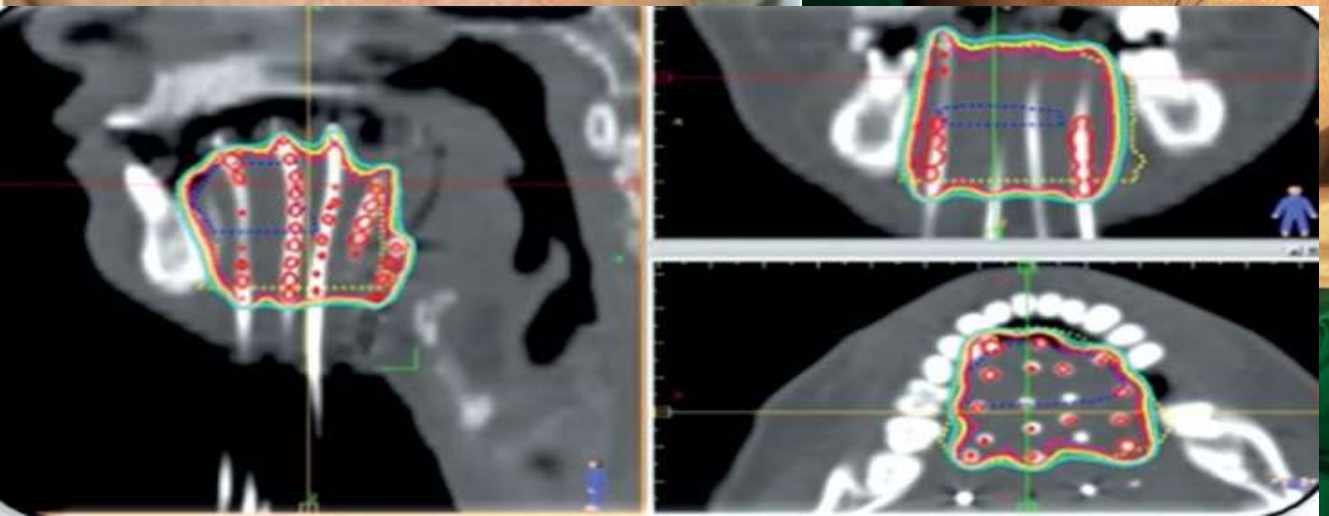


HNSCC – Basic steps

- Pre planning (imaging plus clinical examination)
- Anaesthesia
- Applicator placement (Paris principle – planar, volume implants)
- Target volume / OAR concepts
  - GTV
  - CTV (=PTV)
  - OAR (skin except surface moulds, mucosa, bone)
- Dose prescription CTV D90 > 90%, V100 > 90%
- Optimization – geometric, dwell time, graphical
- Plan evaluation and QA
  - Prescription dose, MCD
  - Coverage of CTV (or CTV with margins), COIN
  - Hyperdose sleeve (200%, 150%), DNR, DHI
- Manual check for catheter patency, maintenance and cleaning.

HNSCC – Examples



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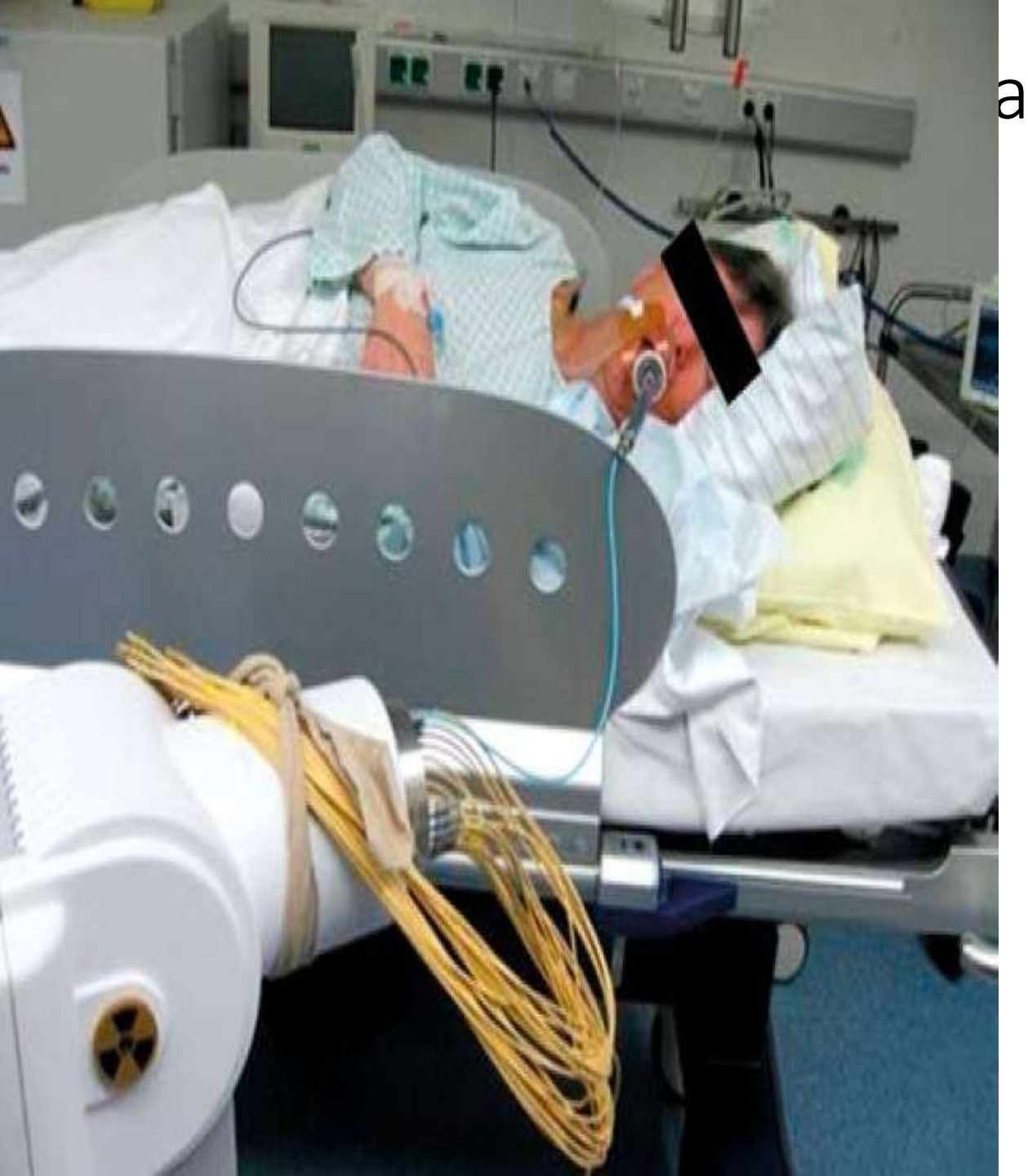
Esophagus



agus ILRT

- Boost after EBRT / palliation of symptoms.
- Thoracic esophageal Ca without bronchial / tracheal involvement.
- Curative
  - EBRT 50Gy; ILRT 10 – 16 Gy
- Palliative (stenosis, dysphagia, bleeding, pain)
  - ILRT only 10 – 28 Gy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Breast

Breast Cancer Guidelines

ELSEVIER

Brachytherapy ■ (2017) ■

BRACHYTHERAPY

The American Brachytherapy Society consensus statement for accelerated partial-breast irradiation

Chirag Shah[1,*], Frank Vicini[2], Simona F. Shaitelman[3], Jaroslaw Hepel[4,5], Martin Keisch[6], Douglas Arthur[7], Atif J. Khan[8], Robert Kuske[9], Rakesh Patel[10], David E. Wazer[4,5]

Boost

APBI

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ESTRO-ACROP Guideline

ESTRO-ACROP guideline: Interstitial multi-catheter breast brachytherapy as Accelerated Partial Breast Irradiation alone or as boost – GEC-ESTRO Breast Cancer Working Group practical recommendations

Vratislav Strnad[a,*], Tibor Major[b], Csaba Polgar[c], Michael Lotter[a], Jose-Luis Guinot[c], Cristina Gutierrez-Miguelez[d], Razvan Galalae[e], Erik Van Limbergen[f], Benjamin Guix[g], Peter Niehoff[h], Kristina Lössl[i], Jean-Michel Hannoun-Levi[j]

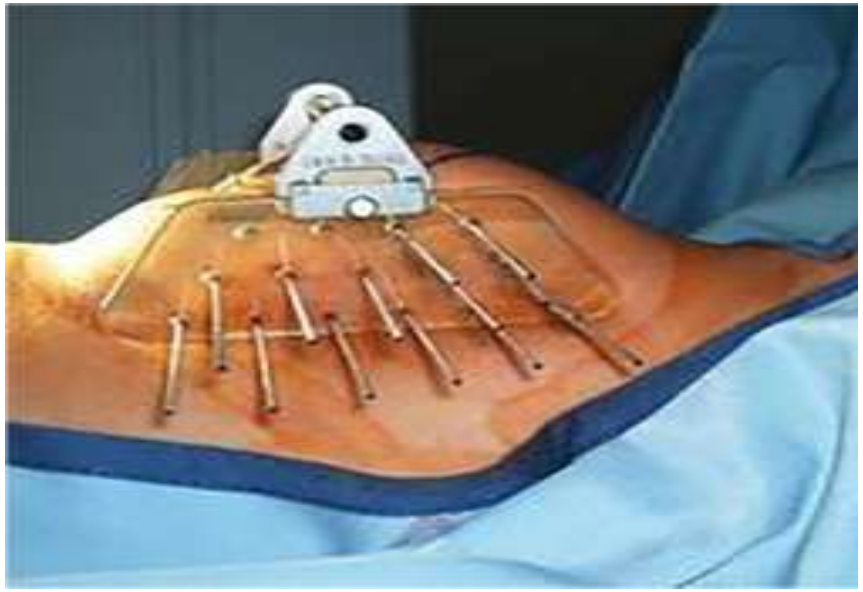
APBI

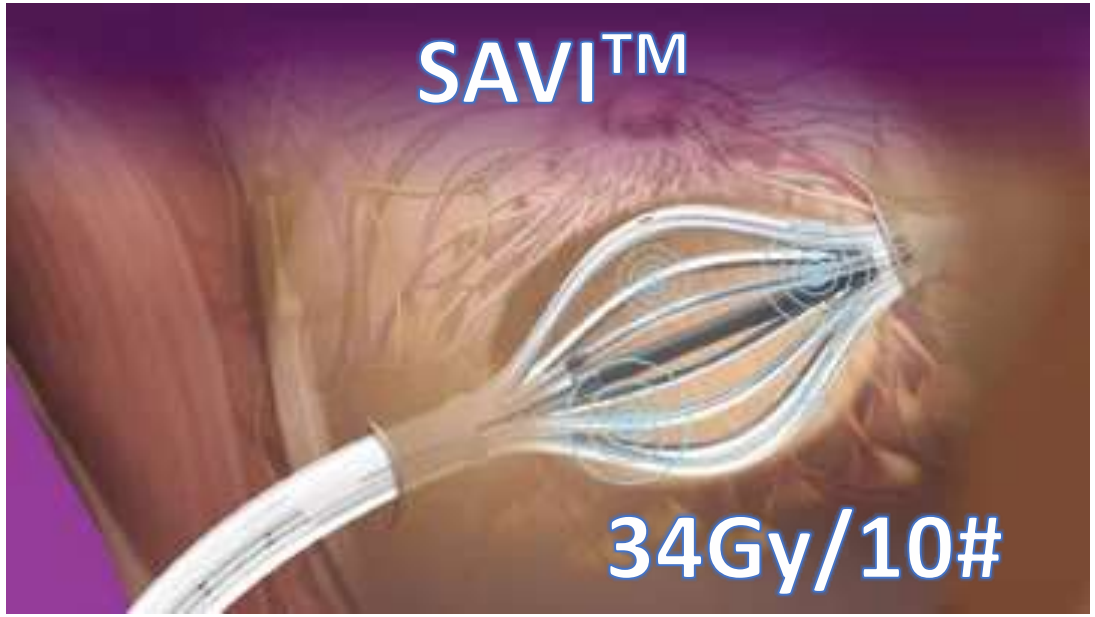
| ASTRO consensus statement* groupings for APBI patient selection

Factors	Suitable criteria	Cautionary criteria	Unsuitable criteria
Age (years)	≥60	50–59	<50
Tumour size (cm)	≤2.0	2.1–3.0	>3.0
LN status	pN0	NS	pN1, pN2, pN3
Margin status	Negative (>2 mm)	Close (<2 mm)	Positive
Grade	Any	NS	NS
ER status	Positive	Negative	NS
DCIS	Not allowed	≤3 cm	>3 cm
LVSI	Not present	Limited or focal	Extensive
EIC	Not allowed	≤3 cm	≥3 cm
Multicentricity	Unicentric	NS	Present
Multifocality	Unifocal with total size ≤2 cm	Clinically unifocal with total size 2.1–3.0 cm	>3 cm or if clinically multifocal
BRCA mutation	Not present	NS	Present

*Non-clinical trial data from Smith, B. D. *et al. Int. J. Radiat. Oncol. Biol. Phys.* **74**, 987–1001 (2009).[34]
Abbreviations: DCIS, ductal carcinoma *in situ*; EIC, extensive intraductal component; ER, oestrogen receptor; LVSI, lymphvascular space invasion; NS, not specified.

Techniques





Interstitial Breast Brachytherapy

Table 3
Recommended dose–volume limits for OAR-s.

Organ	Constraints
Ipsilateral non-target breast	$V_{90} < 10\%$ $V_{50} < 40\%$
Skin*	$D_{1cm3} < 90\%$ $D_{0.2cm3} < 100\%$
Rib	$D_{0.1cm3} < 90\%$ $D_{1cm3} < 80\%$
Heart**	MHD < 8% $D_{0.1cm3} < 50\%$
Ipsilateral lung	MLD < 8% $D_{0.1cm3} < 60\%$

* Skin volume is defined as a 5 mm shell below the body contour.

** Left sided lesion only, MHD: mean heart dose, MLD: mean lung dose

Table 2
Recommended dose–volume limits for implant and PTV.

	Constraints
Implant	$V_{PD} \leq 300\ cm^3$ $DNR \leq 0.35$
PTV	$V_{100} \geq 90\%$ $V_{150} < 65\ cm^3$ $V_{200} < 15\ cm^3$ $COIN \geq 0.65$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Prostate

Prostate Cancer Guidelines

GEC/ESTRO recommendations

GEC/ESTRO recommendations on high dose rate afterloading brachytherapy for localised prostate cancer: An update

Peter J. Hoskin [a,*,1], Alessandro Colombo [b,1], Ann Henry [c,1], Peter Niehoff [d,1], Taran Paulsen Hellebust [e,1], Frank-Andre Siebert [f,1], Gyorgy Kovacs [g,1]

[a] *Mount Vernon Cancer Centre, Northwood, UK;* [b] *Department of Radiotherapy, Manzoni Hospital, Lecco, Italy;* [c] *St. James Institute for Oncology, Leeds, UK;* [d] *Department of Radiotherapy, City Hospital Cologne, Germany;* [e] *DNR Norwegian Radium Hospital, Oslo, Norway;* [f] *Universitätsklinikum Schleswig-Holstein, Kiel; and* [g] *University Hospital Schleswig-Holstein Campus Lübeck, Germany*

Guidelines

GEC-ESTRO ACROP prostate brachytherapy guidelines

Ann Henry [a], Bradley R. Pieters [b], Frank André Siebert [c], Peter Hoskin [d,e,*], on behalf of the UROGEC group of GEC ESTRO with endorsement by the European Association of Urology [1]

[a] *St James University Hospital, Leeds, UK;* [b] *Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, The Netherlands;* [c] *University of Kiel/University Hospital Schleswig-Holstein Campus Kiel, Germany;* [d] *Mount Vernon Cancer Centre, Northwood; and* [e] *University of Manchester, Manchester, UK*

Prostate Interstitial Brachytherapy

- Indication :

Monotherapy / Boost after EBRT

- Dose rate

Permanent implant / HDR

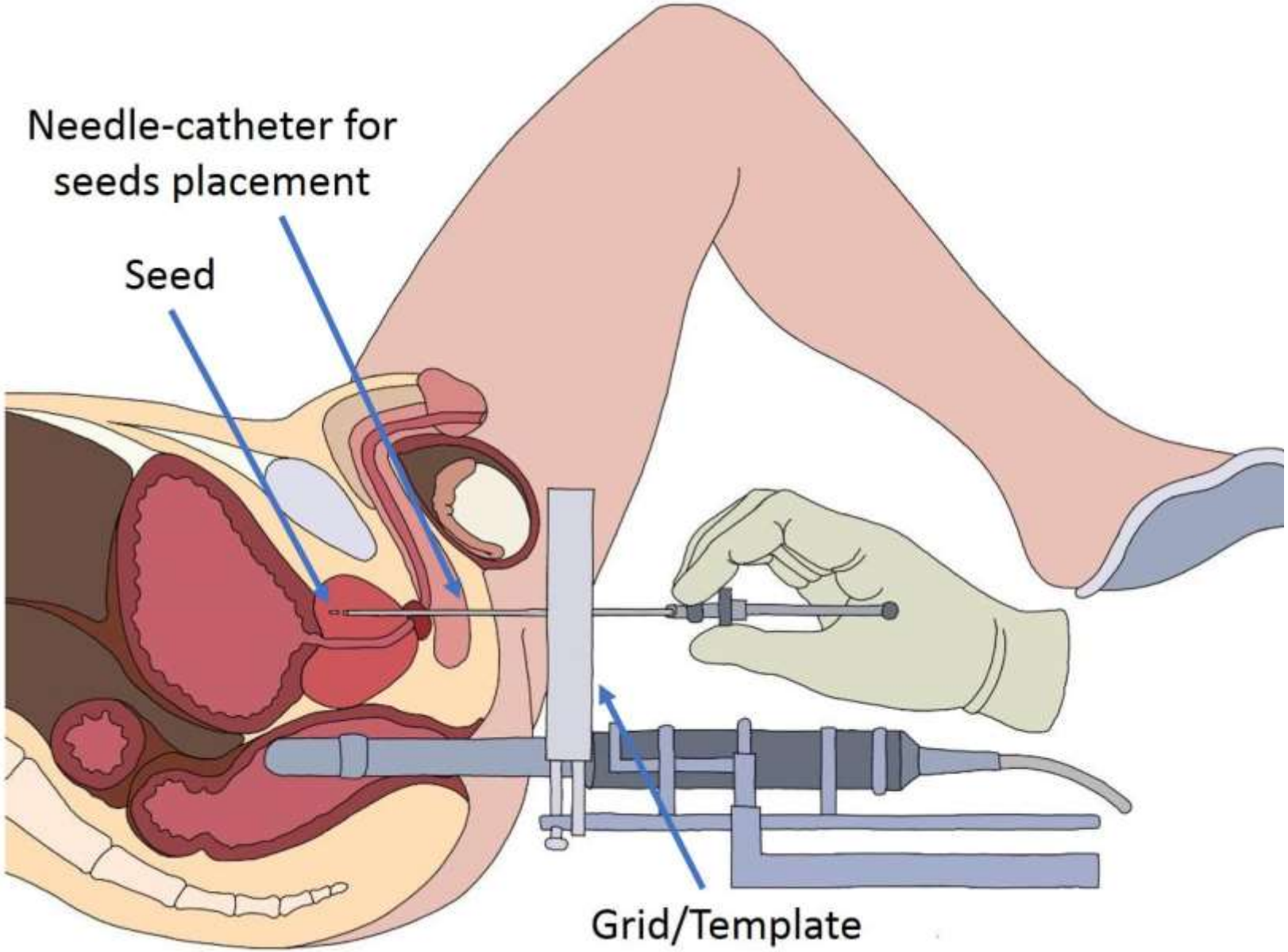
- 15 Gy in 3 fractions.
- 11–22 Gy in 2 fractions.
- 12–15 Gy in 1 fraction.

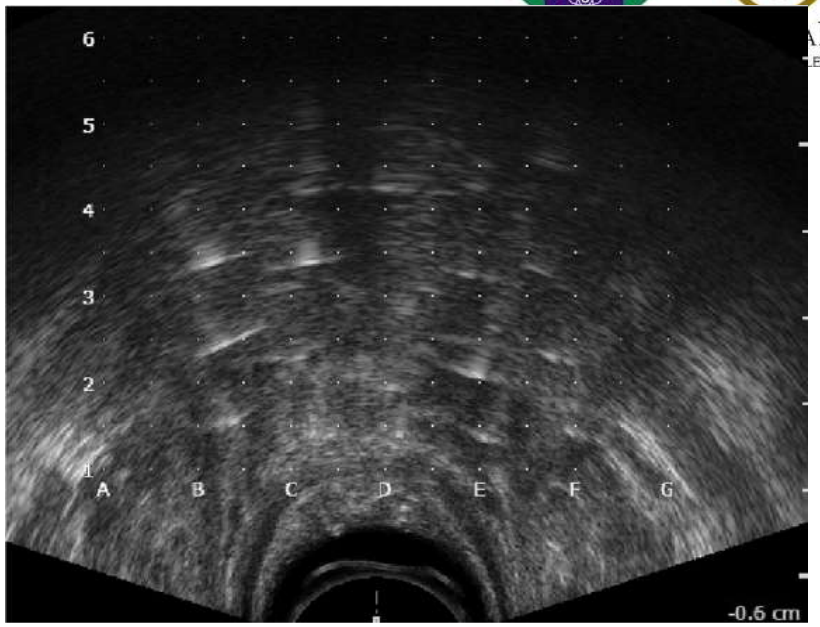
Table 2
Patient selection criteria for a curative combined HD[illegible] treatment.

