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Endometriumkarzinom - Postoperative Radiotherapie

SELECTED ABBREVIATIONS	
VBT	Vaginal Brachytherapy
FU	Follow Ep
P-EBRT	Pelvic External Beam RadioTherapy
P&Pao EBRT	Pelvic & Paraaortic External Beam RadioTherapy
ChT	Chemotherapy
Obt	Obturator
AIE	Arteria Iliaca Externa
AII	Arteria Iliaca Interna
PS	Pre-Sacral
Pao	Paraaortic
S	Serous
CC	Clear Cell
CS	CarcinoSarcoma
UC	Undifferentiated Carcinoma
TRAK	Total Reference Air Kerma
MMRd	Mismatch Repair Deficient
NSMP	Non-Specific Molecular Profile
MP	Molecular Profile
POLEmut	Polymerase mutated
LG	Low Grade (Grade1 & 2)
HG	High Grade (Grade 3)
LVSI -f	Lymphovascular Space Invasion – negative or focal
LVSI s	Lymphovascular Space Invasion – substantial

REFERENCES	
All risk groups	ESGO/ESTRO/ESP Guidelines. Int J Gynecol Cancer 2021 ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma (bmj.com) ESMO/ESGO/ESTRO Guidelines. Int J Gynecol Cancer 2016 https://ijgc.bmj.com/content/ijgc/26/1/2.full.pdf S3 Leitlinie 2018 https://www.leitlinienprogramm-onkologie.de/leitlinien/endometriumkarzinom/ NCCN Guidelines. V 1.2021 https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf
Low risk	Sorbe B, et al. Int J Gynecol Cancer 19:873-8;2009 https://ijgc.bmj.com/content/19/5/873-878.long Klopp, et al Pract Radiat Oncol 4(3): https://www.ncbi.nlm.nih.gov/pubmed/24766678
Intermediate risk	Creutzberg C, et al. PORTEC-1. IJROBP 2011 https://www.sciencedirect.com/science/article/pii/S036030161100530X?via%3Dihub Nout R, et al. PORTEC 2. The Lancet 2010 https://reader.elsevier.com/reader/sd/pii/S0140673609621632?token=69202F9E8FC95B516BCA95D943CC87D92F40756A55EDD05C2039C42D541D5432CE607D203D927F16ABB8CAAAC8DC9ED8&originRegion=eu-west-1&originCreation=20210503135437 Sorbe BG, et al. “Norwegian” RND trial

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High Risk	De Boer S, et al. PORTEC 3. The Lancet Oncology 2018 https://www.sciencedirect.com/science/article/pii/S1470204518300792?via%3Dihub Emons G, et al. AGO Stellungnahme 2018 https://www.thieme-connect.com/products/ejournals/pdf/10.1055/a-0658-1918.pdf
Simulation & Contouring	Small W, et al. NRG/RTOG Consensus Guidelines. IJROBP 2021 https://www.sciencedirect.com/science/article/pii/S0360301620342206?via%3Dihub PORTEC 3 Study protocol: https://www.msbi.nl/promise/Portals/0/Users/027/27/27/Protocol_PORTEC3_FINAL_AMENDMENTS_071116.pdf?ver=Yg4PRXMJNivwhAhFmi-hBQ%3d%3d USZ SOP: Cervix & Endometrium LAG Contouring

PATIENT GROUP

<u>These guidelines cover:</u>

1. Verified non-metastatic & oligometastatic endometrioid adenocarcinoma, serous, clear-cell & undifferentiated carcinoma, carcinosarcoma.
2. Patients after hysterectomy + adnexectomy +/- lymphandenectomy +/- other staging and treatment decision at multidisciplinary tumor board.
3. Patients with signed informed consent to treatment.

