# ICRU REPORT No. 89 PRESCRIBING, RECORDING, AND REPORTING BRACHYTHERAPY FOR CANCER OF THE CERVIX

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#### ICRU GEC ESTRO 89 (published 06/2016)



### **TOPICS COVERED**

- Prevention, Diagnosis, Prognosis, Treatment, and Outcome
- Brachytherapy Techniques and Systems
- Brachytherapy Imaging for Treatment Planning
- Tumor and Target Volumes and Adaptive Radiotherapy
- OAR- and Morbidity-Related Concepts and Volumes
- Radiobiological Considerations
- Dose and Volume Parameters
- Physics Aspects of Three-Dimensional Volumetric Dose Assessment
- Radiographic Localization of Absorbed Dose Points
- Sources and Dose Calculation
- Treatment Planning
- Summary of the Recommendations
- Clinical Examples

#### ABSTRACT

- This ICRU/GEC-ESTRO report starts with the essential background, including a clinical introduction, historical and current techniques including the concepts of volumetric imaging for cervix cancer.
- One key element is the four-dimensional adaptive target concept at certain time points during treatment by clinical examination and imaging.

#### ABSTRACT

- The radiobiology chapter explains the limitations of the linear quadratic model, but encourages the use of the EQD2 concept as the current best option for treatment planning and overall dose reporting.
- A detailed concept is recommended to report dose and volume parameters related to contours and reference points.
- The report includes detailed chapters on treatment planning, especially for three-dimensional volumetric approach, but also the underlying concepts of dosimetry which remains essential for volumetric and radiography-based planning.

Prevention, Diagnosis, Prognosis, Treatment, and Outcome

• To provide an overview of cancer of the cervix, Section2 begins with an outline of the currently available methods of prevention (vaccination), screening, diagnosis, and staging, followed by a discussion of stage- and risk-adapted treatment strategies, which consist of conservative and radical surgical interventions, radiotherapy, and chemotherapy alone or in various combinations.

## Brachytherapy Techniques and Systems

- Intracavitary gynecologic brachytherapy is the most widely used application of brachytherapy.
- A major aim of this report is to provide definitions of concepts and terms to enable valid and reliable exchange of information about treatment methods and clinical results.

 Brachytherapy "dosimetric systems" refer to specific, comprehensive sets of rules, adjusted for applicator type and radioactive isotope, distribution of sources in the applicator, and the consequent absorbed-dose distribution in a defined target

- The systems established in the early 1900s include the
- "Stockholm System,
- the Paris Method, and
- the Manchester System."



PARIS SYSTEM



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- The Manchester System, pervasive in current brachytherapy, includes dose specification at
- Point A,
- vaginal packing,
- and rectum and bladder dosimetry to limit the absorbed doses to the latter organs.



MANCHESTER SYSTEM

**Point A**: 2 cm lateral to the central canal of the uterus and 2 cm up from the mucous membrane of the lateral fornix in the axis of the uterus. (In practice, 2 cm up from the flange and 2cm lateral from the central axis)

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Point B : Being in the transverse axis through points A , 5 cm from midline

 In the Fletcher System, also pervasive in contemporary brachytherapy, ideal applicator geometry is key as is consideration of the absorbed-dose distribution relative to tumor volume.



# **TECHNIQUES**



- Tendem and Ring (Modified Stcokholm Technique)- for shallow fornices
- Tendem and Ovoid (Modified Manchester Technique)-barrel shaped cervix, using largest ovoid. To cover cervix, uterus, medial parametrium and upper 1-2 cm of vagina
- Tendem and Ring/Ovoids + interstitial needles (Modified Fletcher Technique) –large bulky tumors (for tumour coverage and OAR sparing), vaginal extension of disease, fistulae, pelvic side wall invasion



### **TECHNIQUES**

- Tendem and Ring-shallow fornices
- Tendem and Cylinder- upper vaginal stenosis/narrowing, superficial disease (5mm thick) in lower vagina
- Ovoids or Cylinders alone-for post op cases
- Interstitial only- Large lesions, lower vaginal disease, applicators not fitting