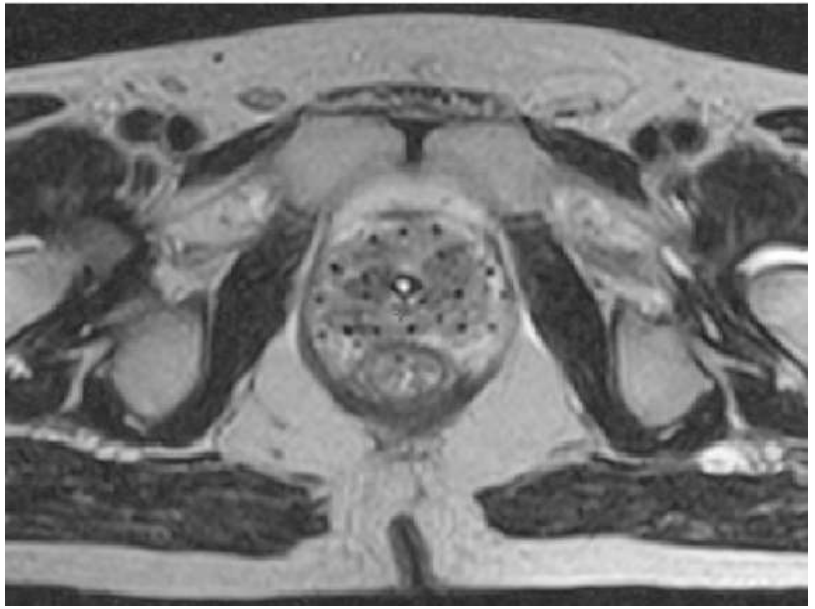
Inclusion criteria
Stages T1b–T3b
Any Gleason score
Any PSA level
Exclusion criteria
TURP within 3–6 months
Maximum urinary flow rate (Qmax) <10 ml/s
IPSS > 20
Pubic arch interference
Lithotomy position or anaesthesia not possible
Rectal fistula

- Pre-planning
- Anaesthesia
- Positioning with TRUS placement
- [illegible]S guided applicator insertion
- [illegible]ging
- Applicator reconstruction
- Dose prescription
- Plan optimization
- Treatment delivery

Prostate Interstitial Brachytherapy : Technique







Prostate Interstitial Brachytherapy : Doses

- HDR Monotherapy doses :

Low acute toxicity and high biochemical control rates but limited data.

34 Gy in 4 fractions.

36 – 38 Gy in 4 fractions.

31.5 Gy in 3 fractions.

26 Gy in 2 fractions.

- Dose rate

After 45Gy EBRT,

17 Gy in 2 fractions.

22 in single fractions.

15 Gy in single fraction.

Table 2
Planning aims and objectives of temporary HDR brachytherapy.

Organ	Parameter	Objective (*)	Objective for 15 Gy brachytherapy boost only
CTV	V_{100}	>95%	>95% (14.3 Gy)
	D_{90}	>100% (121 Gy EQD2)	>100% (15 Gy)
	V_{150}	≤40%	≤40% (6 Gy)
Rectum	D_{2cc}	≤75 Gy EQD2	≤10 Gy
Urethra	D_{10}	≤120 Gy EQD2	≤17 Gy
	D_{30}	≤105 Gy EQD2	≤15 Gy

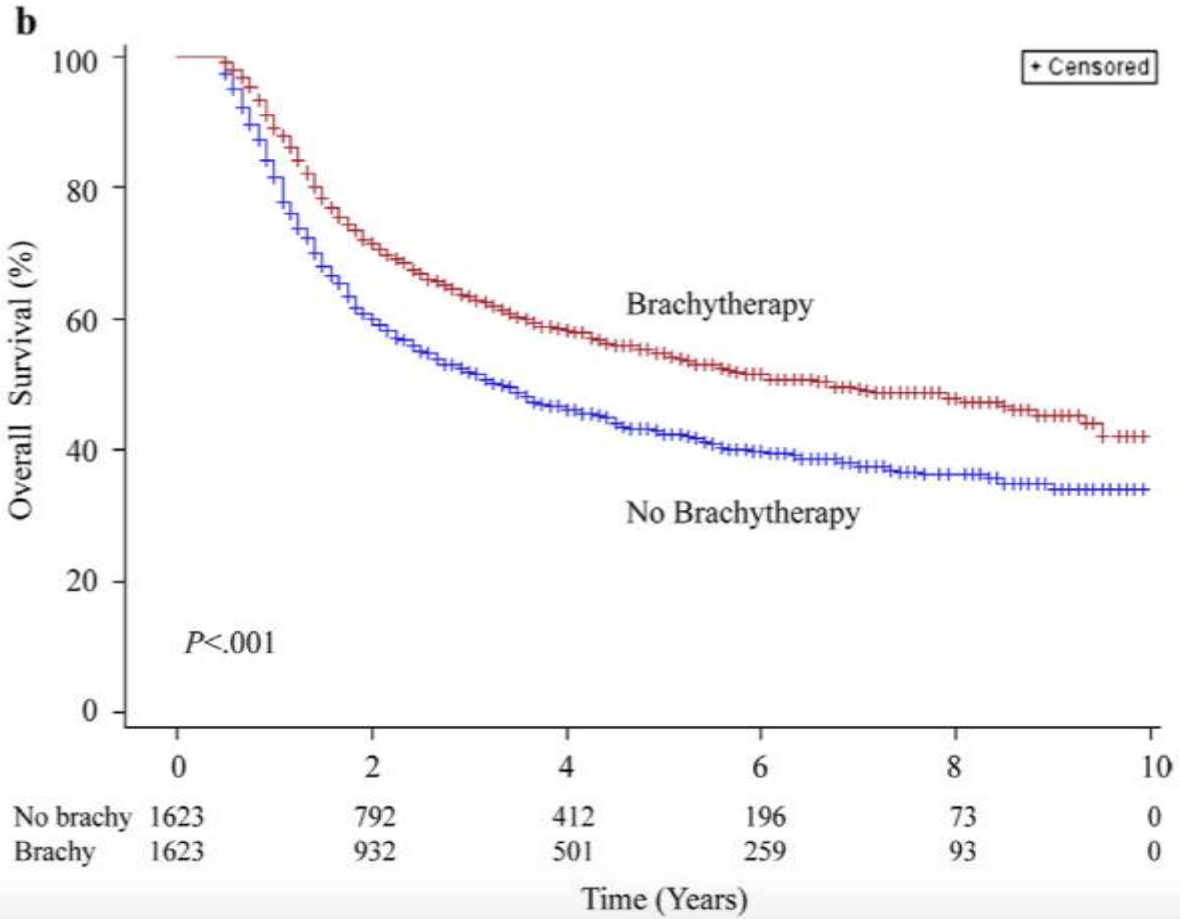
(*) EQD2 dose was calculated using the following concept: prescribed dose: external.
25x2Gy, HDR brachytherapy 1x15Gy, α/β-ratio = 1.5 Gy, EQD2: 50 Gy + 70.7 Gy ≈ 121 Gy.

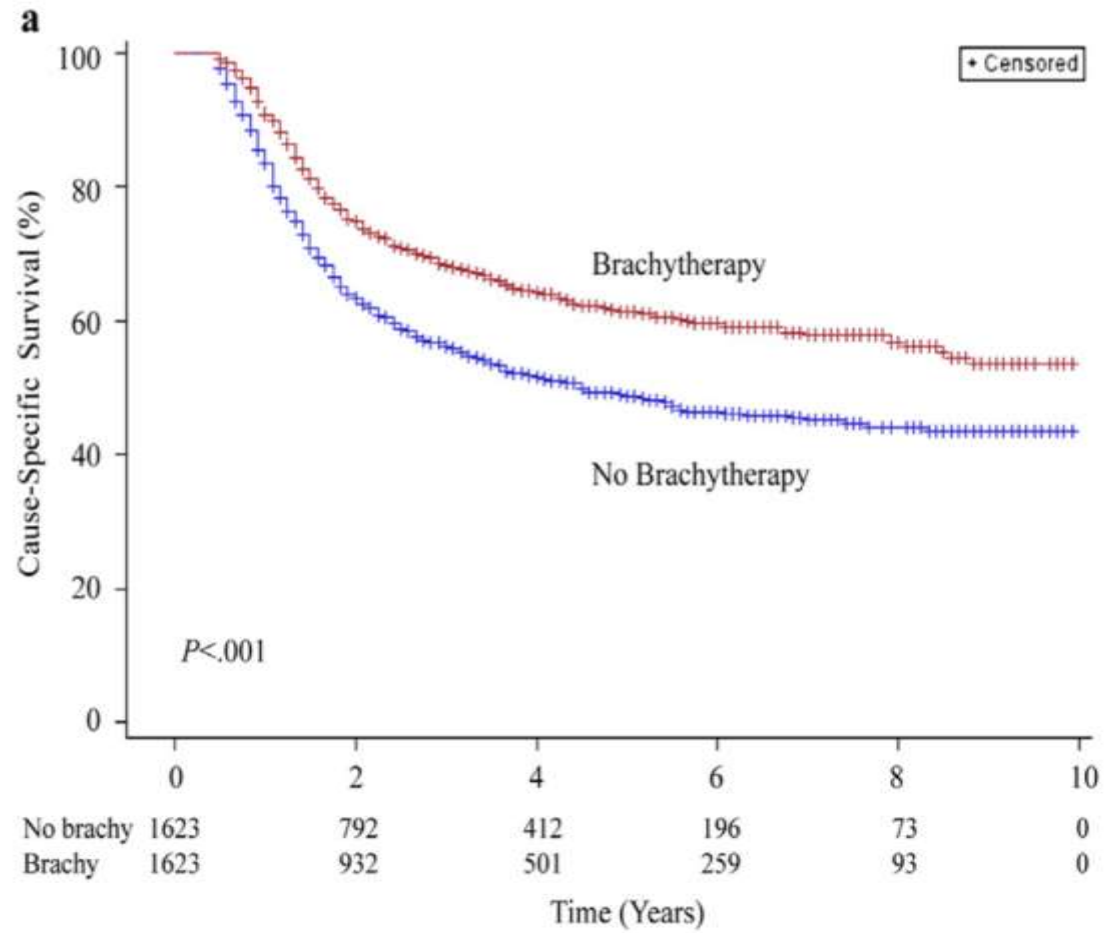
Brachytherapy in Gynaecological Cancer

EDITORIAL

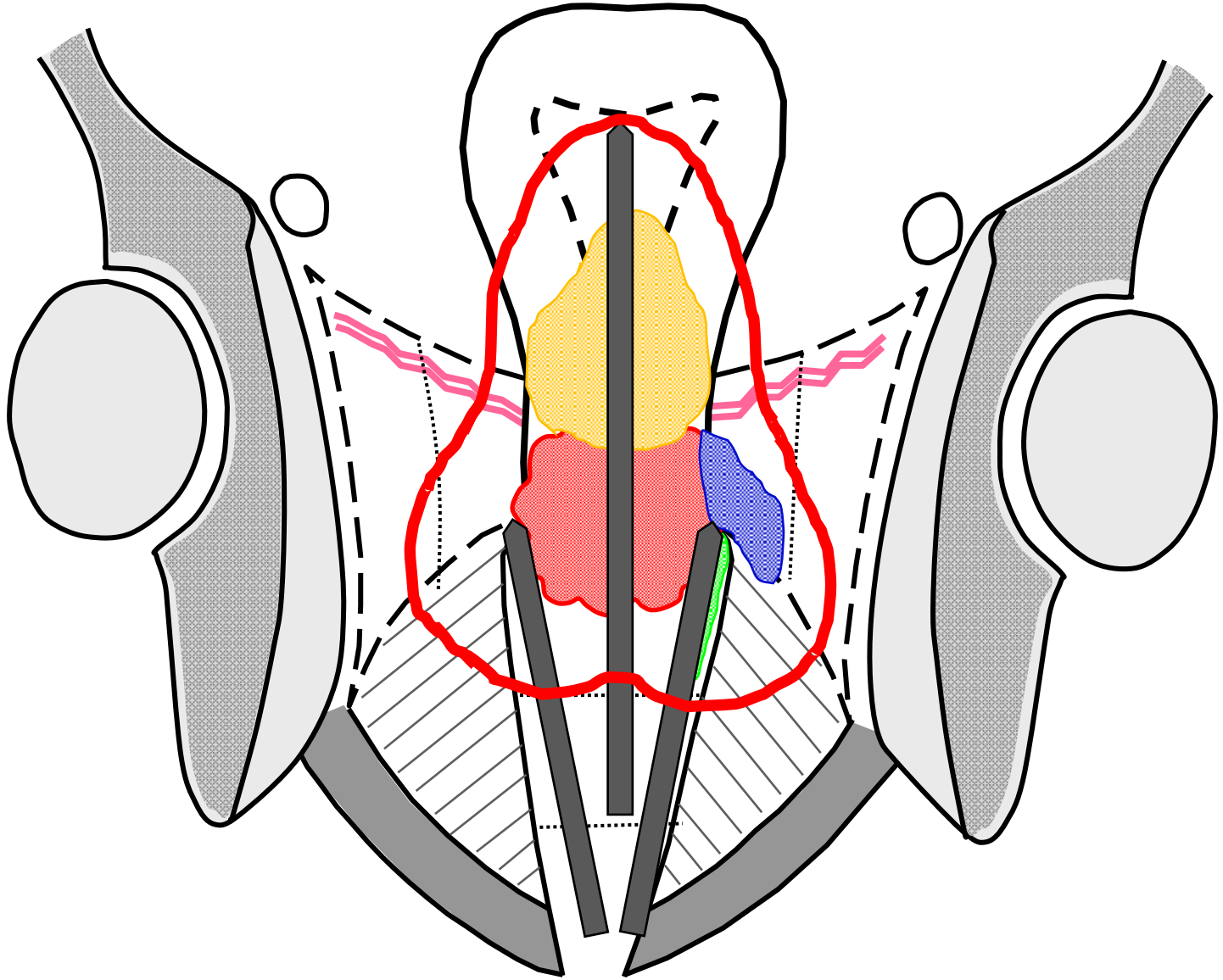
Curative Radiation Therapy for Locally Advanced Cervical Cancer: Brachytherapy Is NOT Optional

Kari Tanderup, PhD,*,† Patricia J. Eifel, MD,‡ Catheryn M. Yashar, MD,§ Richard Pötter, MD,‖ and Perry W. Grigsby, MD*



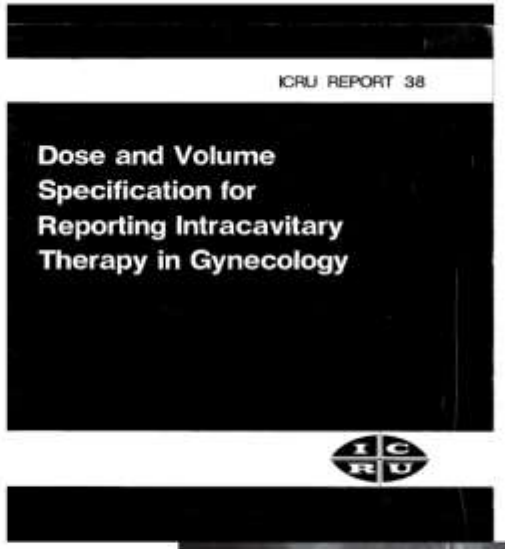


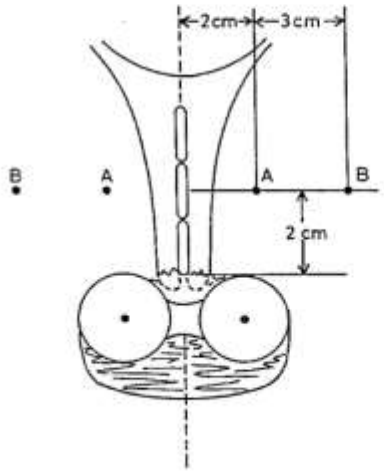
Advantages of BT : Cervix

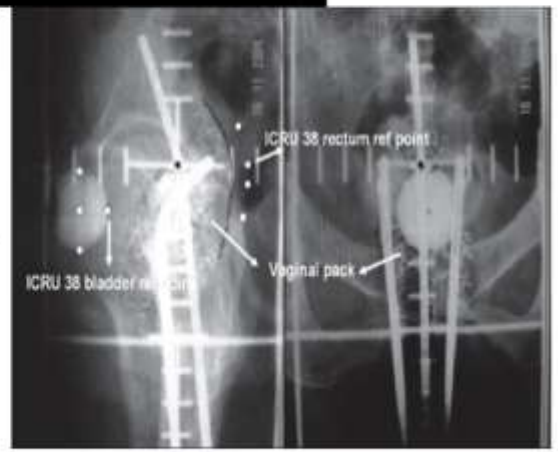


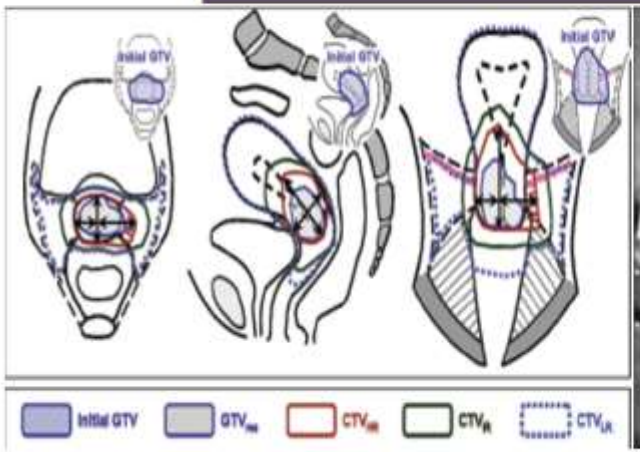
Journey from 2D to 3D

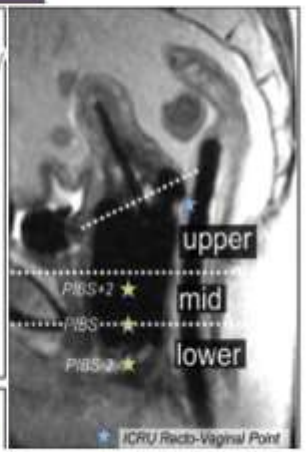
The GYN GEC ESTRO I – IV recommendations











Journey from 2D to 3D

The Indian Brachytherapy Society recommendations

Educational Article

Original paper

Indian Brachytherapy Society Guidelines for radiotherapeutic management of cervical cancer with special emphasis on high-dose-rate brachytherapy

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Brachytherapy steps / workflow

- Pre BT imaging / clin exam
- PAC
- Applicator selection
- Imaging slot booking

- MRI / CT
- Protocols
- Targets
- OARs
- Others

- Check and connect transfer tubes
- Treat
- Remove, inspect
- Post procedure treatment

Preplanning → **Brachy procedure** → **Imaging / delineation** → **Planning and evaluation** → **Treatment and removal**

- Anaesthesia
- Bladder / bowel
- Topography
- Applicator insertion
- Packing
- Fixation / stabilization

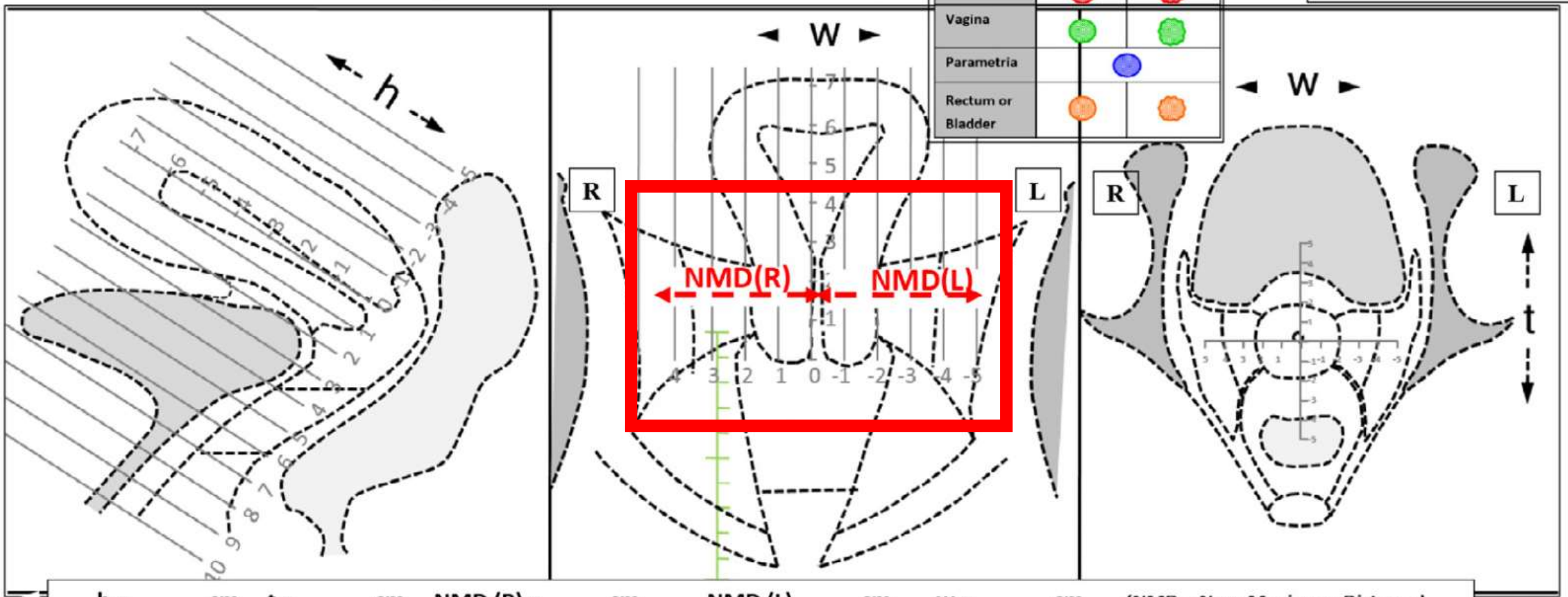
- Applicator reconstruction
- Standard Loading
- Optimization
- Dosimetry : LQ spreadsheet for EQD2s - recording