<u>These guidelines do not cover:</u>

1. Inoperable patients.
2. Sarcoma, small cell carcinoma & other non-epithelial histologies.

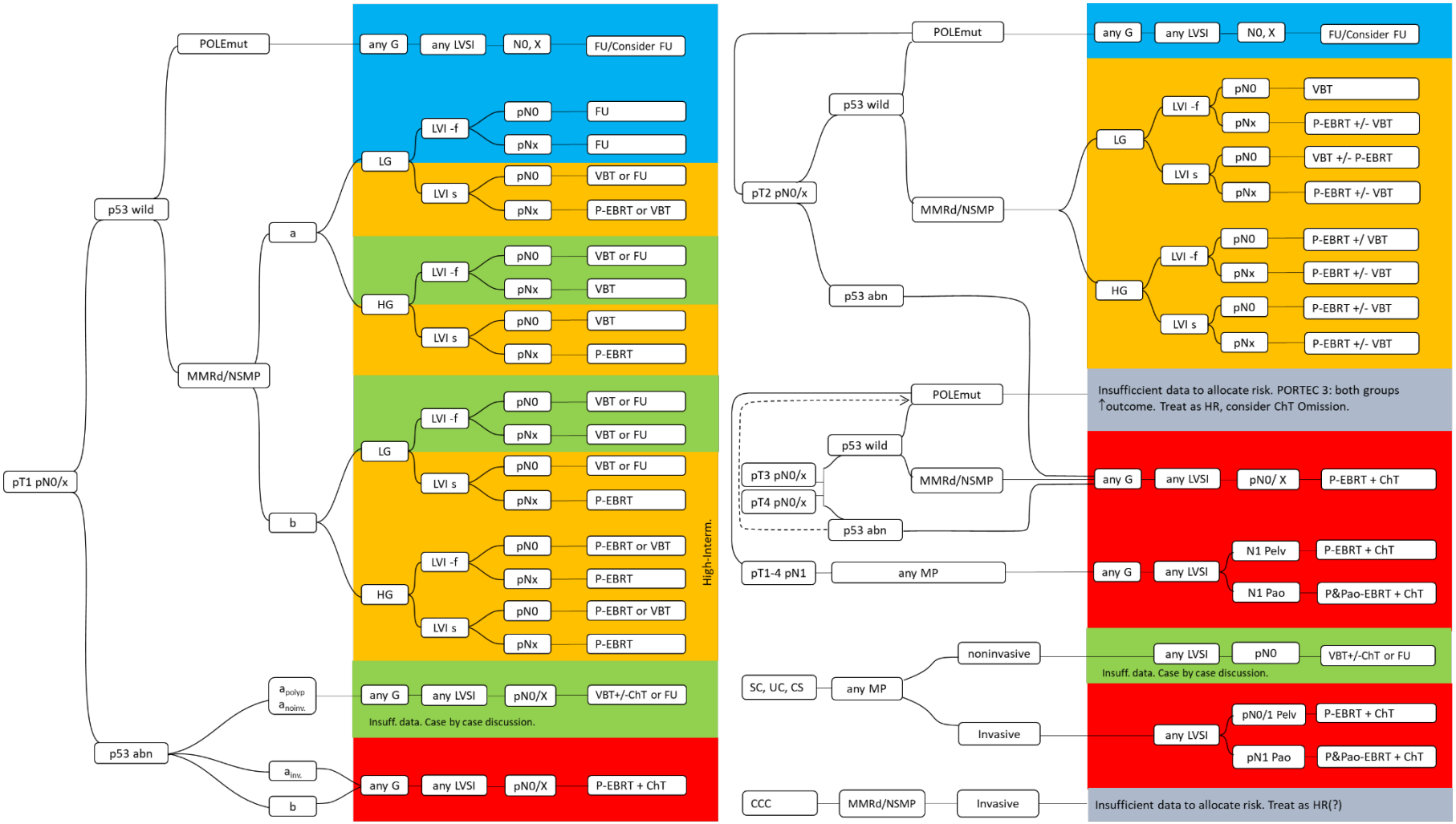
PRE-RADIOTHERAPY WORKUP

1. Family history, co-morbidities, RT contraindications?
2. General & Gynecological examination.
3. Imaging: preop. PET CT or CT of thorax & abdomen, pelvic MRI and/or TVUS
4. Conventional pre- & postop. pathology: T, type, G, MI, LVSI (no/focal/substantial), N…
5. Postop. IHC for MMR status (+MLH1 promotor methylation status if IHC loss of MLH1/PMS2) or MSI tests.
6. Genetic counselling if increased risk of Lynch syndrome.
7. IHC markers status: p53, MSH6, PMS2.
8. POLE molecular test (may be omitted in LR and IR cancer with low-grade histology).

RADIOTHERAPY 1st CONSULTATION

1. Consent, RT Scheduling
2. If BT: document vaginal length, diameter, and applicator dimensions
    - Plan 1st VBT appointment:
        - VBT alone: 4-6 weeks after surgery.
        - EBRT + VBT: immediately after EBRT.

POSTOPERATIVE MANAGEMENT ACCORDING TO RISK, Molecular status known (Abbreviations – page1)



LEGEND: Low risk; Intermediate risk; High-intermediate risk; High risk; ⇢ If p53 abn & POLEmut: manage as POLEmut. a and b designate the depth of invasion.