#### Manchester Applicators



#### **MRI compatible applicators-**





#### **Modern manchester applicator**







#### **Fletcher-suit applicator set**



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#### HDR SORBO APPLICATOR SET





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### **APPLICATOR SELECTION**

- Intact uterus should always have a tendem placed
- Supracervical hysterectomy –short tendem
- Intact uterus with extensive disease-tendem with interstitial needles

### **APPLICATOR INSERTION**

- Tandem and ovoid, tandem and ring or tandem and cylinders for intracavitary applications, inserted free hand
- Hollow interstitial needles inserted either freehand or with template or ultrasound guidance

#### Imaging after applicator insertion

- X ray
- USG
- CT
- MRI

### Reference volume and dose

- Absorbed dose of 60 Gy as the reference level volume
- Reference volume described is pear shaped co-incident with intra –uterine sources
- Reference volume is defined by 3 dimensions
- Height (dh): Maximum dimension along the intrauterine source, measured in oblique frontal plane
- Width(dw): Maximum dimension perpendicular to the intra-uterine source, measured in oblique frontal plane
- Thickness (dt): Maximum dimension perpendicular to the intrauterine sources and measured in saggital plane

#### CLINICAL DIAGRAM TEMPLATE



Figure 4.1. Clinical diagram template taken from the EMBRACE protocol (www.embracestudy.dk) (see also Supplementary appendix) (EMBRACE, 2015). Tumor delineation is done at the time of diagnosis, during treatment for response monitoring, and at the time of brachytherapy insertion.

#### **Reference volume and dose**





#### **Reference volume and dose**



Figure 10.4. Determination of the RPWRP and LPWRP. The lateral figure shows only the placement of the RPWRP due to space limitations. The placement of the left would be similar but with the point Ridder, to the "kell's marked [26:0steadBof 3. Adapted from Chassagne and Horight ((Shashagger and Horiot, 1977; ICRU, 1985).

### LIMITATIONS OF (2 D)RADIOGRAPHIC IMAGING







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# For determination of target

#### • point based dosimetry

• point A may overestimate or underestimate the tumor dose based on 3D imaging\*

#### no optimization:

- tumor coverage relies on tumor volume at time of BT, larger tumors requiring greater optimization to be adequately covered by the prescribed isodose line
- Kim et al<sup>\*\*</sup> found that dose to point A was significantly lower than the  $D_{90}$  for HR-CTV calculated using 3D image-based optimization

dose escalation not possible



Figure 10.6. Determination of the reference points for the bladder and rectum (Chassagne and Horiot, 1977; ICRU, 1985). The ICRU-rectum reference point (ICRU, 1985) is in this report called the ICRU-recto-vaginal reference point.

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#### For determination of OAR

#### **Bladder Point**

•ICRU bladder point:

wide range of **anatomic variations** in bladder points along the length of implant

•doses may be different at bladder **base & neck**, multiple points have to be taken

**HCRU** point may underestimate maximum doses to the OAR, in particular for the bladder

•ICRU bladder volume point does not represent the hottest part of the bladder that usually falls about 2 cm superior. highest dose often is about 2-4 times the dose at the bulb



# **Rectal point**

- ICRU rectal point:
- rectal markers is used which tend to lie on posterior wall of rectum while the **anterior wall is at greater risk**
- Stiff markers can move rectum, flimsy ones are difficult to push deep.
- ICRU rectal point doesn't usually represent the maximum rectal does, which, again often is **2-4 cm cephalad**.
- maximum does is up to **3 times the** ICRU point

None of this localizes the superior bowel - an organ very much at risk.