Imaging and documenting disease

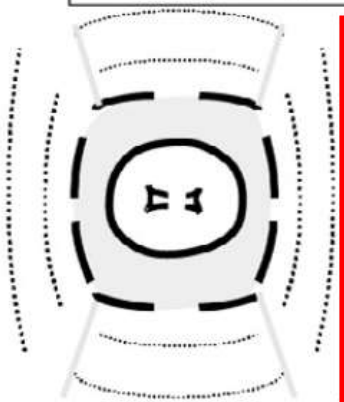
Patient Initials : | **ID :**

	Infiltrative	Exophytic
Cervix		
Vagina		
Parametria		
Rectum or Bladder		

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

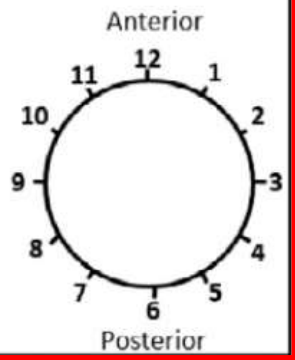


h = _____cm t = _____cm NMD (R) = _____cm NMD (L) _____cm w = _____cm *(NMD = Near Maximum Distance)*



Vaginal Disease

Ant : ___ cm
Post :___ cm
Rt Lat: ___cm
Lt Lat: ___cm



FIGO (2018)

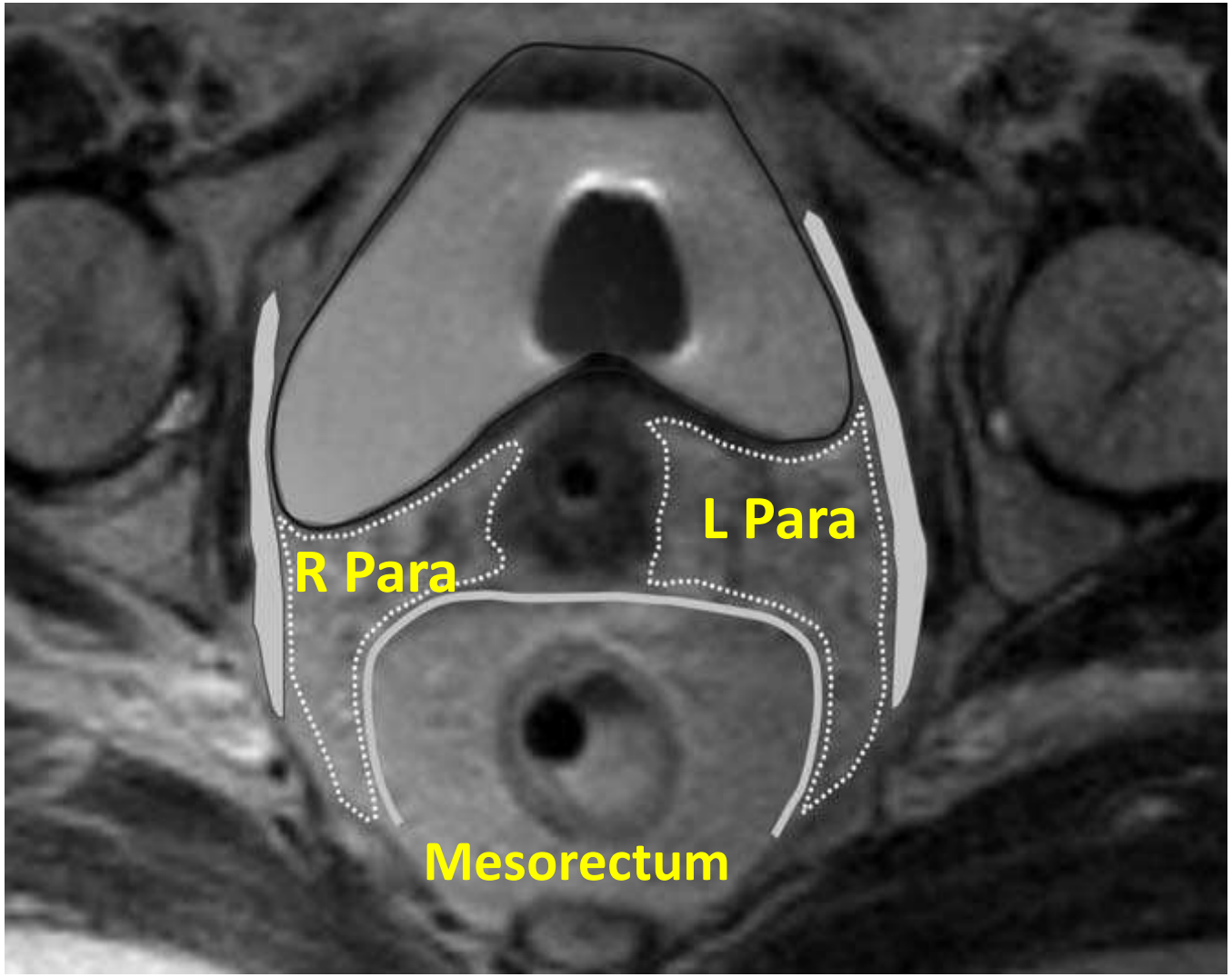
T N M ( )

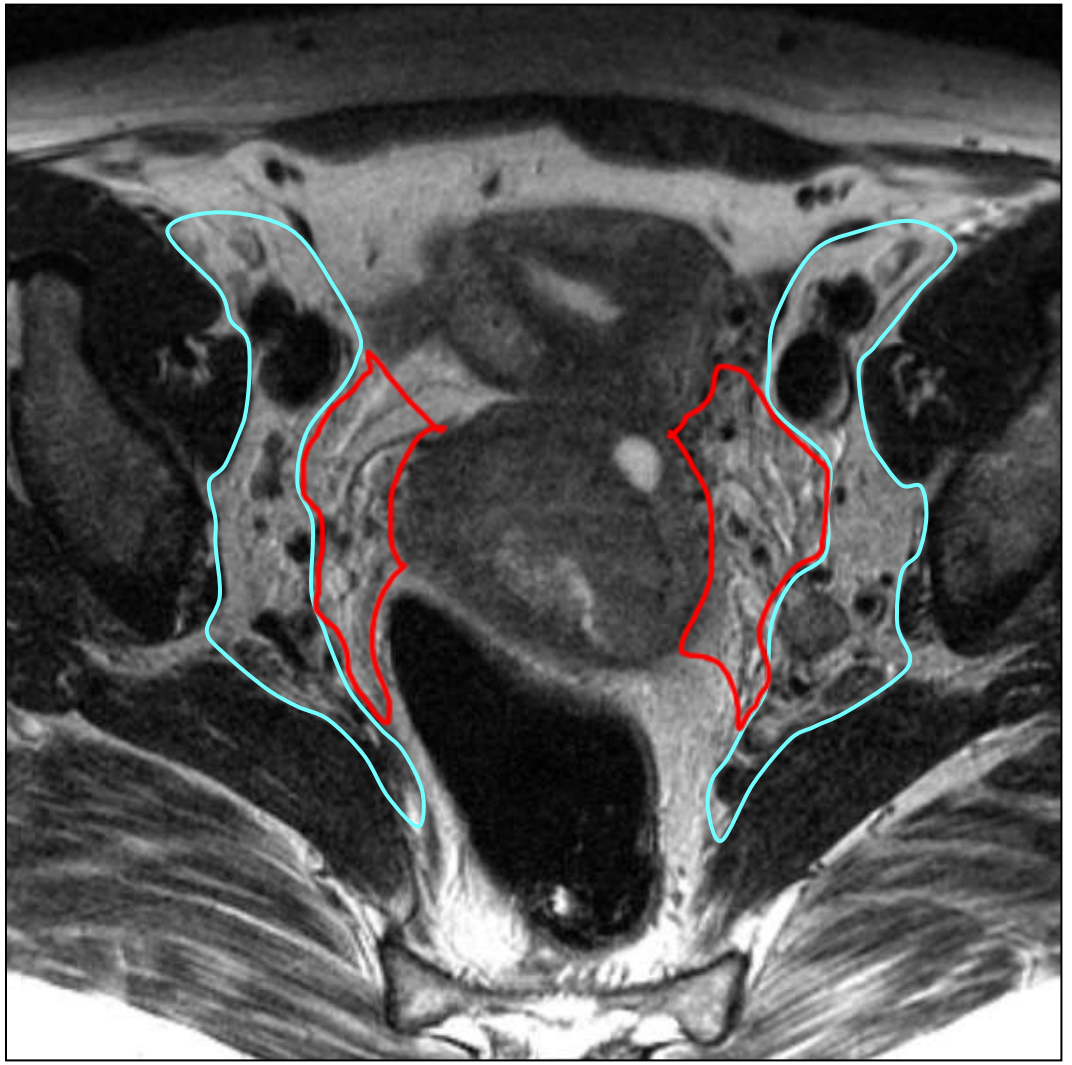
$BT_{category}$: I_{BT} / II_{BT} / III_{BT} / IV_{BT}

Remarks:

Signature & Date :