POSTOPERATIVE MANAGEMENT ACCORDING TO RISK, Molecular status unknown (Abbreviations – page1)

ENDOMETRIOID ADENOCARCINOMA						
Risk Group	**pT**	**G**	**LVI**	**pN**	**Adjuvant RT**	**Adjuvant ChT**
Low	1a	1, 2	-	0, x	FU	No
Intermediate	1b	1, 2	-	0, x	VBT or FU[a]	No
High-Intermediate	1a	1, 2	+	0	VBT or FU[a]	No
	1a	1, 2	+	x	P-EBRT	No
	1a	3	- , +	0	VBT or FU[a]	No
	1a	3	+	x	P-EBRT	No
	1a	3	-	x	VBT	No
	1a	3	+	x	EBRT	No
	1b	1, 2	+	0	VBT or FU[a]	No
	1b	1, 2	+	x	EBRT	No
High	1b	3	-	0	EBRT or VBT	No
	1b	3	-	x	EBRT	No
	1b	3	+	0	EBRT or VBT	No
	1b	3	+	X	EBRT	No
	2	1, 2	-	0	VBT	No
	2	1 ,2	+	0	EBRT + consider VBT	No
	2	3	-, +	0	EBRT + consider VBT	No / Consider
	2	1, 2, 3	-, +	x	EBRT + consider VBT	No /Cons.(G3)
	3a	1, 2, 3	-, +	0, x	EBRT[b]	Yes
	3b	1, 2, 3	-, +	0, x	EBRT + VBT	Yes
	Any	1, 2, 3	-, +	1	EBRT[b]	Yes
	Any	1, 2, 3	-, +	2	EBRT[b]	Yes
NON-ENDOMETRIOID HISTOLOGIES						
Risk Group	**pT**	**Hyst.**	**LVI**	**pN**	**Adjuvant RT**	**Adjuvant ChT**
High	1a	S, CC	-	0	VBT	No / Consider
	Any	S, CC	-, +	Any	P-EBRT	Yes
	Any	CS, UC	-, +	Any	Consider P-EBRT	Yes

EBRT CT SIMULATION	
1. Position: ○ Supine, arms on chest, bra removed, leg support. 2. Bladder filling: ○ Reproducible protocol at simulation & treatment. ○ 2 scans: full & empty bladder (CT_{FB} & CT_{EB}). 3. i.v. Contrast for full-bladder scan. 4. Rectal / sigmoid colon filling: ○ Patient empties the rectum at simulation & each RT. ○ If rectal diameter >4 cm on ≥1 transverse slice (≅ mid-V): empty rectum & rescan. ○ If persistence: laxatives & CT re-appointment. 5. Scanning: ○ 2 mm slices. ○ Region: • Pelvic RT: L 1/2 to upper 1/3 of femur. • Pelvic + paraaortic RT: T8/9 to upper 1/3 of femur. • Inguinal RT planned: lower border mid-femur.	

EBRT CONTOURING		
Target Volumes		Cervix & Endometrium LAG Contouring
1. CTV T LR init FB	Initial Low-Risk CTV of 1° tumor, FB scan ○ Proximal 1/2 of vagina ○ Supravaginal scar ○ Parametria bilaterally	
2. CTV T LR init EB	Initial Low-Risk CTV of 1° tumor, EB scan ○ Same structures as 1.	
3. ITV T LR	Internal Target Volume of 1° tumor = 1 + 2 + adaptations	
4. CTV E	Elective nodal CTV:	
	○ Stage I: Obt, AIE, AII, distal AIC to L5/S1	
	○ Stage II: Obt, AIE, AII, PS, AIC to aortic bifurcation.	
	○ Stage IIIA: based on tumor growth.	
	○ Stage IIIB: Obt, AIE, AII, PS, AIC to aort. bif.; + Ing, if lower vaginal 1/3.	
	○ Stage IIIC1: Obt, AIE, AII, PS, AIC to aortic bifurcation +/- Pao up to 1-1.5 cm above left renal vessels. Min. 2 cm above the highest involved N.	
	○ Stage IIIC2: Obt, AIE, AII, PS, AIC, Pao up to 1-1.5 cm above left renal vessels. Min. 2 cm above the highest involved N.	
5. V homogen	Vaginal cuff + 1 cm margin (only if VBT planned)	
6. ITV1_V1_1a	Internal target volume = ITV T LR + CTV E	
7. PTV1_V1_1a	Planning target volume = ITV1_V1_1a + 5 mm	
Organs at risk		
1. Rectum	Ano-rectal to recto-sigmoid junction.	
2. Sigmoid colon	Recto-sigmoid to sigmoid-descendens junction.	
3. Bladder	Urethral-vesical junction to bladder dome.	
4. Bowel	Bowel loops + mesentery, ≥1 cm above PTV. Not sigmoid colon.	
5. Femurs	Proximal femur; separate L/R	
6. Bones / marrow	L4/L5 - under ischial bone. If Paraaortic: upper border 1 vertebra above PTV.	
7. Spinal cord	≥1 cm above PTV	