Neither the vagina- which again is an organ at risk





 Therefore a transition from point based (2D) to volume based(3D) brachytherapy is the key to modern techniques



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#### Tumor and Target Volumes and Adaptive Radiotherapy

- Brachytherapy in cancer of the uterine cervix can be adaptive and provide better dose conformation if the tumor/target can be precisely assessed and delineated in three dimensions, taking into account the tumor-growth pattern, change during the course of radio-chemotherapy, and the topography of the adjacent OAR.
- At the time of publication of ICRU Report 38 (ICRU, 1985), treatment planning for cervical cancer was based on gynecologic examination at diagnosis and radiography without the benefit of time dependent volumetric imaging.
- The target approach was recommended, referring to the clinical tumor presentation at diagnosis.
- Reporting the maximum width, thickness, and height of the 60 Gy reference volume covering this target was recommended.
- It is now well documented that major shrinkage of the initial gross tumor volume (GTV) and variation of topography occurs regularly during treatment, which typically begins with EBRTand simultaneous chemotherapy, leaving various amounts of residual GTV at the time of brachytherapy.

#### The Challenge: Tumour size and topography change during treatment



#### The evolution of the concept of residual GTV and HR CTV



### Tumor and Target Volumes and Adaptive Radiotherapy

- To allow adaptations of the treatment, repetitive gynecologic examinations and imaging are essential to determine tumor width, thickness, and height as a function of time.
- The high-risk CTV-T (CTV-THR), an adaptive CTV-T,1 includes the residual tumor, the cervix, and residual adjacent pathologic tissue.
- A second CTV, the intermediate-risk CTV-T (CTV-TIR), includes the initial tumor extent and the CTV-THR with a margin. The area of potential microscopic tumor spread is called the low-risk tumor related CTV-T (CTV-TLR).








## Tumor and Target Volumes and Adaptive Radiotherapy

- The general concepts, terms, and definitions enunciated in the series of recent ICRU reports on prescribing, recording, and reporting different radiotherapy (ICRU, 1993a; 2000; 2004; 2007; 2010) are integrated into the present report, which unlike these previous reports deals with a specific disease site.
- The GEC ESTRO Recommendations (Haie-Meder et al., 2005), generally accepted worldwide, form the basis of this adaptive strategy. Some attention is paid also to the use of the planning target volume (PTV), which plays a major role in planning and delivering EBRT.

## Tumor and Target Volumes and Adaptive Radiotherapy

- However, specific considerations have to be taken into account for brachytherapy due to the inherent absorbed-dose distribution characteristics, with large absorbed-dose in homogeneities throughout the target volume and steep absorbed-dose gradients adjacent to the target surface.
- Therefore, PTV margins have to be utilized with great care in intracavitary brachytherapy.
- Due to very limited target movement in relation to the position of the applicator, margins for compensation of geometric uncertainties playa minor role.
- Addition of margins in the orthogonal direction should be avoided as they would lead to a considerable absorbed dose increase in the whole volume.

### Example: cervical cancer IIIB: GTV shrinkage + adaptive $CTV_{HR}$ **EBRT dose**

**9 Gy** Cisplatin (40 mg/m<sup>2</sup>) x1

27 Gy Cisplatin (40 mg/m<sup>2</sup>) x3

36 Gy Cisplatin (40 mg/m<sup>2</sup>) x4

**0** Gy

**Initial GTV** 

18 Gy

Volume 75 ccm

Cisplatin (40 mg/m<sup>2</sup>) x2



Cisplatin (40 mg/m<sup>2</sup>) x5

G7X01/2018 CTV



### **Example: cervical cancer, FIGO IIIB**



# Applicator for up to mid-parametrial residual GTV and residual pathologic tissue



### The<sup>07</sup> Vienna Applicator

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# Applicator for up to distal parametrial residual GTV and residual pathologic tissue disease

### The<sup>97</sup>Vienna II Applicator

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### additional divergent template guided needles

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- Radiotherapy-related morbidity endpoints and (sub-) volumes of OAR are selected based on the typical morbidity profiles as known from clinical experience in cervical cancer radiotherapy.
- Certain targets in the OAR are selected that correspond to the typical pathology and morbidity patterns [e.g., rectal wall area (vasculature), telangiectasia/bleeding].