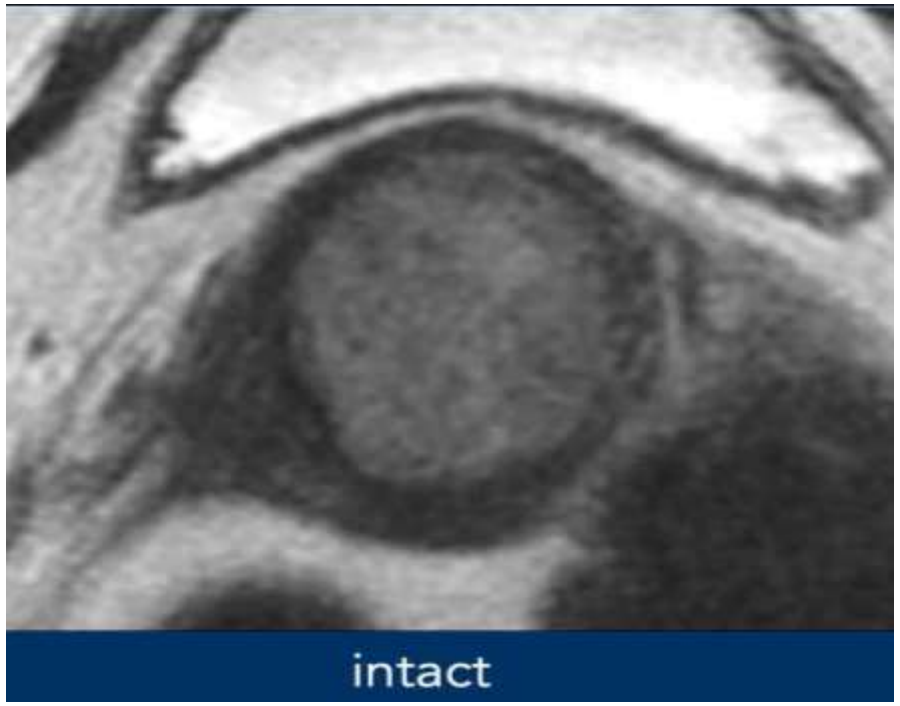
The parametrium on MRI

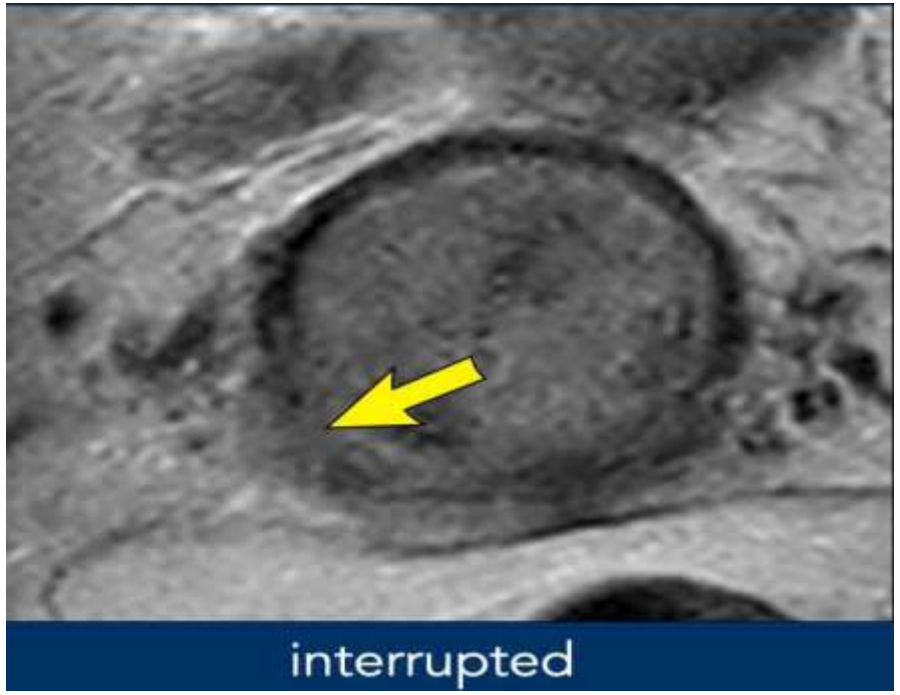


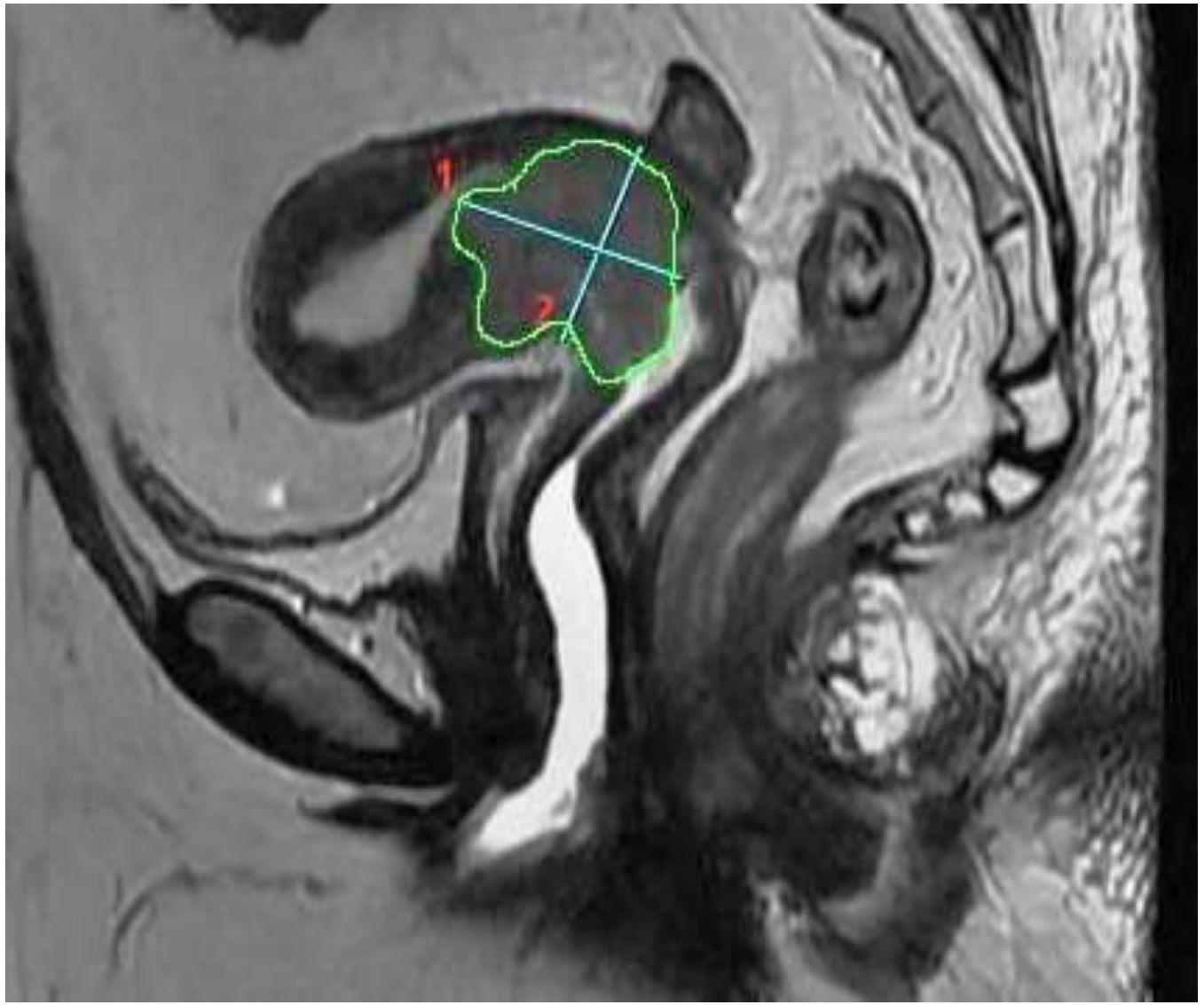


Courtesy of J. Dimoupoulos, P. Petric

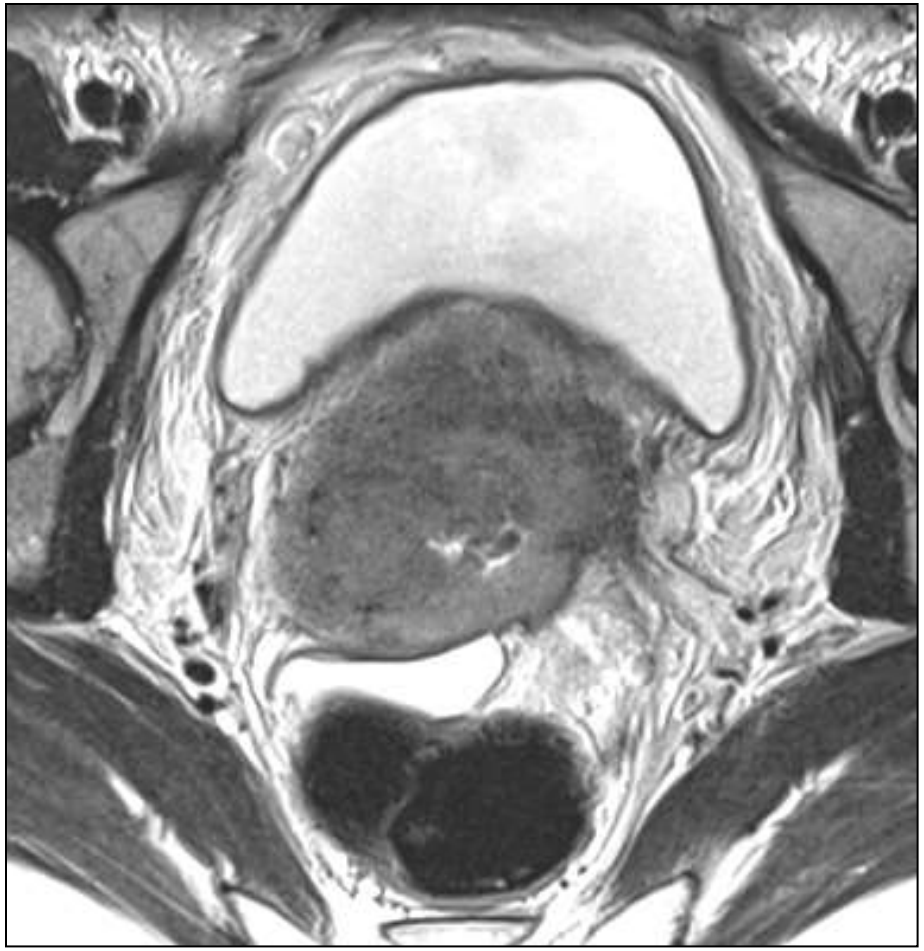
Parametrial / vaginal invasion



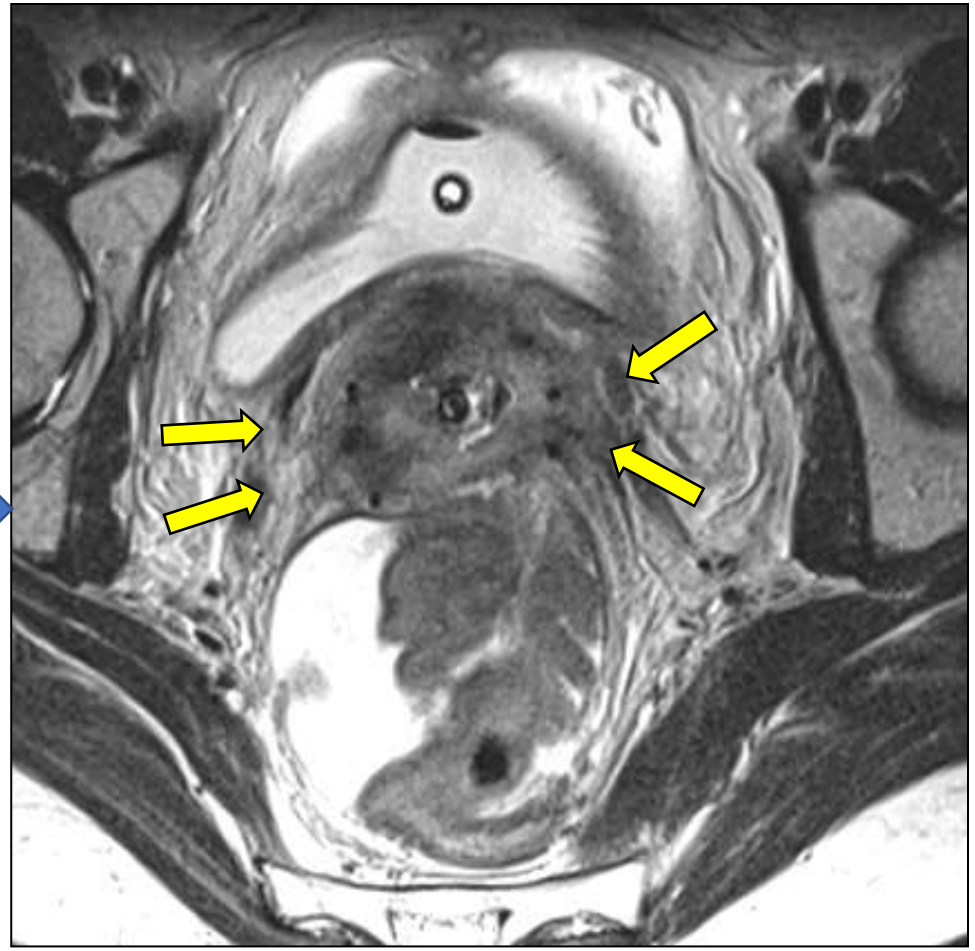




Grey Zones Residual pathologic disease on MRI



EBRT + ChT



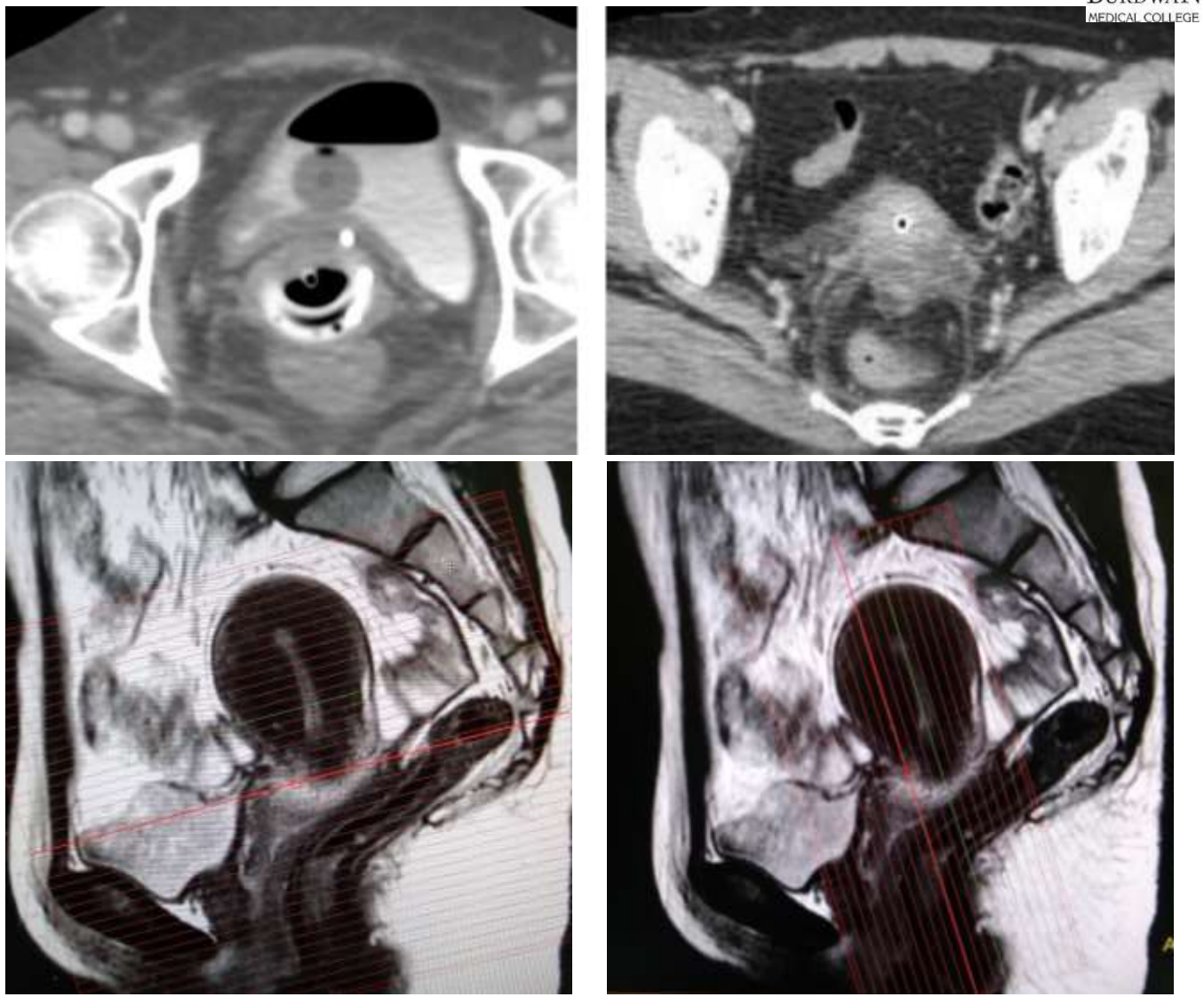
Courtesy of P. Petric

Issues for imaging – CT / MRI

- Blood tests – KFT, Electrolytes.
- Bowel prep.

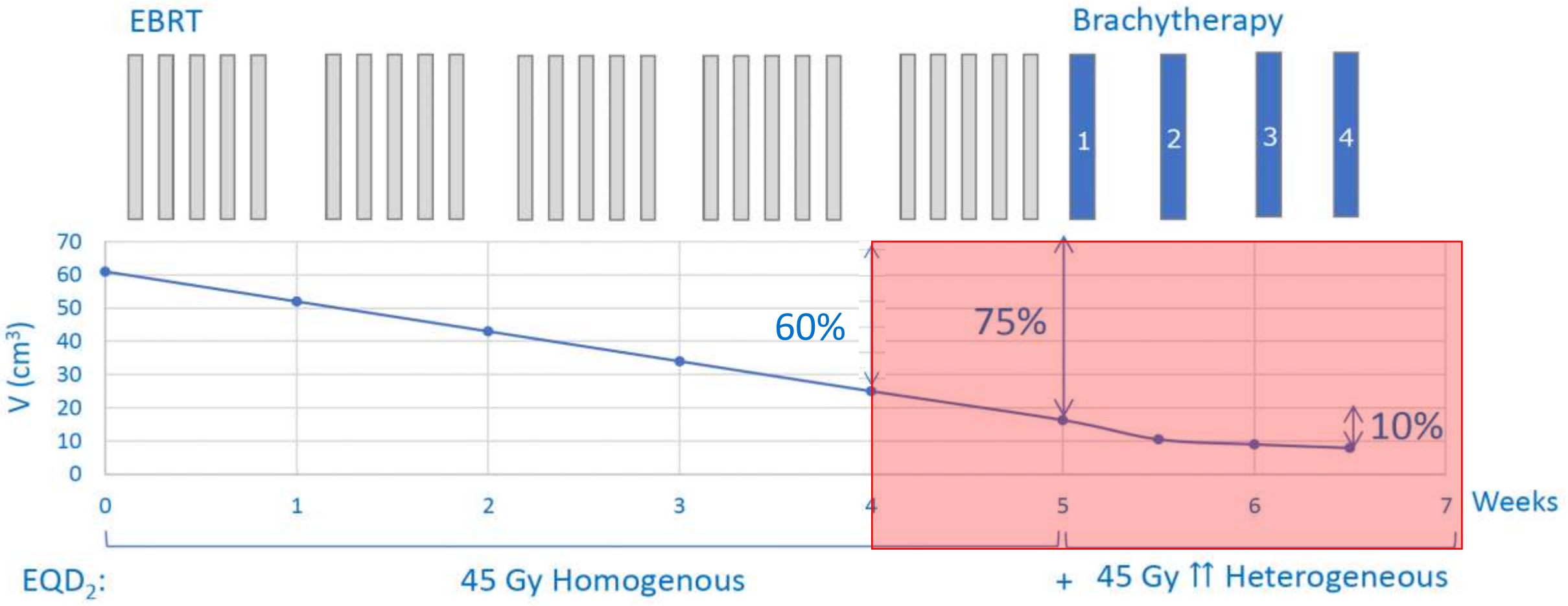
- CT scan
  - IV contrast – arterial phase.
  - Dilute bladder contrast.
  - ≤ 3mm slice cuts.

- MRI
  - 1.5T.
  - T2w FSE para.
  - ≤ 3mm slice cuts. Zero gap.



Courtesy of Mahantshetty U and Ghosh P;
Mahantshetty U et al IBS CT guidelines 2021, GEC ESTRO IV guidelines

Disease assessment time points



OTT < 50 days

Dimopoulos et al 2006, Mary An et al 2006

Applicator selection

Table 1: Definition of four BT target categories according to assessment and restaging taking into account the pattern of residual disease at BT for CT based contouring of the adaptive HR CTV_{CT}

Category of BT HR CTV_{CT}	Cervix	Parametrium	Vagina	Uterine corpus
I_{BT}	No residual disease Or Residual disease confined to cervix	No residual disease	No residual disease Or Residual disease < 2cm of upper vagina	No residual disease Or Residual disease in proximal third of utero-cervical junction
II_{BT}	Significant residual disease	Proximal parametrial disease	Residual disease within upper one third	Residual disease not beyond mid corpus

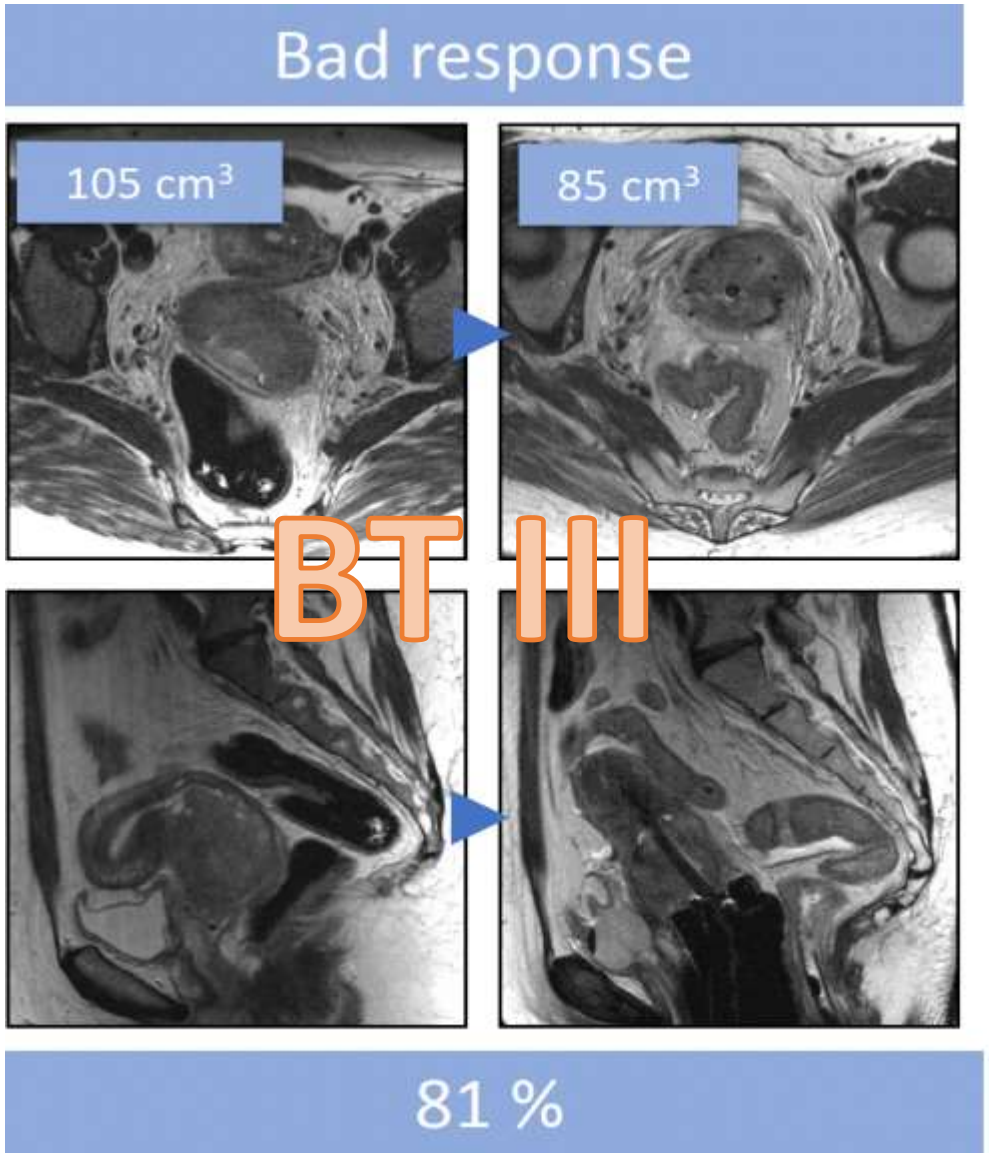
Mahantshetty et al, Radiother Oncol 2021

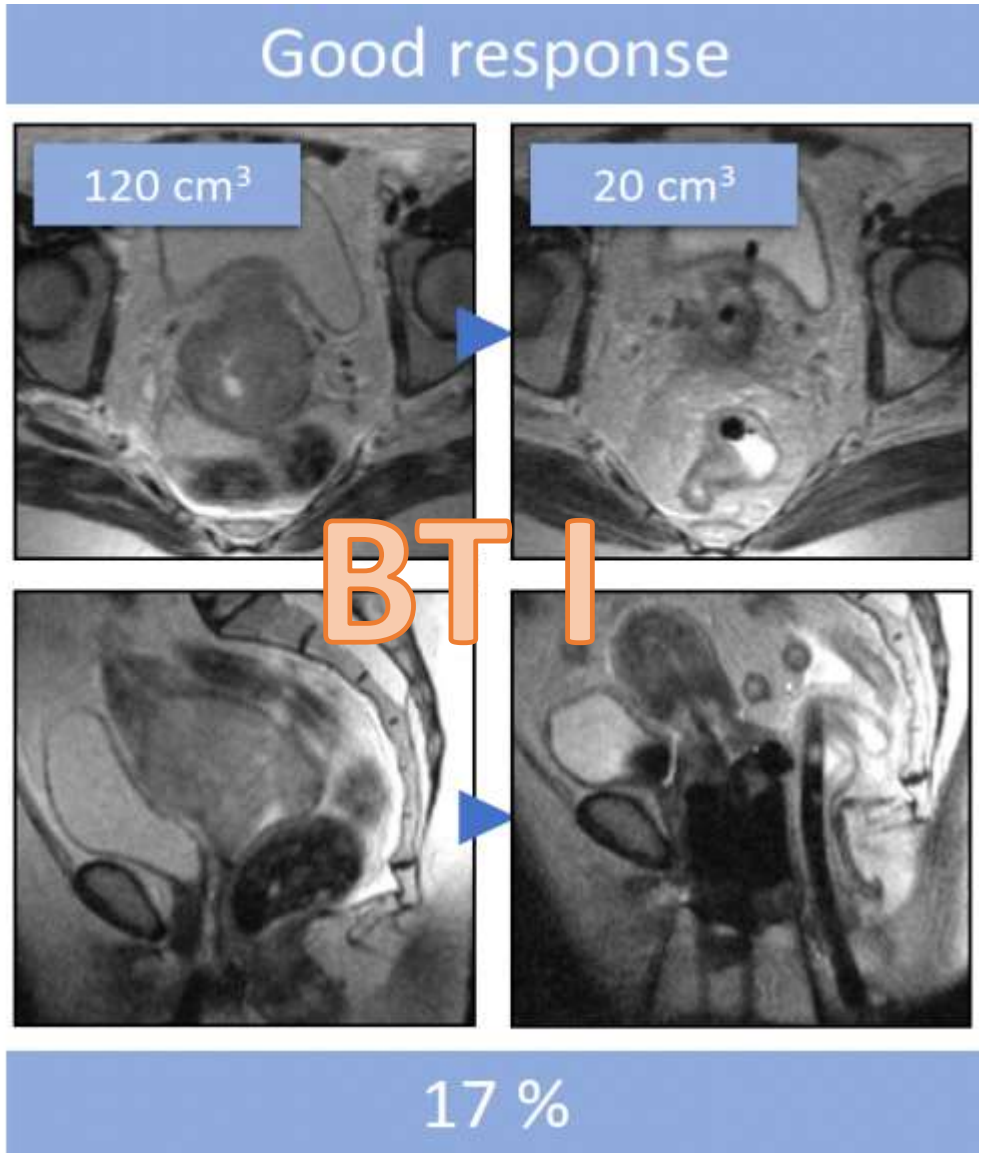
Table 1: Definition of four BT target categories according to assessment and restaging taking into account the pattern of residual disease at BT for CT based contouring of the adaptive HR CTV_{CT}

Category of BT HR CTV_{CT}	Cervix	Parametrium	Vagina	Uterine corpus
III_{BT}	Significant residual disease	Distal / Up to pelvic wall parametrial disease	Residual disease in mid or lower third	Residual disease into distal corpus / Up to fundus
IV_{BT}	Significant residual disease involving neighbouring organ wall/ mucosae (bladder/ rectum)	Proximal parametrial disease	Residual disease within upper one third	Residual disease not beyond mid corpus
		Distal / Up to pelvic wall parametrial disease	Residual disease in mid or lower third	Residual disease into distal corpus / Up to fundus

Mahantshetty et al, Radiother Oncol 2021

Degrees of response





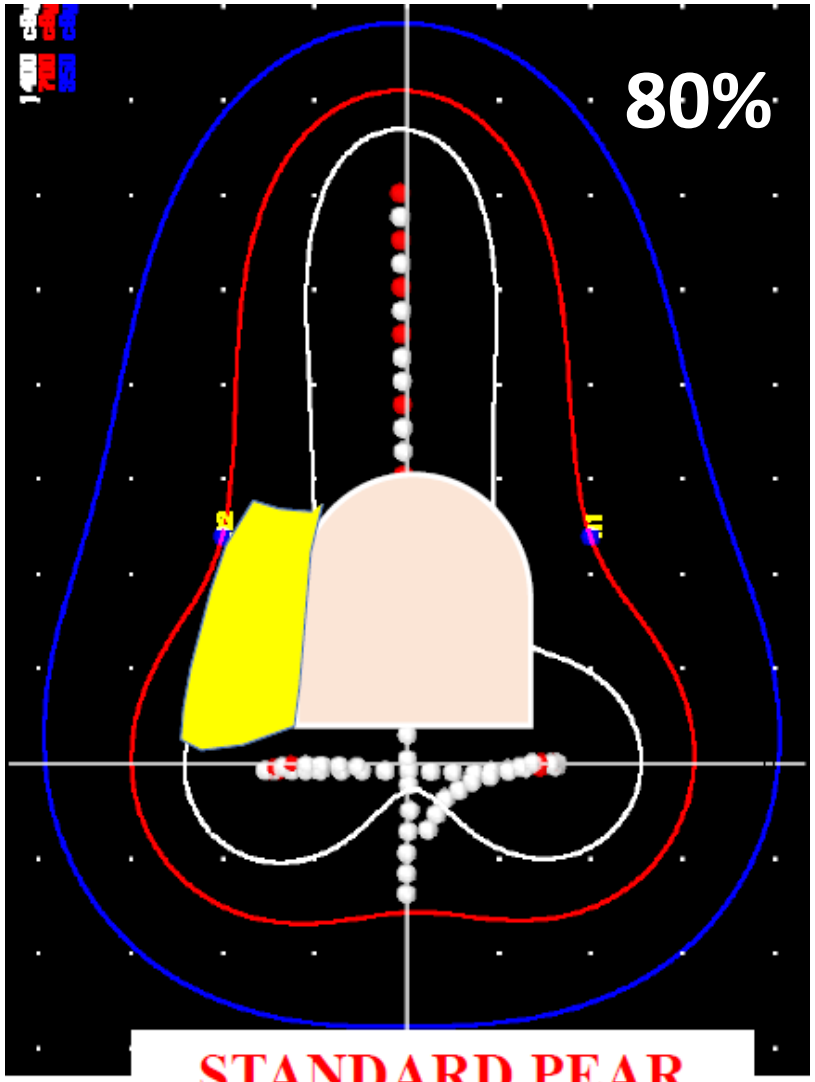
Imaging modalities for each component

	MRI	Clinical	CT* alone
GTV_{BT}	Excellent	Poor	Poor
Cervix	Excellent	Fair	Good
Parametria	Excellent	Fair	Good
Uterine corpus	Excellent	Poor	Poor
Vagina	Good	Excellent	Good