8. Kidneys	Parenchyma; separate L/R.	

EBRT Dose Prescription	
Intermediate risk:	45 Gy, 25 fractions a 1.8 Gy.
High risk:	48.6 Gy, 27 fractions a 1.8 Gy.

Concomitant chemotherapy		
High risk:	Cisplatin 50 mg/m2 week 1 & 4. After RT, 4 cycles of Paclitaxel / Carboplatin (gyn).	

EBRT TREATMENT PLANNING	
Plan on CT_{FB}.	

EBRT PLAN REVIEW, APPROVAL & PRESENTATION	
According to planning aims & constraints. Present at Mittagsrapport.	

EBRT TREATMENT

1. Linear accelerator, VMAT.
2. Full bladder, empty rectum.
3. Daily CBCT, offline review by RO.
4. Weekly review by RO.
5. If chemotherapy: weekly lab.

VBT pre-planning	
1. CT with VC in place just before 1st VBT. 2. Contour Bladder, Rectum, Sigmoid colon, Small bowel.	

VBT Procedure	
1. Position: lithotomy or normal supine	
2. Gynecological examination.	
3. Disinfect Vagina.	
4. Cover applicator with condom & lubricate with gel.	
5. Insert applicator.	
6. Reposition: lithotomy to supine.	
7. Fix applicator midline, horizontal.	
8. Knee support.	

VBT prescription and fractionation (Figure 2)

Use EQD2 VC Template K:\RAO_Aerzte\Anforderung_Planungsauftrag\HDR_Planungsauftrag\1. TOOLS\Endometrium - VC

1. Specify clinical target length. Standard: upper 1/3 of vagina.
2. Specify prescription depth. Standard: 5 mm.
3. Specify D & Fractionation:

○ VBT alone:	20 Gy / 4 fractions a 5 Gy, 2x/week
○ VBT alone in pT2:	25 Gy / 5 fractions a 5 Gy, 2x/week
○ VBT after EBRT:	10 Gy / 2 fractions a 5 Gy, 2x/week

VBT planning

1. Apply library plan.

2. Review D on CT – only at 1st VBT.
3. Optimize plan or technique if needed.

VBT PLAN REVIEW AND APPROVAL	
1. Plan review & approval (RO). 2. Plan review & approval (MP & 2nd MP).	

PRE-TREATMENT CHECKS & TREATMENT
1. Afterloader morning QA check (MTRA). 2. Emergency equipment check (MTRA). 3. Import approved plan to afterloader console (MTRA). 4. Check channel treatment times (MTRA & MP). 5. Approve plan (MTRA). 6. Time-out: patient, procedure, applicator, positions, times, plan name, source strength (MTRA). 7. Remove afterloader from safe (MTRA). 8. Connect transfer tubes to applicator (RO) & afterloader (MTRA). Check visually & verbally. 9. Push Test & Length Test (MTRA). 10. Last Man Out sequence (MTRA). 11. Adjust treatment room cameras (MTRA). 12. Specify team member for the case of emergency entry in BT room (MTRA). 13. Inform RO that pre-treatment checks are completed (MTRA). 14. Signal treatment start (RO). 15. Start treatment (MTRA). 16. Import & approve Treatment Report in ARIA (MTRA).

APPLICATOR REMOVAL (RO)
1. Position: supine. 2. Remove fixating device (RO) 3. Remove applicator (RO)

VBT PLAN PRESENTATION AND EVALUATION	
Present 1st VBT fraction after 1st treatment at Mittagsrapport.	

VBT reporting (See Figure 1) *Use EQD2 VC Template* K:\RAO_Aerzte\Anforderung_Planungsauftrag\HDR_Planungsauftrag\1. TOOLS\Endometrium - VC		
General		
○ FIGO Stage	○ Histology	○ Grade
○ EBRT nominal D	○ EBRT D/fraction	○ EBRT duration
○ BT Protocol	○ BT prescription depth	○ BT prescription length
○ TRAK	○ Active length	○ Reference V length
EQD2 point-doses (EBRT + BT)		EQD2 DVH parameters (EBRT + BT*)
○ A	○ $A_{surface}$	○ Bladder D2cc
○ A1	○ $A1_{surface}$	○ Rectum D2cc
○ A3	○ PD	○ Sigmoid Colon D2cc
		○ Bowel D2cc

FOLLOW UP
○ Vaginal dilatator + instructions given to the patient after VBT.