- This selection implies multiple targets within one organ according to different morbidity endpoints (e.g., bleeding versus urgency/frequency in the rectum).
- Small absolute volumes (e.g., 2 cm3, 0.1 cm 3) correspond to typical brachytherapy-related morbidity, such as teleangiectasia and ulceration/fistula.
- These volumes can have different locations in the OARs depending on the application technique

- The location of such volumes within a given organ can be reflected by anatomically defined points in OARs (e.g., ICRU bladder point at the bladder floor, mid- and inferior vaginal points) and/or by application-related points (upper vaginal points,ICRU recto-vaginal point).
- Larger volumes are also of interest for morbidity, including the whole circumference of a hollow organ (e.g., for stenosis, shrinkage).

- Due to contouring uncertainties, the latter approach is at present not recommended for the vagina. Protocols to ascertain a particular organ-filling status, as well as specific delineation protocols, are essential. Variations and uncertainties due to internal motion are known for OARs but should not be compensated for by adding shell margins around the OARs as suggested for EBRT.
- Organ motion in between imaging and absorbed-dose delivery leads to discrepancies between prescribed and delivered absorbed dose.
- Rather, these variations should be assessed through repetitive imaging and corrected for as appropriate.
- The assumption of static anatomical location of hotspots is recommended for small volumes in fractionated brachytherapy to assess the accumulated high-absorbed-dose region for a certain treatment.
- There is some evidence that such an approach is valid and reliable within reasonable confidence intervals.

- Volume selection and delineation of the hollow OARs adjacent to the CTV, such as rectum, sigmoid colon, adjacent small bowel, bladder (vagina, anus, ureter, and urethra) is performed along their walls, either as outer contour or as wall contour.
- For small absolute volumes, outer contour delineation is sufficient, whereas organ-wall contouring is recommended for volumes larger than 2 cm3.



Figure 6.1. MRI sagittal view of the vagina with applicator, rectal probe, and bladder balloon in place. Lines indicate the cranial borders of the upper, mid, and lower portion of the vagina. The lower vaginal line, as the transition between lower and mid-vagina, is defined at the level of the posterior-inferior border of the symphysis (PIBS, as denoted by asterisk, together with the other vaginal points in Figure 6.4). Endoscopic views of typical vaginal morbidity in the upper, mid, and lower portion: dome shape indicative of fibrosis, multiple telangiectasia, and mucosal pallor in the upper vagina; telangiectasia, mucosal pallor, and reduced rugae in the mid vagina; some pallor in lower vagina. 07/01/2018



Figure 6.2. MRI sagittal and transversal views with utero-vaginal applicator in place and probe in the rectum with three transverse lines, indicating the distal, middle, and proximal third of the rectum (a) and the ICRU recto-vaginal point (RVICRU, blue star in a and b). Lower line is at the level of the pelvic diaphragm, which is indicated by the PIBS (yellow star) and also shows the beginning of the anal canal (see Figure 6.4). The highest absorbed dose is at the level of the vaginal sources above the middle line in the mid-rectum. The 2 cm<sup>3</sup> rectal volume is shown on the anterior wall (c). The  $D_{2cm^3}$  and the  $D_{0.1cm^3}$  for the rectum and the corresponding isodose lines (67%/87% of the prescribed absorbed dose) are shown and correspond to 71 and 103 Gy EQD2<sub>3</sub>, respectively (a) (see Section 8.4.1; compare examples in the Appendix). Endoscopic images of multiple teleanglestasia/peterbianci celeated ROUD046terior wall 2 cm<sup>3</sup> volume after 18 months (d). Note 53