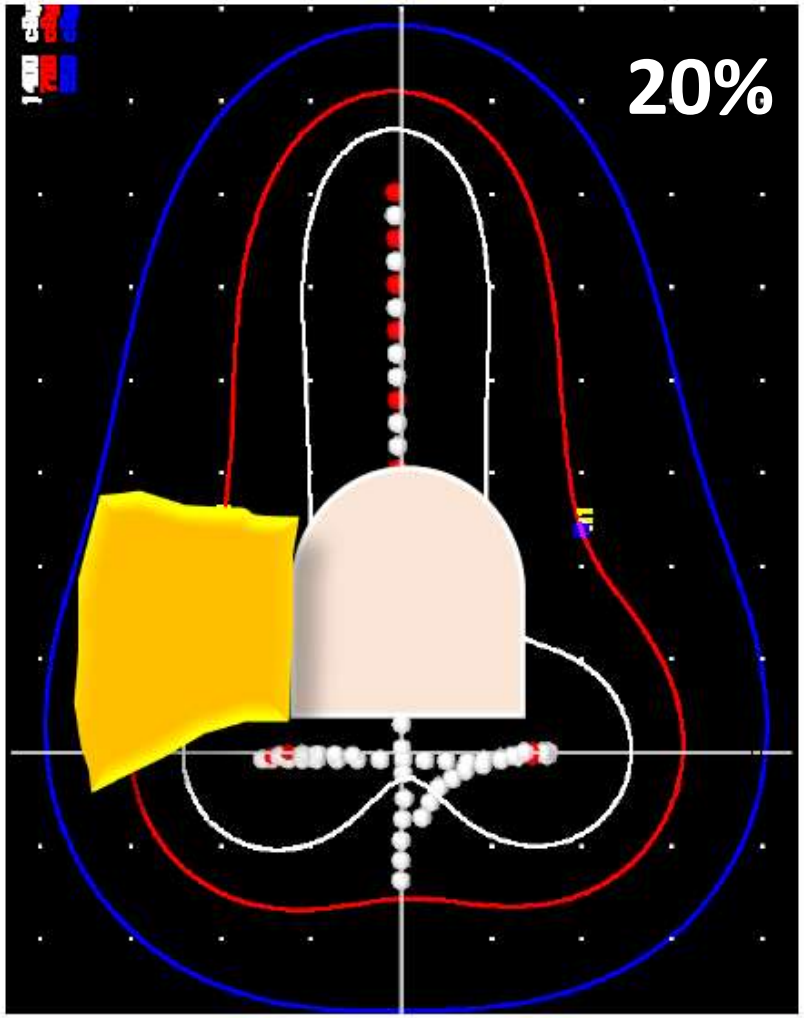
* - with arterial phase IV contrast

Adapted from Primoz Petric

Applicator selection based on tumour topography



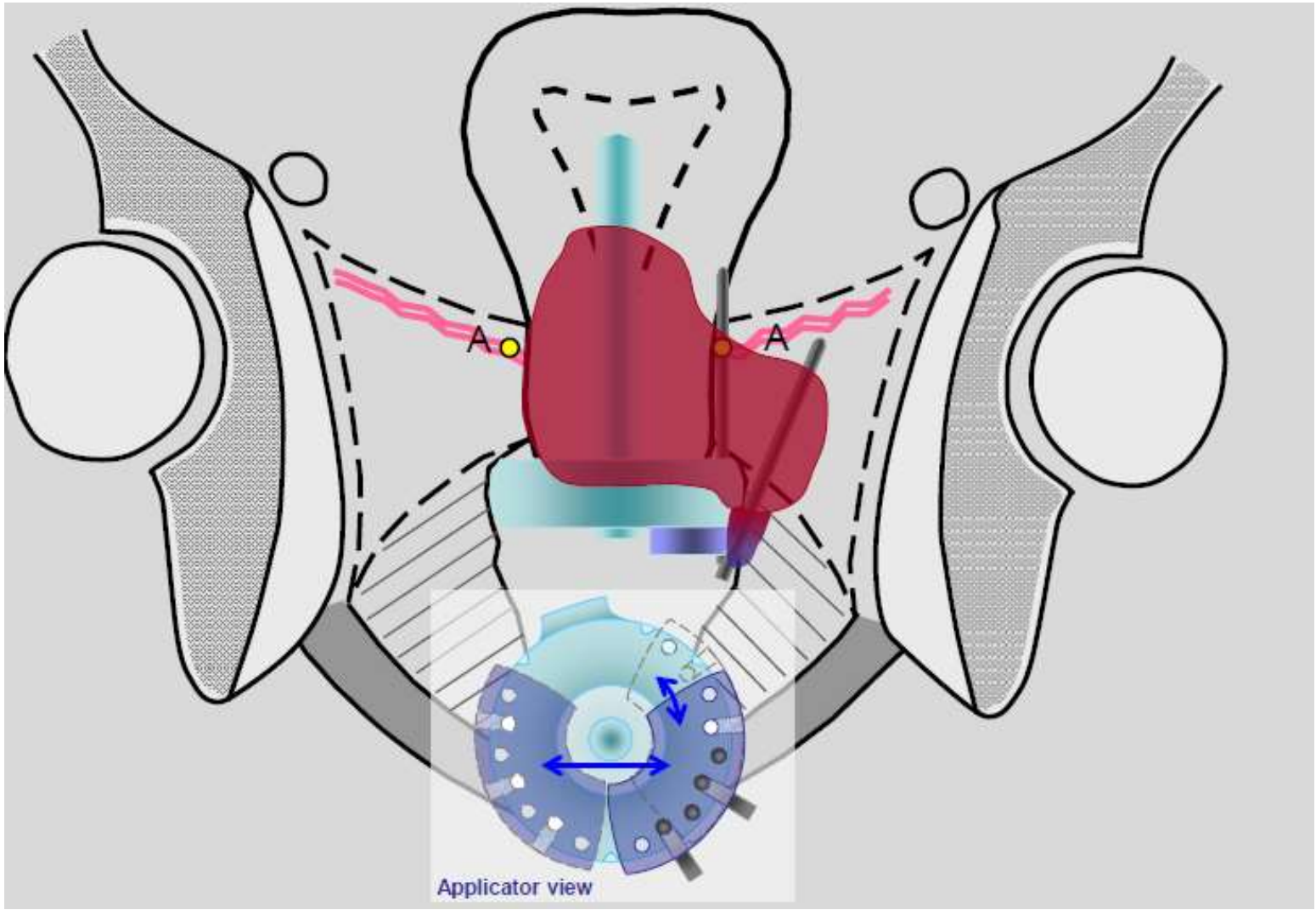
STANDARD PEAR



LIMITATION OF STANDARD PEAR

Courtesy of Daniel Berger and Primoz Petric

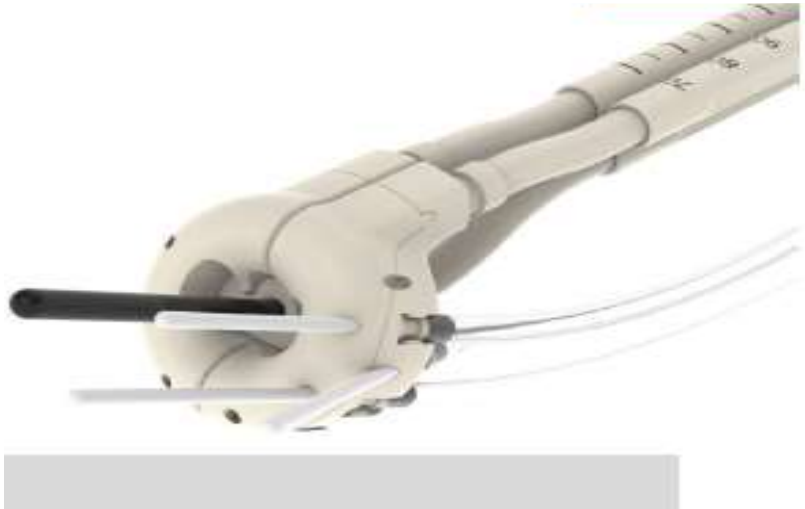
Applicator selection based on tumour topography



Courtesy of Daniel Berger and Primoz Petric

Advanced (hybrid) gyn applicators

IC + IS, ring / ovoid based

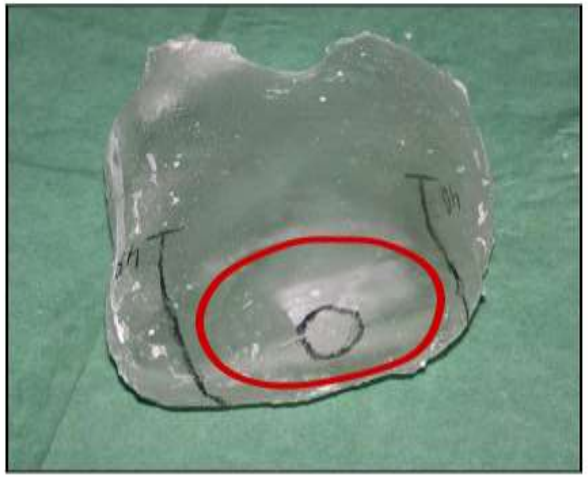


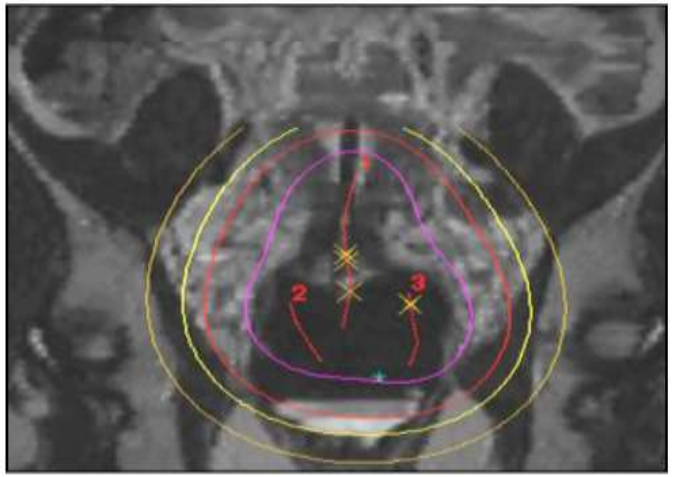
Courtesy of Daniel Berger and Primoz Petric

Custom made applicators

Personalized applicators

- Individually adapted to anatomy & tumour
- Good patient tolerance
- No need for vaginal packing
- MRI compatibility
- Prolonged bed rest avoided





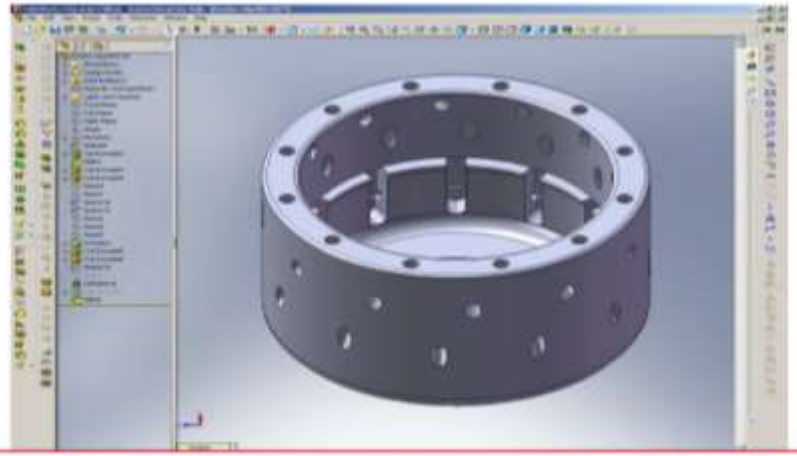
Courtesy of Christine Haie Meder

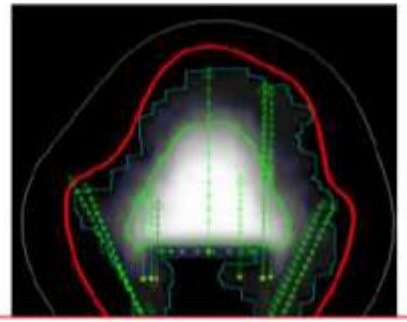
Custom made applicators

Adaptive BT applicators

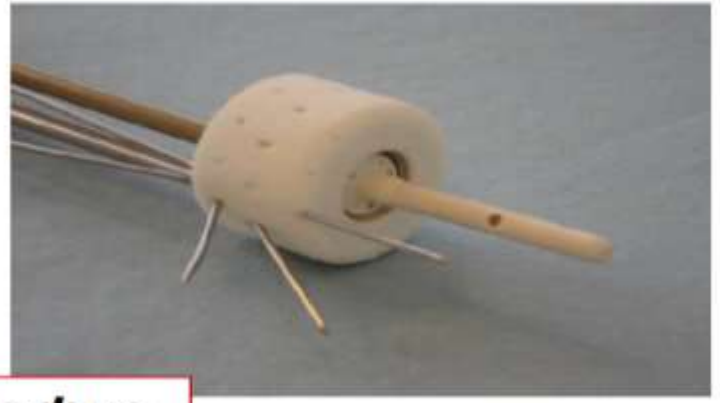
3D Printing

Virtual applicator





New applicator

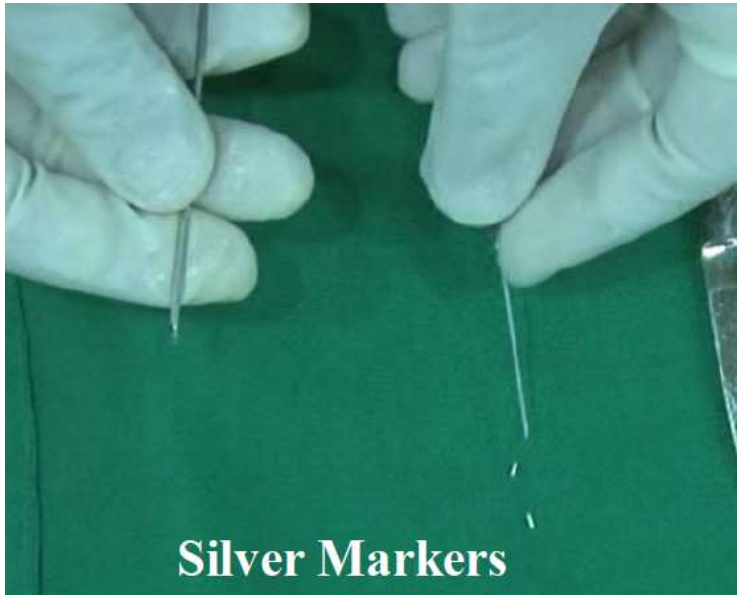


264 patients with tumour mapping Ljubljana, Vienna, Aarhus

Provided by Primoz Petric and Jacob Lindegaard Ljubljana/Aarhus

Brachytherapy application

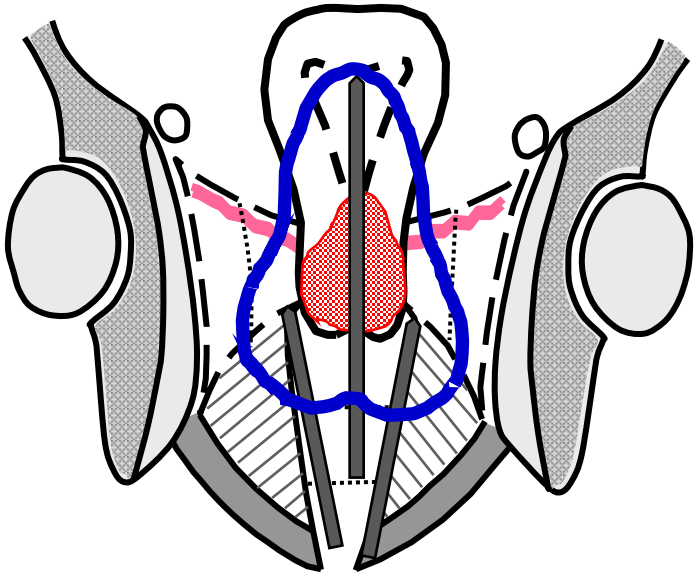
Instruments and applicators



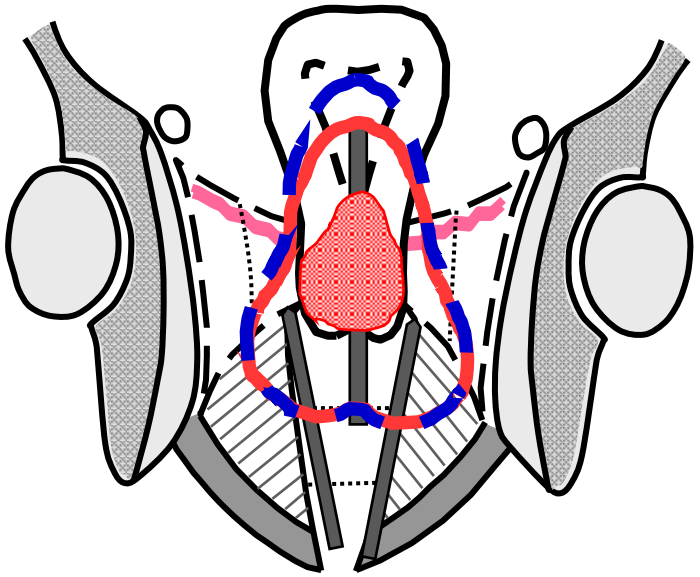
Brachytherapy application protocol

- *Anesthesia* / deep sedation.
- Lithotomy position, Antiseptic dressing / draping.
- *Clinical assessment on table.*
- *Bladder and bowel protocols*.
  - Empty vs full bladder
  - Flatus tube
- Uterine sounding – length / version. *TRUS guidance*
- *Dilatation of the uterine canal.*
- Placement of the uterine tandem (longest, appropriately curved).
- Placement of vaginal ovoids or ring *(largest) or template.*
- Insertion of needles. *No force, TRUS guidance.*
- *Securing applicators in place with one another.*
- Avoiding tissue injury.
- *Avoiding overzealous packing.*
- Securing applicators to patient.
- Final check before imaging.
  - Correct applicators, Appropriate fixation, No rotation.

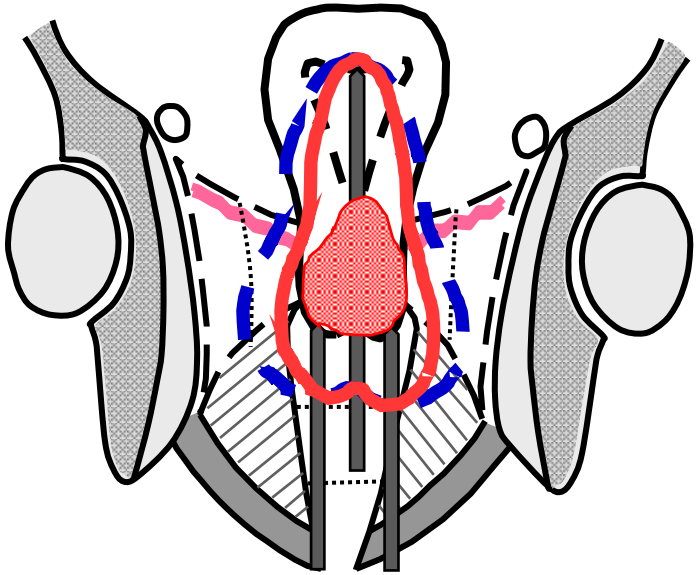
Longest tandem, largest ovoids



Ideal application
Longest tandem
Largest ovoids
Perfect pear



Poor application
Shorter tandem
Largest ovoids
Flattened pear



Poor application
Longest tandem
Smaller ovoids
Narrowed pear

Optimal packing

Applicators

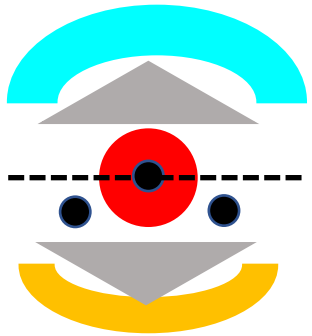
Rectum

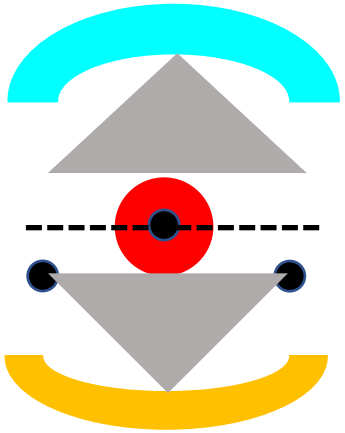
Bladder

Cervical tumour

Midline

Correct



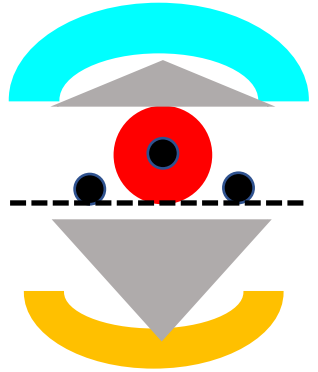


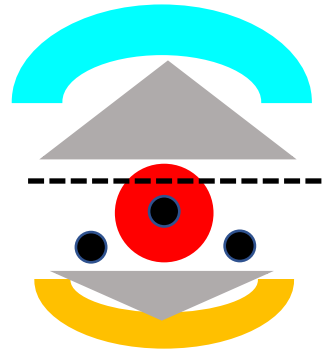
Incorrect

Ovoids displaced

Incorrect

Bladder excess dose



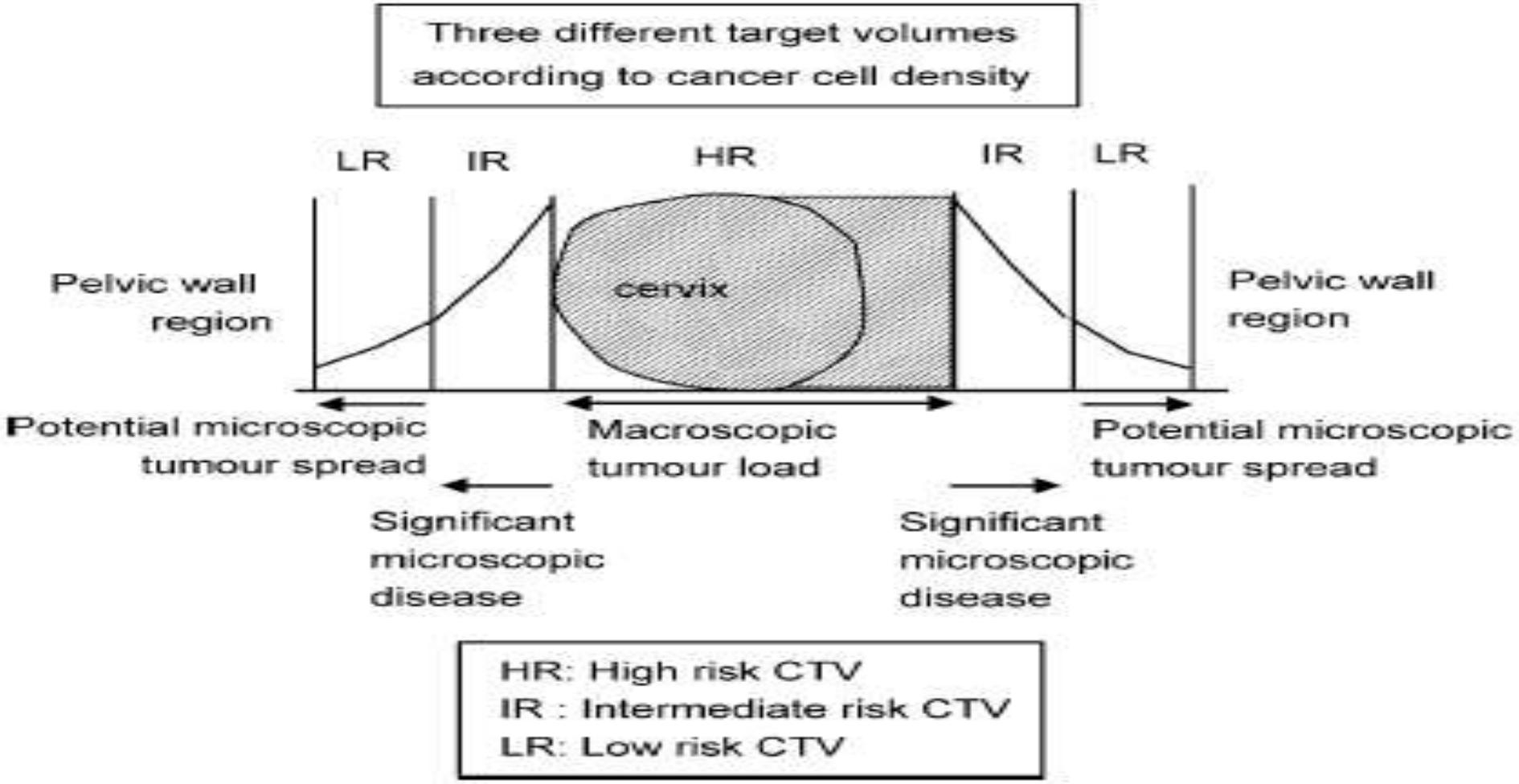


Incorrect

Rectum excess dose

Target concepts

GYN GEC ESTRO concepts



GYN GES ESTRO recommendations 2005

GYN GEC ESTRO / ICRU 89 concepts

GTV_B ($GTV\text{-}T_{res}$)

- Gross residual at the time of BT.
- Only visualized on MRI / clin exam. **Not on CT.**
- Usually central.
- To receive highest dose.