- First follow up 4-6 Weeks After RT.
- Further follow ups at radio-oncology: 1 / year.
- Regular gynaecological / oncological follow ups need to be ensured.

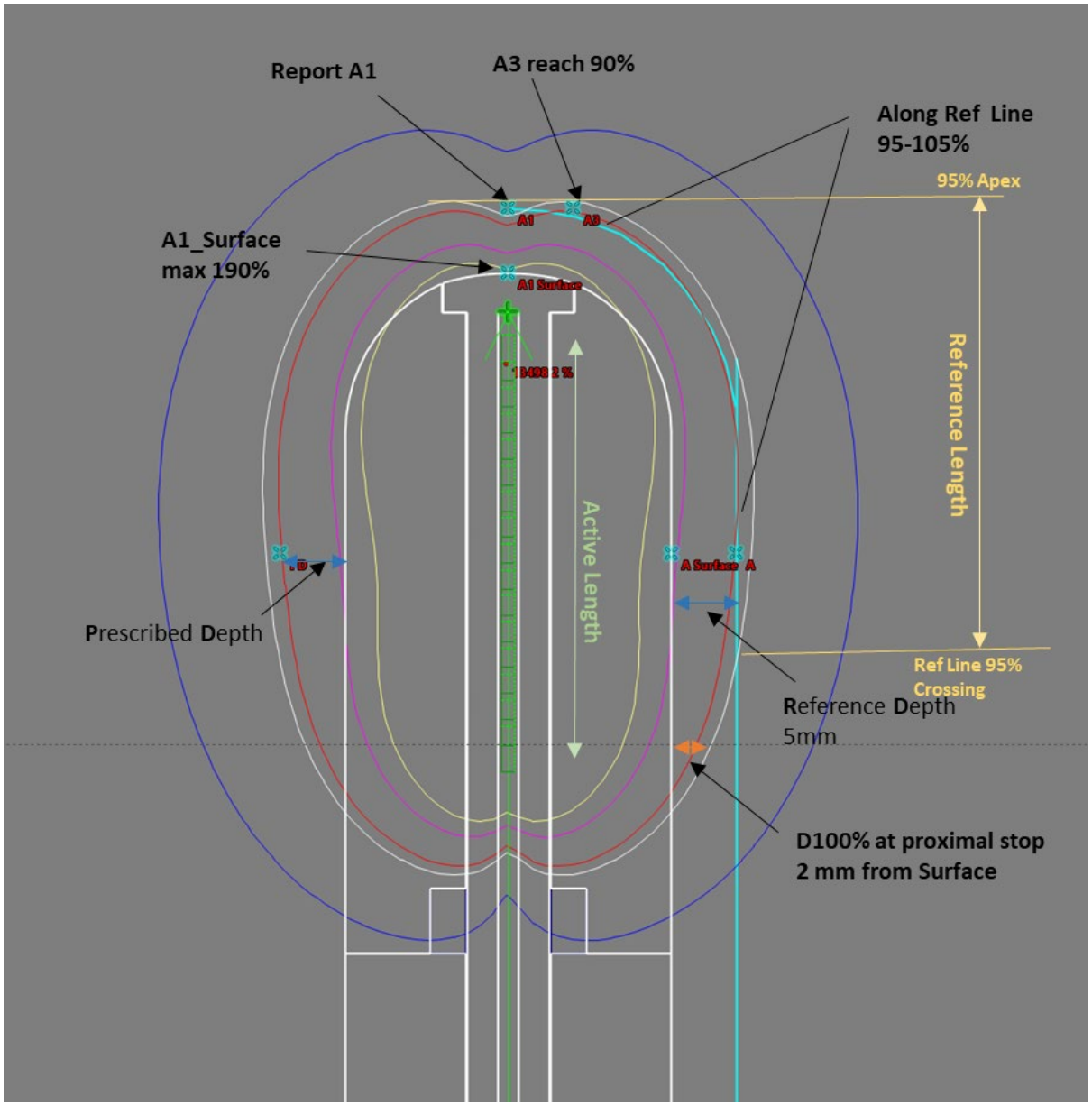


Figure 1. Concepts for basic VBT reporting.