Figure 6.3. MRI sagittal and transversal views with utero-vaginal applicator in place and a rectal probe with three transverse lines, indicating the distal, middle, and proximal third of the rectum (a and b) and the ICRU recto-vaginal point RVICRU (a and b, blue star). Lower line is at the level of the pelvic diaphragm, which is indicated by the PIBS (yellow star) and demonstrates also the beginning of the anal canal (see Figure 6.4), which for this patient is not far from the vaginal sources (compare Figures 6.2 and 6.4). The 0.1 cm<sup>3</sup> rectal volume is shown on the anterior wall (c). The highest rectal absorbed dose is at the level of the vaginal sources below the middle line in the distal rectum. The  $D_{0.1 \text{cm}^3}$  for the rectum (arrow) is 108 Gy EQD2<sub>3</sub> and  $D_{0.000}$  is 80 Gy EQD2<sub>4</sub> (see Section 8.4.8); compare examples in the Appendix). Endoscopic images 07/01/26 theansient, asymptomatic ulteration (G2) of the anterior wall after 24 months (d) (modified from Georg et al., 2009). 54



Figure 6.4. Schematic anatomical diagrams (sagittal view) showing two different positions of the vaginal part of the utero-vaginal applicators, the cervix tumor, the uterus, and the reference volumes of OARs in two different patients. The most irradiated-tissue volumes adjacent to the applicator, *i.e.*, the reference volumes  $0.1 \text{ cm}^3$ ,  $2 \text{ cm}^3$ , and  $5 \text{ cm}^3$ , are illustrated for the various adjacent organs such as the bladder (neck), rectum (anus), sigmoid, and small bowel (see Section 8.4.1). The two panels show the different locations of the  $0.1 \text{ cm}^3$  and  $2 \text{ cm}^3$  reference volumes in the adjacent OARs [modified from GEC ESTRO Recommendations II; see also Westerveld *et al.* (2013)]. Reference points are indicated for the bladder (ICRU, 1985), the rectum and upper vagina (ICRU, 1985), and the mid- and lower vagina (PIBS  $\pm 2 \text{ cm}$ ). The vaginal reference length (VRL) (PIBS to midpoint between the vaginal sources) can serve as an indicator to assess the vagying position of the vaginal sources relative to the surrounding hormal discuestion structures (Westerveld *et al.*, 2013).

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#### 6.6 Recommendations on Morbidity-Related **Volumes and Points**

#### Level 1: Minimum standard for reporting

Volumetric imaging approximation based on:	Radiographic approxims based on:
Baseline morbidity and QoL assessment according to international classification systems	Baseline morbidity and assessment according to international classificati systems
Reference volumes on 3D images: Assessment of small organ volumes (0.1 cm <sup>3</sup> and 2 cm <sup>3</sup> ) for brachytherapy-related morbidity through outer-wall contouring on volumetric images in the	Reference point location radiographs or on a treatment plan:
treatment planning system:	
<ol> <li>(1) bladder contour/volume;</li> <li>(2) Rectum contour/volume.</li> </ol>	<ol> <li>Bladder reference po</li> <li>Recto-vaginal reference point</li> </ol>
Recto-vaginal reference point (positioned on volumetric images)	

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#### Level 2: Advanced standard for reporting All that is reported in level 1 plus:

Volumetric-imaging approximation based on:	Radiographic approximation based on:
Bladder reference point (positioned on volumetric images)	Vagina reference points (on radiographs):
Assessment of small organ volumes (0.1 cm <sup>3</sup> and 2 cm <sup>3</sup> ) for brachytherapy-related morbidity	Upper-vagina points (5 mm lateral from vaginal applicator surface, right and left) for brachytherapy-related morbidity Anatomical points for
volumetric images in the treatment-planning system:	(PIBS, PIBS ± 2 cm), for morbidity from EBRT
(1) Sigmoid-colon contour/volume;	and brachytherapy (on radiographs)
<ul> <li>(2) Bowel contour/volume (adjacent, fixed)</li> <li>Assessment of intermediate- and large-organ volumes for EBRT- and brachytherapy-related morbidity through outer-wall contouring on volumetric images in the</li> </ul>	