Priority 2

HRCTV ($CTV\text{-}T_{HR}$)

- GTV_B + Entire cervix.
- Includes "*grey zones*".
- Best visualized on MRI, possible on CT.
- Region of residual pathologic disease.
- To receive high dose.

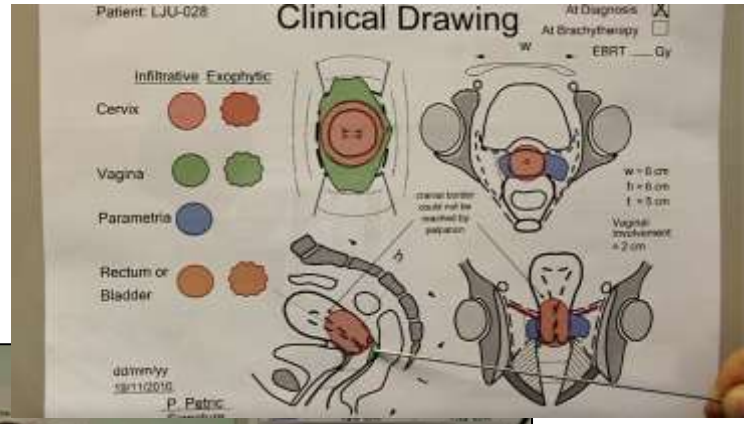
Priority 1

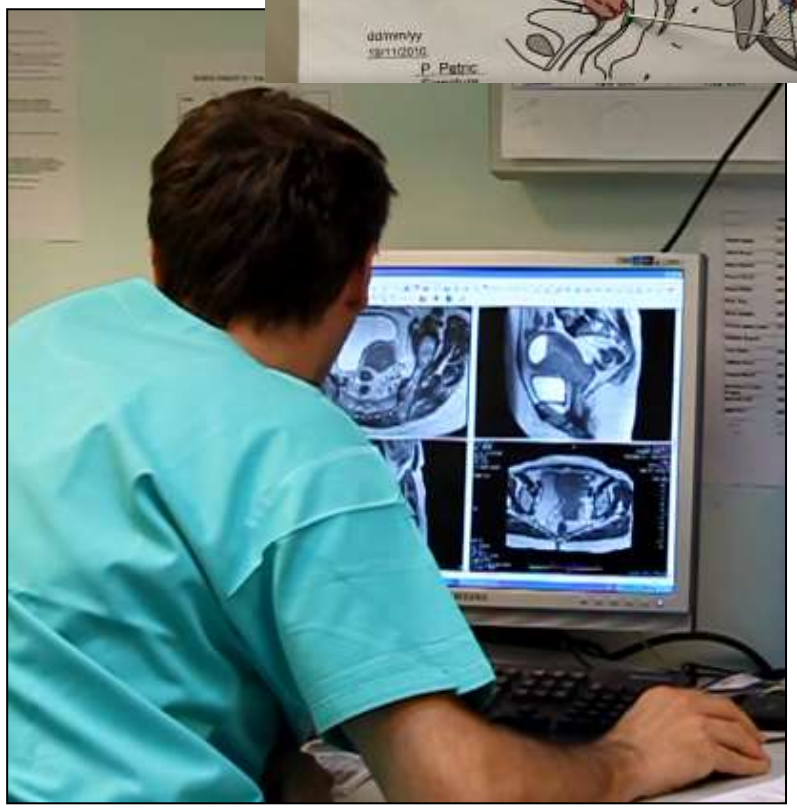
IRCTV ($CTV\text{-}T_{IR}$)

- HRCTV with margins (5 – 15 mm), must include GTV_{Diag}.
- Requires imaging at diagnosis.
- Region of potential microscopic disease.
- To receive intermediate dose.

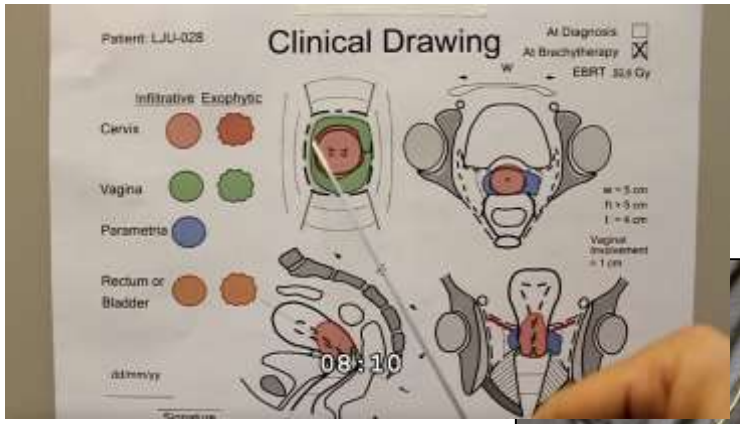
Priority 3

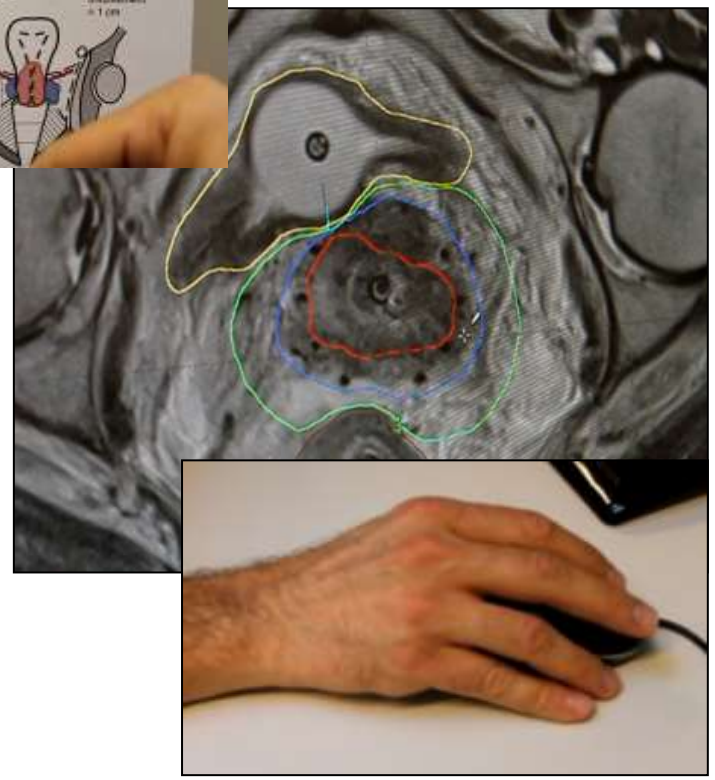
At Diagnosis





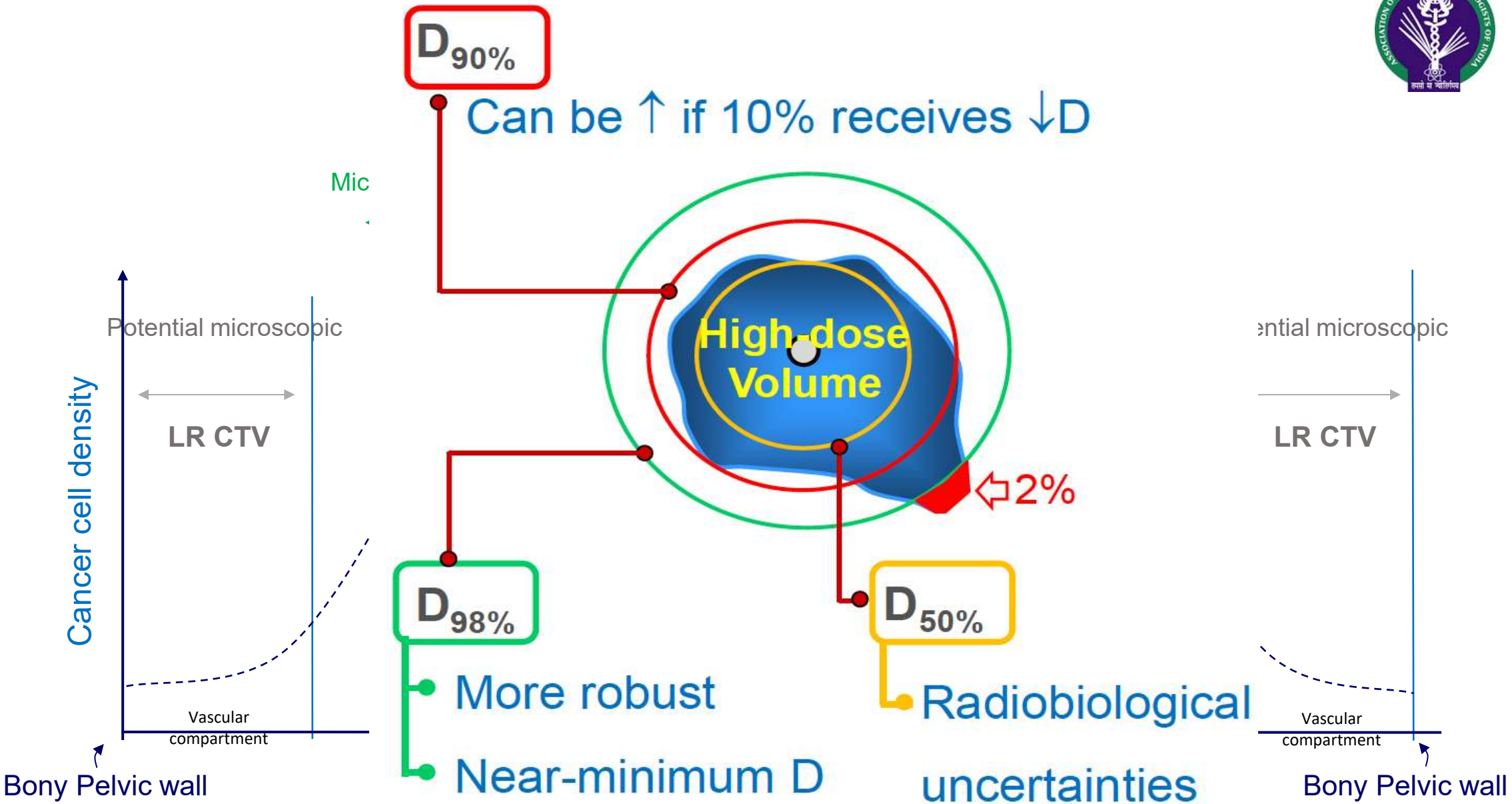
At Brachytherapy





The target delineation process

Courtesy of Dr. Primoz Petric



Different dose levels required to sterilize the three CTVs

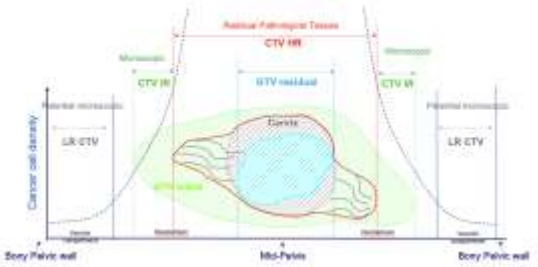
GTV diag

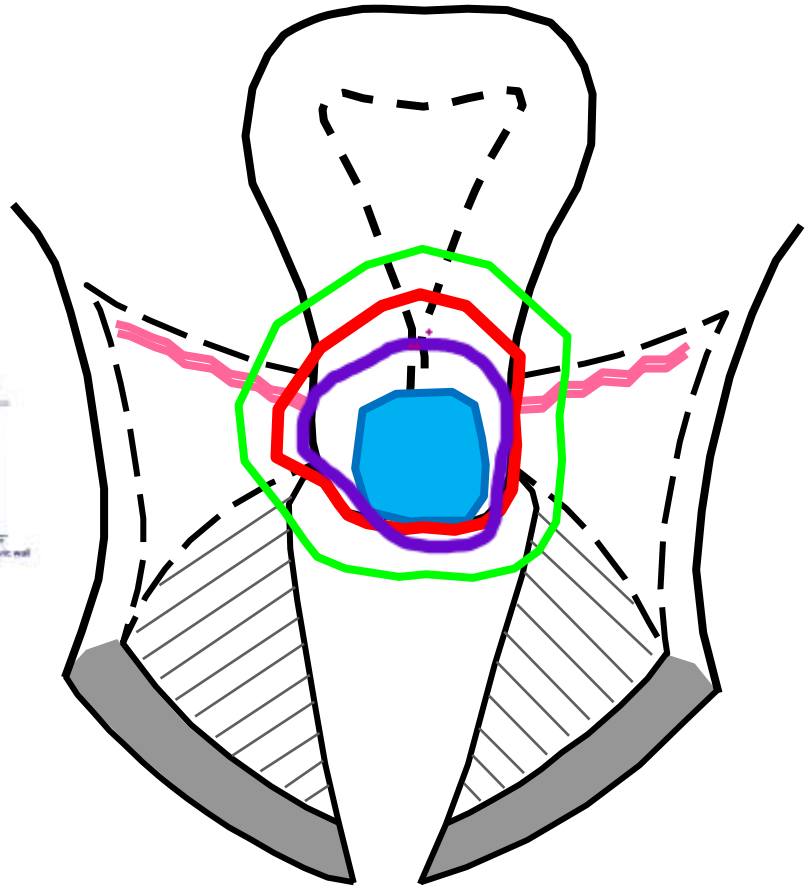
GTV res

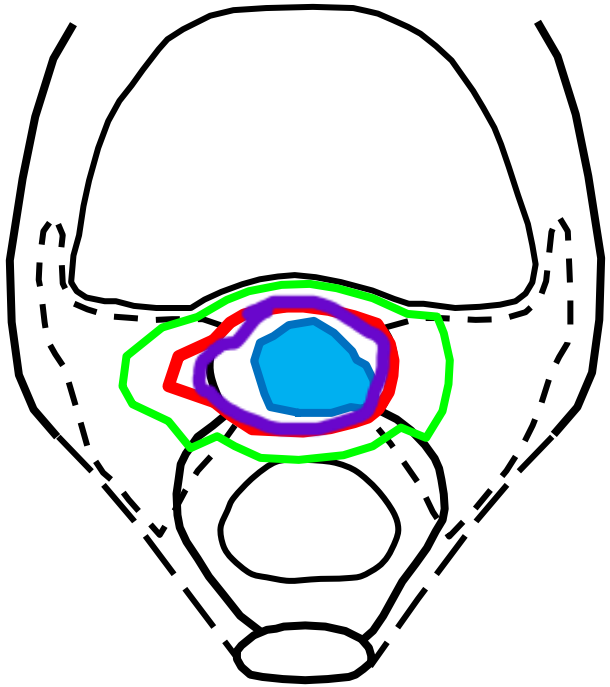
CTV-HR

CTV-IR

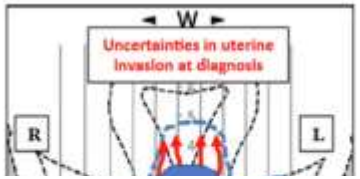
HRCTV is almost always overdrawn on CT compared to MRI, especially cranially.

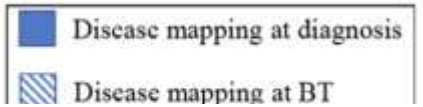




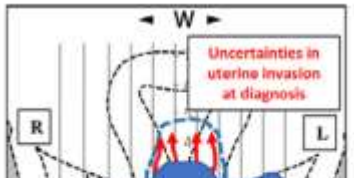


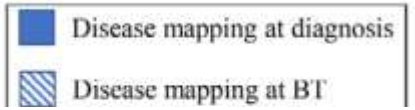
CT_{DG} – CT_{BT} Environment



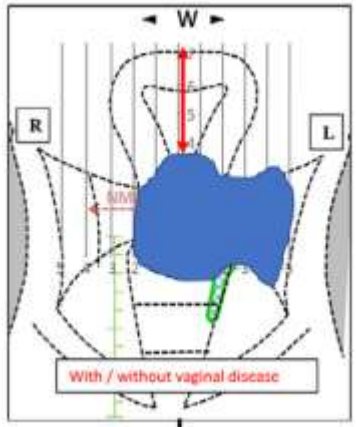


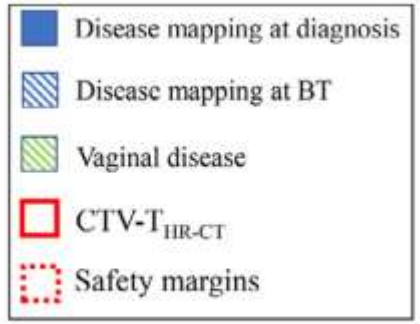
CT_{DG} – Pre BT MRI and CT_{BT} Environment

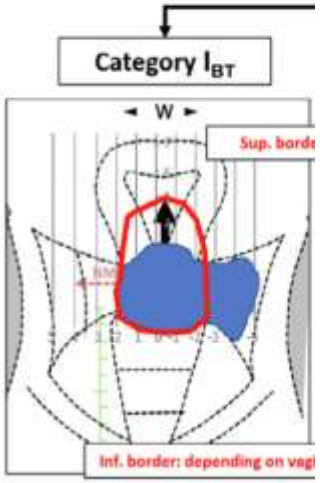


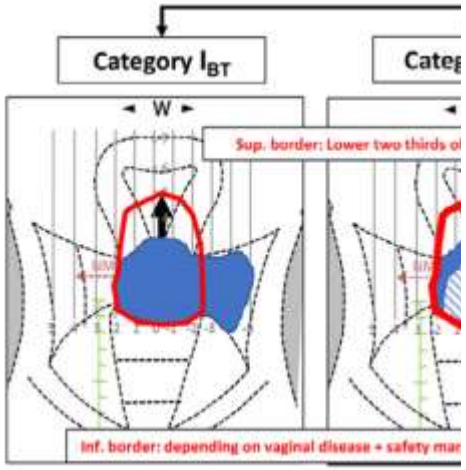


MR_{DG} – Pre BT MRI and CT_{BT} Environment

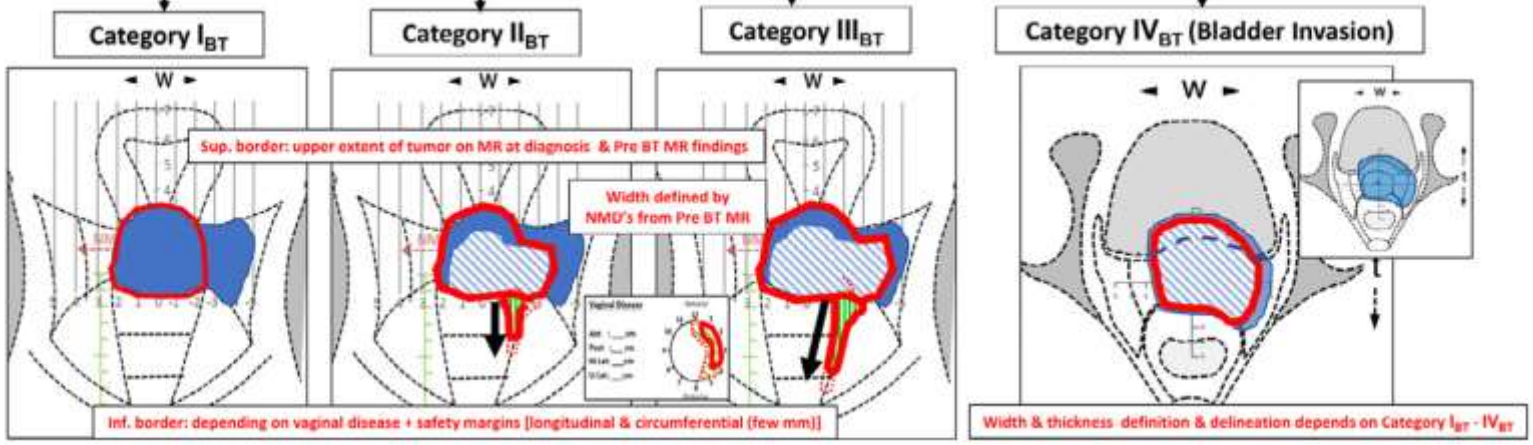






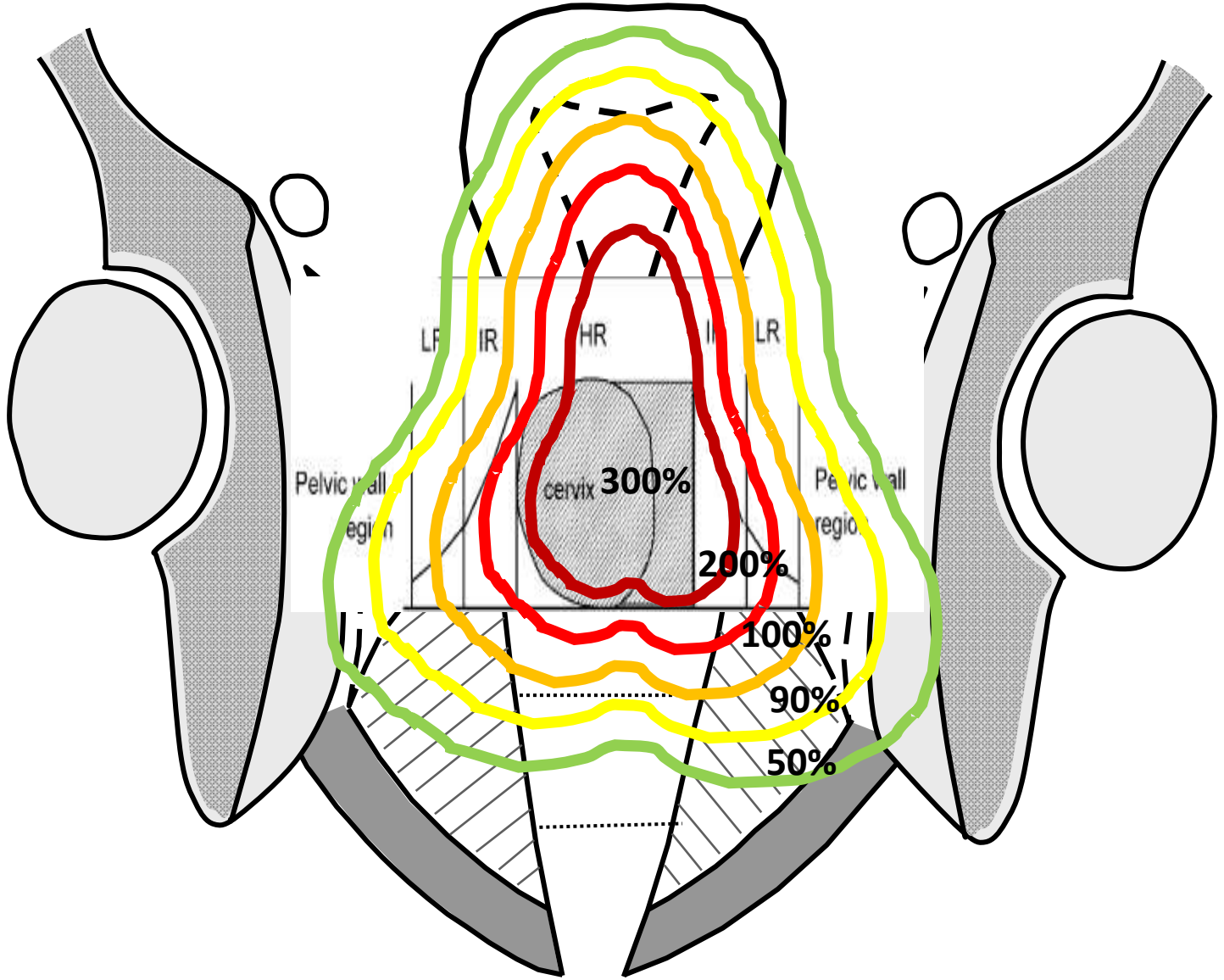


II_{BT}	Sign dise	
III_{BT}	Sign disease	parametrial disease
IV_{BT}	Any residual disease	Proximal parametri disease
		Distal/upto pelvic w parametrial disease



Mahantshetty U et al, R & O 2021

Brachytherapy dose gradient mimics disease



Organs At Risk

Contouring OARs

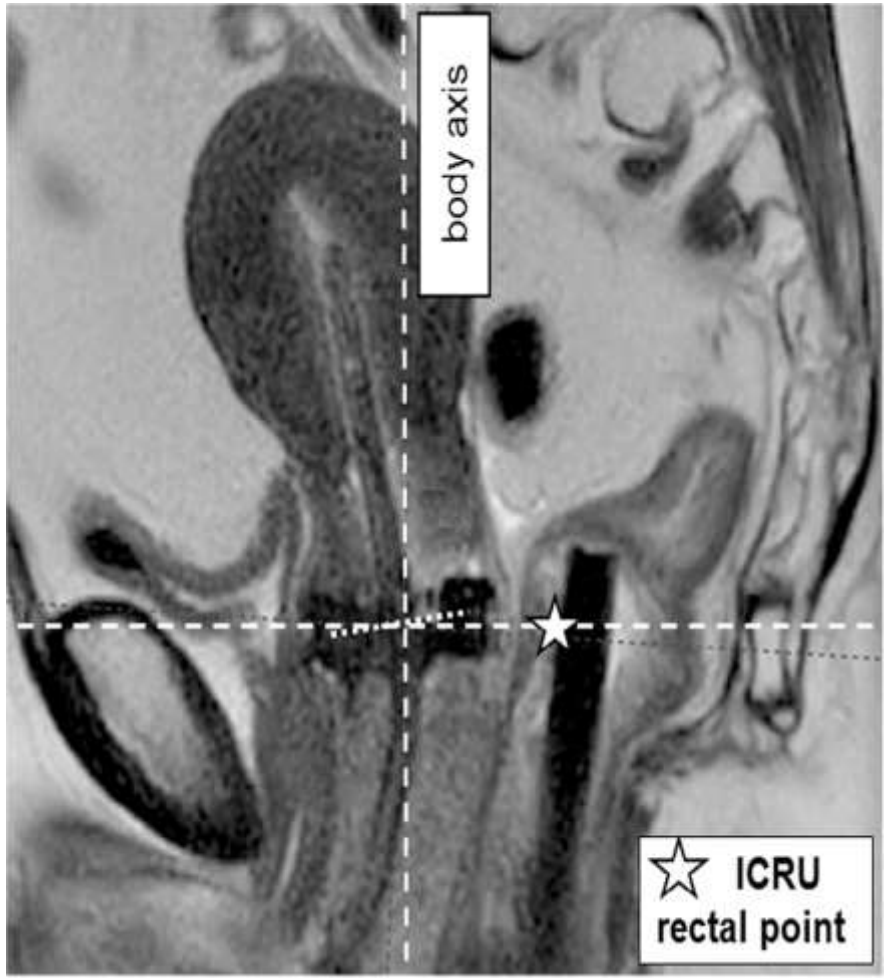
- The following organs are contoured (from at least *2 cm below the IR-CTV to 2 cm above the uterus*):
  - *Bladder*: Outer bladder wall including the bladder neck.
  - *Rectum*: Outer rectal wall from the anal sphincter to the transition into the sigmoid.
  - *Sigmoid*: Outer sigmoid wall from the recto-sigmoid flexure to at least 2 cm above the parametria and the uterus.
  - *Bowel loops*: Outer contours of loops positioned within 3-4 cm to the uterus and applicator
- For specific endpoints, small sub-volumes (bladder trigone/neck, anterior rectal wall) may be contoured.

Pötter et al et al 2006; ICRU 83 Section 6.2

Rectovaginal reference point

- The recto-vaginal reference point is positioned at the intersection level between tandem and the source positions in the ovoids or ring and *5 mm dorsal of the posterior vaginal wall* on the axis perpendicular to the body axis.

- Keeping the steep dose gradient of brachytherapy in mind, the 5 mm distance provides a more reliable dose estimate compared to points very close to or on the surface of the applicator.



Kirchheiner et al et al 2016; ICRU 83 Section 6.2

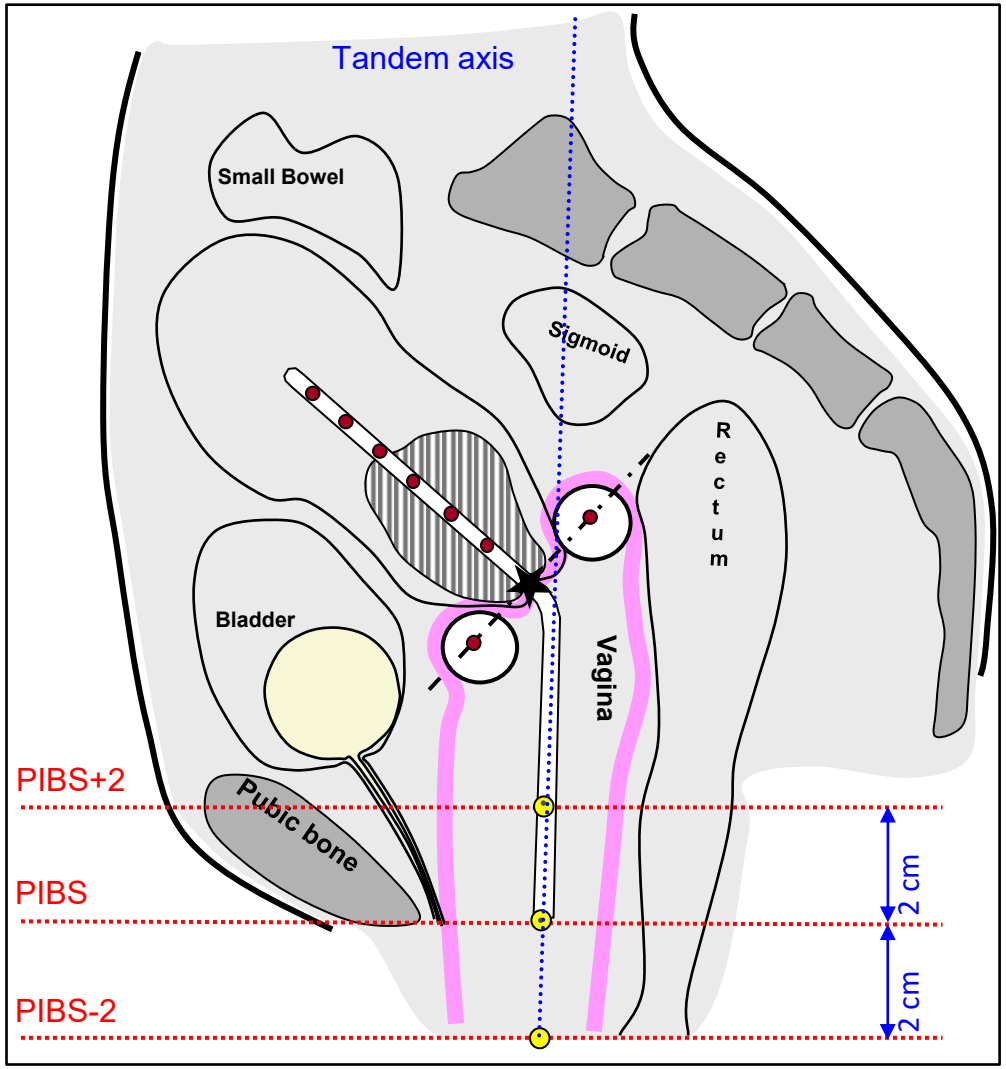
Posterior Inferior Border of Symphysis (PIBS) Points

Brachytherapy

PIBS +2
Upper vaginal dose

PIBS
Mid vaginal dose

PIBS – 2
Lower vaginal dose



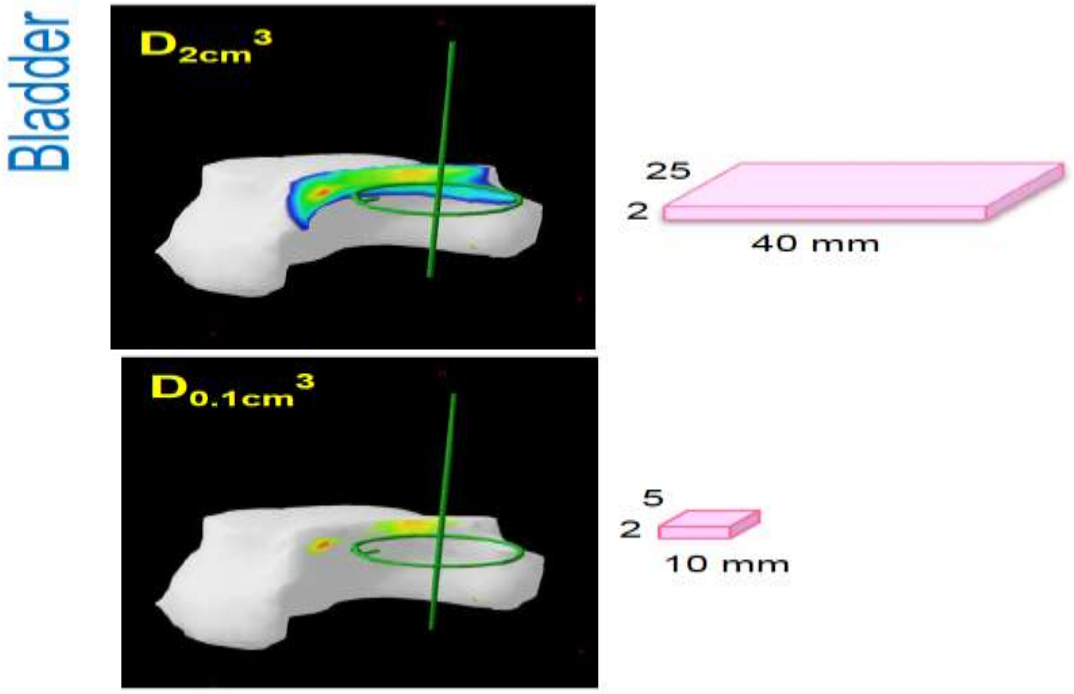
VRL

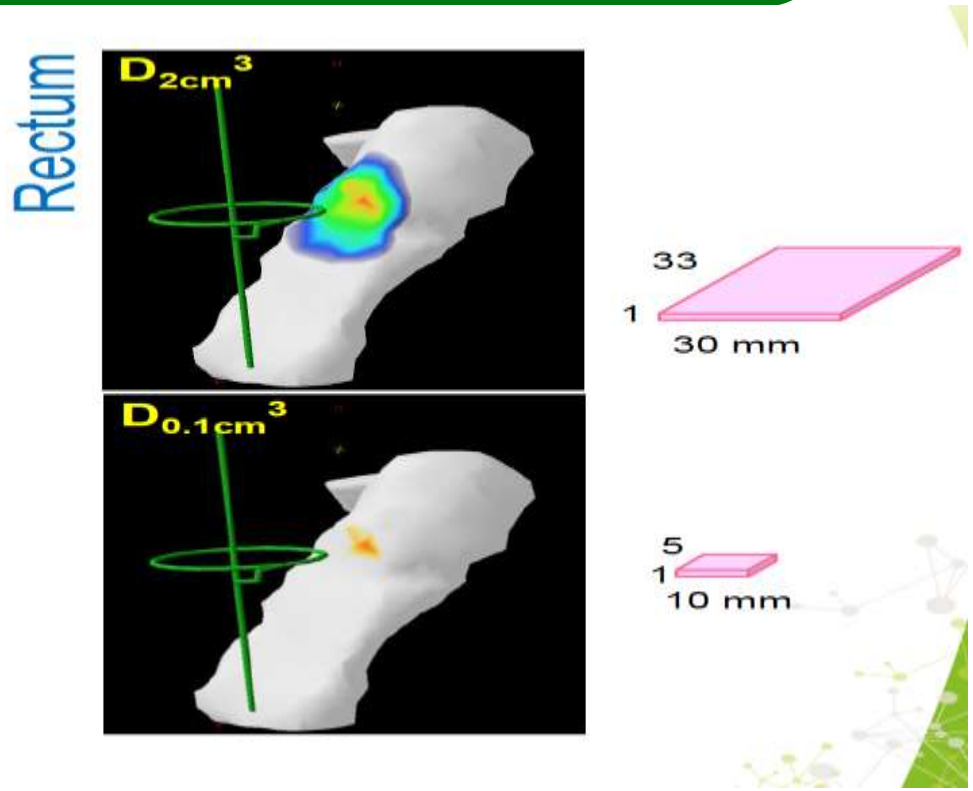
Vaginal reference length has a direct implication on PIBS doses and ***must be*** mentioned along with the PIBS doses.

Westerveld et al. R&O 2013;107:99-105.
Westerveld, et al. R&O 2016;120:420-7.
ICRU/GEC ESTRO Report 89, 2016.

Dose volumes for Organs at risk

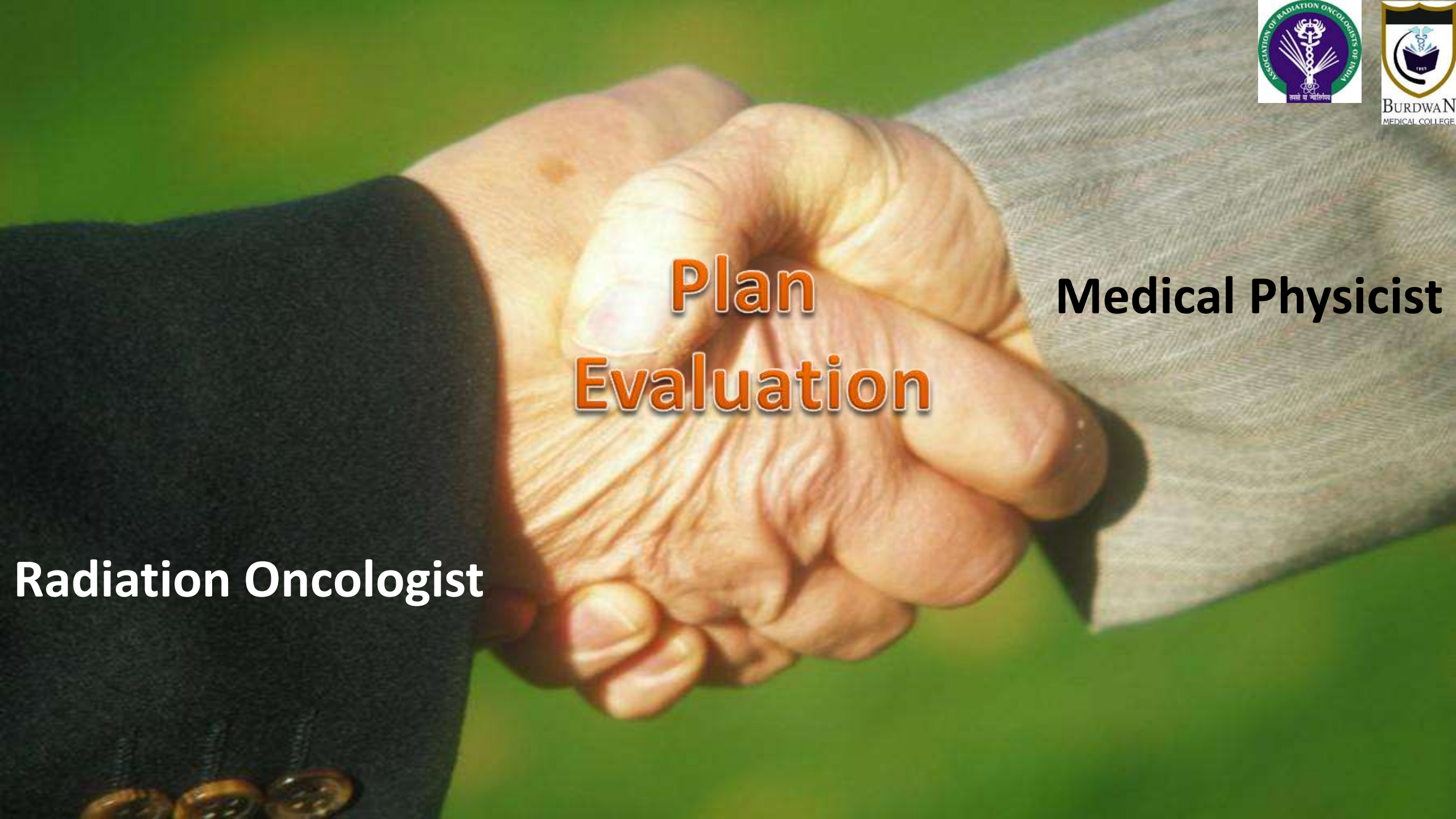
The ***minimum*** dose received by the ***maximally irradiated*** volume of the organ.





Westerveld et al 2013; ICRU 83 Section 6.2

Planning and plan evaluation


Plan
Evaluation
Medical Physicist
Radiation Oncologist

Planning Aim and Dose Limits

Target	D90 CTV_{HR} $EQD2_{10}$	D98 CTV_{HR} $EQD2_{10}$	D98 GTV_{res} $EQD2_{10}$	D98 CTV_{IR} $EQD2_{10}$	Point A $EQD2_{10}$
Planning Aims	> 90 Gy < 95 Gy	> 75 Gy	>95 Gy	> 60 Gy	> 65 Gy
Limits for Prescribed Dose	> 85 Gy	-	>90 Gy	-	-
OAR	Bladder D_{2cm^3} $EQD2_3$	Rectum D_{2cm^3} $EQD2_3$	Recto-vaginal point $EQD2_3$	Sigmoid D_{2cm^3} $EQD2_3$	Bowel D_{2cm^3} $EQD2_3$
Planning Aims	< 80 Gy	< 65 Gy	< 65 Gy	< 70 Gy*	< 70 Gy*
Limits for Prescribed Dose	< 90 Gy	< 75 Gy	< 75 Gy	< 75 Gy*	< 75 Gy*

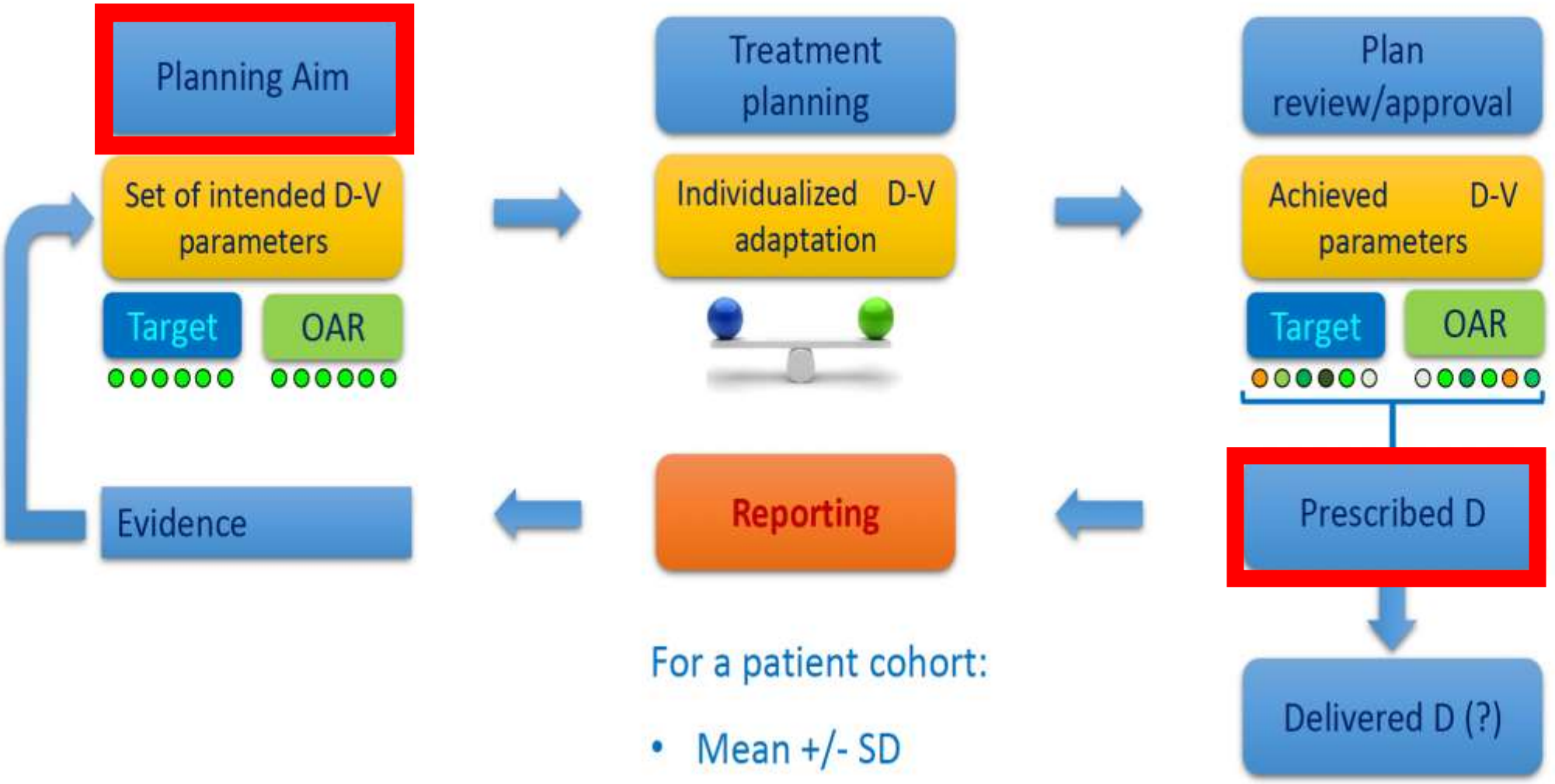
** for the sigmoid/bowel structures these dose constraints are valid in case of non-mobile bowel loops resulting in the situation that the most exposed volume is located at a similar part of the organ*

EMBRACE II protocol, Tanderup et al

Workflow of planning

1. Applicator reconstruction – *Manual* vs *Library* based, using *CT* vs *MRI*
2. Standard Loading - based on the traditional systems
3. Normalization to point A – *Planning Aim versus Prescribed dose*
4. Optimization – *Manual dwell time >>> Geometric > Graphical (not recommended)*
5. Additional needles – minimal loading only up to 15 – 20%
6. Recording, verification, audit

How to add EBRT and BT doses ?
Conversion of physical doses to EQD2 and simple addition

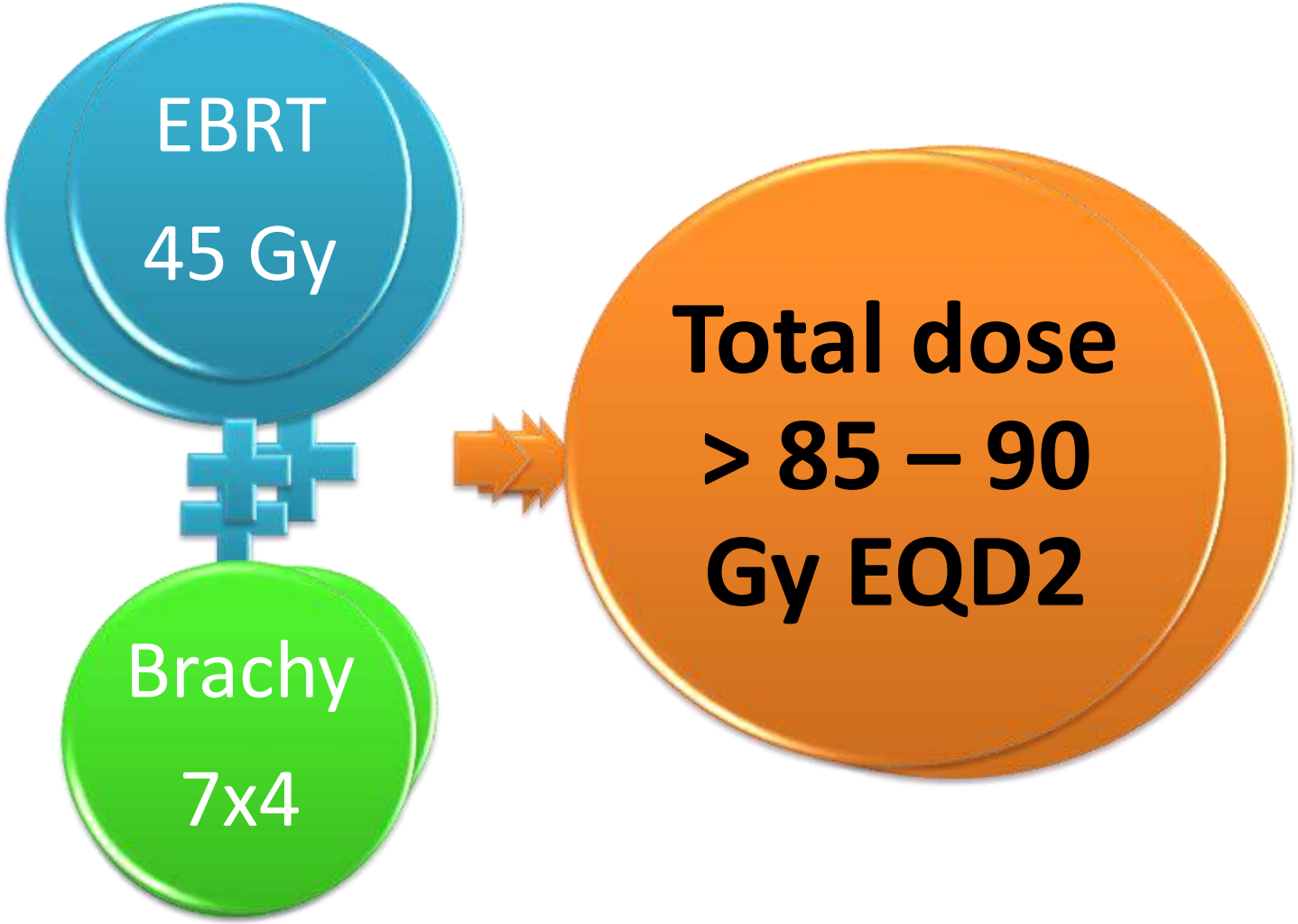


For a patient cohort:

- Mean +/- SD
- Unlikely = Planning Aim!

Courtesy of Dr. Primoz Petric

Relative contribution of EBRT vs Brachytherapy



Aim : Complete treatment within 7 to 8 weeks, ideally 50 days

LQ spreadsheet (absolute doses)

PHYSICAL - BIOLOGICAL DOCUMENTATION OF GYNAECOLOGICAL HDR BT

PATIENT , ID-number								tumour entity	
EXTERNAL BEAM THERAPY			**TUMOUR**		**OAR**			FIGO, TNM	
dose per fraction	1.8		$D_{1/2}$ [α/β=10Gy]		$D_{1/2}$ [α/β=3 Gy]				
fractions without central shield	25		44.3		43.2				
fractions with central shield			0.0		0.0			GTV at diag.	cm³
total dose	**45.0**		**44.3**		**43.2**			chemoth.	
Total volume (body contour) treated to 43 Gy	[cm³]								
Total volume (body contour) treated to 57 Gy	[cm³]								
BRACHYTHERAPY	**F 1**	**F 2**	**F 3**	**F 4**	**F 5**	**F 6**		dose values in Gy	
date									
physicist									
MR / CT	MRI							**TOTAL BT**	**TOTAL BT + EBT**
applicator(s): type, # needles									
applicator(s): dimensions									
Plan, remarks								*mean*	*sudder*
TRAK [cGy at 1m]		0.00	0.00	0.00				**0.00**	
TRAK intrauterine [%]		0.0%							
TRAK vaginal [%]		0.0%							
TRAK interstitial [%]		0.0%							
Planning aim for D_{90} CTV_{HR}		0	0	0					
planning aim $EQD2_{10}$	0.0	0.0	0.0	0.0	0.0	0.0		0.0	**44.3**
dose to + A left	7.0	7.0	7.0	0.0					
A_{left} $EQD2_{10}$	9.9	9.9	9.9	0.0	0.0	0.0		29.8	**74.0**
dose to – A right	7.0	7.0	7.0	0.0					
A_{right} $EQD2_{10}$	9.9	9.9	9.9	0.0	0.0	0.0		29.8	**74.0**
dose to A mean	H	7.0	7.0	0.0	0.0	0.0			
A_{mean} $EQD2_{10}$	#VALUE!	9.9	9.9	0.0	0.0	0.0		#VALUE!	**#VALUE!**
GTV_{res} [cm³]		0						*0.0*	*0.0*
D_{90}		0.0	0.0	0.0					
D_{90} $EQD2_{10}$	0.0	0.0	0.0	0.0	0.0	0.0		0.0	**44.3**
CTV_{HR} [cm³]		0.00						*0.0*	*0.0*
D_{90}		0.0	0.0	0.0					
D_{90} $EQD2_{10}$	0.0	0.0	0.0	0.0	0.0	0.0		0.0	**44.3**
D_{90}	8.5	8.5	8.5	0.0					
D_{90} $EQD2_{10}$	13.1	13.1	13.1	0.0	0.0	0.0		39.3	**83.6**
D_{50}		0.0	0.0	0.0					
D_{50} $EQD2_{10}$	0.0	0.0	0.0	0.0	0.0	0.0		0.0	**44.3**
CTV_{IR} [cm³]		0						*0.0*	*0.0*
D_{90}		0.0	0.0	0.0					
D_{90} $EQD2_{10}$	0.0	0.0	0.0	0.0	0.0	0.0		0.0	**44.3**
D_{90}		0.0	0.0	0.0					
D_{90} $EQD2_{10}$	0.0	0.0	0.0	0.0	0.0	0.0		0.0	**44.3**
BLADDER [cm³]		0						*0.0*	*0.0*
Bladder reference point		0.0	0.0	0.0					
ICRU $EQD2_3$	0.0	0.0	0.0	0.0	0.0	0.0		0.0	**43.2**
$D_{0.1cm^3}$		0.0	0.0	0.0					
$D_{0.1cm^3}$ $EQD2_3$	0.0	0.0	0.0	0.0	0.0	0.0		0.0	43.2
D_{2cm^3}	6.4	6.4	6.4	0.0					
D_{2cm^3} $EQD2_3$	12.0	12.0	12.0	0.0	0.0	0.0		36.1	**79.3**
RECTUM [cm³]		0						*0.0*	*0.0*
Recto–vaginal reference point		0.0	0.0	0.0					
ICRU $EQD2_3$	0.0	0.0	0.0	0.0	0.0	0.0		0.0	**43.2**
$D_{0.1cm^3}$		0.0	0.0	0.0					
$D_{0.1cm^3}$ $EQD2_3$	0.0	0.0	0.0	0.0	0.0	0.0		0.0	43.2
D_{2cm^3}	5.6	5.6	5.6	0.0					
D_{2cm^3} $EQD2_3$	9.6	9.6	9.6	0.0	0.0	0.0		28.9	**72.1**
SIGMOID [cm³]		0						*0.0*	*0.0*

Clinical outcomes

The EMBRACE journey

RETROEMBRACE

Retrospective.

Multi-institutional.

No fixed protocol.

EMBRACE I

Prospective.

Multi-institutional.

Fixed protocol.

MRI based adaptive BT.

EMBRACE II

Prospective.

Multi-institutional.

Fixed protocol.

IG-IMRT.

MRI based adaptive BT with more IC+IS.

EMBRACE III

Risk stratification.

BioEMBRACE.

MRI EMBRACE.

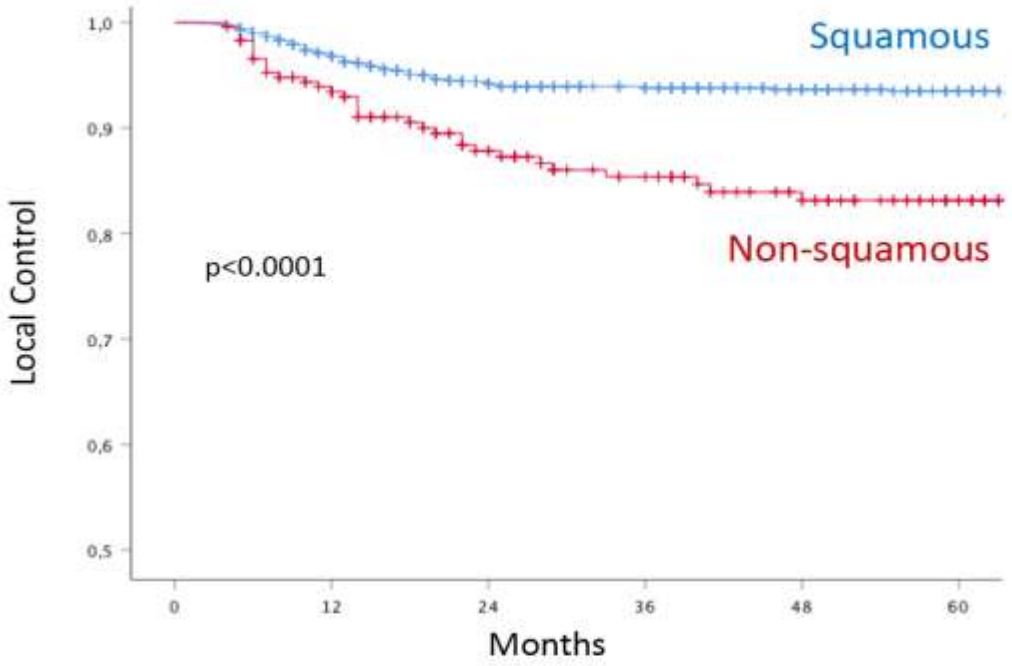
CT EMBRACE.

Real world data.

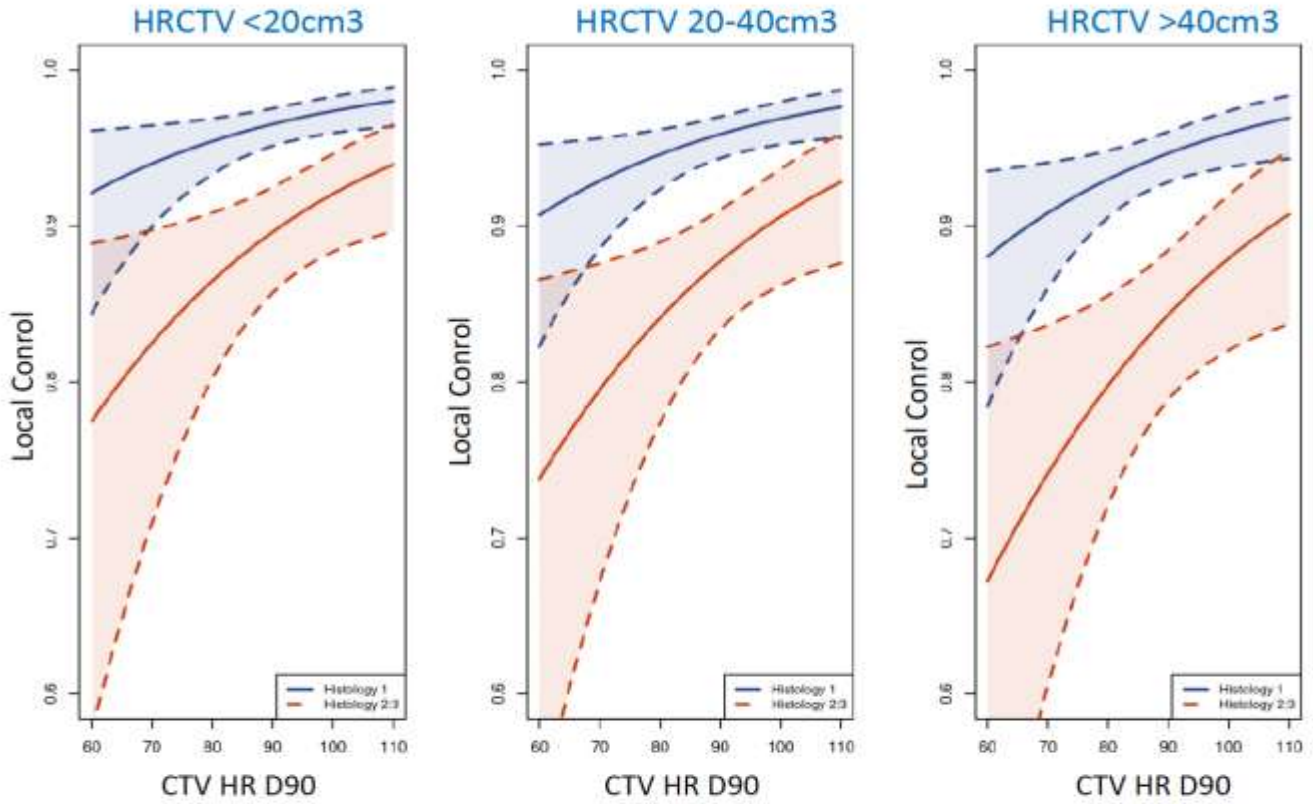
Outcome and predictors : Target

Histology and Local Control (EMBRACE 1)

N = 1291

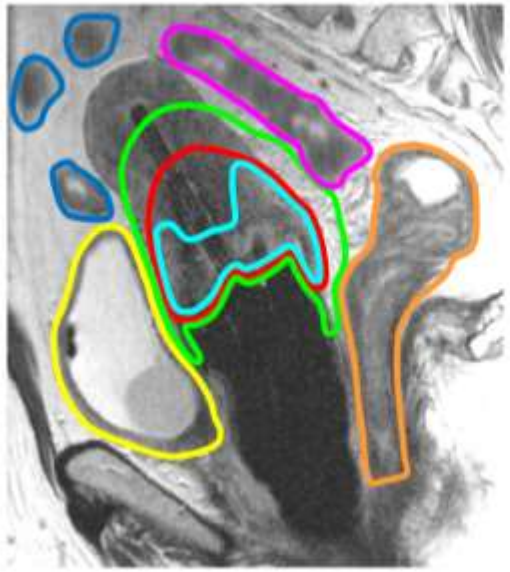


MVA: HR = **3.67**; (95% CI: 2.37-5.7); p<0.0001



Schmid M, et al. 2023

Outcome and predictors : OARs



Pötter R, et al. Lancet Oncol, 2021
Bahn E, Alber M. Radiother Oncol 144 (2020) 148-151.
Dimopoulos JC, et al. Radiother Oncol 93(2) (2009) 311-5.
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Spampinato S, et al. Int J Radiat Oncol Biol Phys 112(3) (2022) 681-693.
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Westerveld H, et al. Radiother Oncol 168 (2022) 8-15.
Smet S, et al. Int J Radiat Oncol Biol Phys 112(5) (2022) 1177-1189.
Serban M, et al. Brachytherapy 20(4) (2021) 796-806.

High Level of Evidence

Bladder	D_{2cm3}	→	Bleeding, Cystitis, Fistula
	ICRU Bl. point	→	Incontinence
Rectum	D_{2cm3}	→	Bleeding, Proctitis, Fistula
	ICRU RV point	→	Bleeding, Proctitis, Fistula
Bowel	D_{2cm3}	→	Diarrh, Bleed, Incont, Strict, Fist
Vagina	ICRU RV point	→	Stenosis
	PIBS point	→	Stenosis
Normal Tissue	V60Gy	→	Pooled GI, Cystitis, Fatigue

Under Investigation

Sigmoid c.	D_{2cm3}	→	Diarrh, Fist, Strict, Bleeding
Vagina	D-Surface maps	→	Stenosis
Ureters	$D_{0.1cm3}$	→	Stenosis

Outcome and predictors : Overall Treatment Time

Aim : Complete treatment < 50 days

1 week extra OTT ~ 5Gy less to CTV_{HR}

1 week extra OTT ~ loss of 2.5% local control

- How to keep overall treatment time limited?
- Primary tumour:
  - Start BT towards the end of EBRT or immediately after end of EBRT
  - With the help of IC/IS it is not necessary to wait further for tumour shrinkage
- Pathological lymph nodes
  - Simultaneously integrated boost

What we expect in the next decade?

Functional / biological imaging

Personalized applicators

Peeping into the future of brachytherapy

Automation and AI in contouring

Biology based dosing

Thank You!

drabhishekbasu@yahoo.com

45

AROICON 2025

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