(1) Bladder contour/volume

treatment-planning system:

(2) Rectum contour/volume

(3) Sigmoid-colon contour/volume

(4) Bowel (adjacent) contour/volume

Vagina reference points (all contoured on volumetric images):

(1) Upper-vagina points (5 mm lateral from vaginal applicator surface,

07/@ht/a@fil@ft) for brachytherapy-related morbidity; ICRU 89, Misbah Hamid for ICRO-2018, SKIMS, Srinagar

### Level 3: Research-oriented reporting All that is reported in Level 1 and 2 plus:

Volumetric-imaging approximation based on:

- Volumes or surface for vagina;
- (2) Vaginal reference length/volume
- (3) Bladder sub-volumes, for example, the neck or wall;
- (4) Small volumes for anus; anal reference point;
- (5) Remaining volume of interest: body outline;
- (6) Other sub-volumes of potential interest

### Radiographic approximation based on:

- (1) Other bladder points;
- (2) Anatomical anal reference point;
- (3) Sigmoid-colon and small/large bowel reference points;
- (4) Vaginal reference length

## **Radiobiological Considerations**

- Intracavitary brachytherapy always results in a range of highly heterogeneous absorbed-dose rates and absorbed doses per fraction in the different tissues of the patient, with different absorbed-dose distributions characterizing each application.
- In addition, a large variety of dose and fractionation schedules are in current use.
- These variations in absorbed dose and absorbeddose rate have a major impact on tumor and normal-tissue effects.

## **Radiobiological Considerations**

- To assess and communicate the effects of such complex dosimetric and clinical situations with such large absorbed-dose inhomogeneities, it is evident that bio-mathematical models would be useful.
- Such models could serve to describe the assumed biological consequences of the various absorbed doses and absorbed-dose rates encountered.

## **Radiobiological Considerations**

- ICRU 89 proposes the concepts and methods to make such complex dosimetric, biological, and clinical scenarios meaningful, valid and reliable. In concordance with this ongoing work.
- the concept of equi-effective dose (EQD2), based on the linear-quadratic model, and EQD2 is recommended for gynecologic brachytherapy.
- These concepts provide a common basis for comparisons of absorbed dose, absorbed-dose rate, and absorbed dose per fraction (rate), and clinical results among different radiotherapy treatment techniques and departments.

- These are discussed in this report in Section 7, and recommendations are made concerning the choice of alpha/beta values in the linear quadratic model in the application of the EQD2 concept.
- Practical ways to implement such concepts into clinical practice are demonstrated in Section 7 (using a spreadsheet). For their application, one must be aware of the limitations of the models, as these concepts still require clinical validation, in particular for their use in brachytherapy.

Recommendation: for reporting Dose-Time Parameters Level 1: Minimum standard for reporting

Dose delivery pattern: 1. A. LDR (a) Absorbed dose (Gy) (b) Dose rate (Gy h<sup>-1</sup>) (c) Number of fractions (d) Time between fractions (h) B. HDR (e) Absorbed dose per fraction (Gy) (f) Number of fractions (g) Time between fractions (h) C. PDR (h) Absorbed dose (Gy) (i) Number of fractions, interval between fractions (j) Pulse size (Gy) (k) Number of pulses (1) Time between pulses (h) 2. Total treatment time (TT) in hours or days of EBRT, brachytherapy, and overall TT of combined modality

3. EQD2 values where available

Level 2: Advanced standard

All that is reported in Level 1 plus:

- 1. EQD2 values for target and OAR biological endpoints
- 2. Respective α/β values for the target and OAR,\*
- 3. Respective T1/2 of recovery\*
- 4. Applied recovery model, mono- or bi-exponential

\*For the moment, the advice is to follow the GEC-ESTR0 recommendations  $\alpha/\beta = 3$  Gy for late effects in OAR and 10 Gy for tumor response, and a  $T_{1/2}$  of 1.5 h for both

Level 3: Research-oriented reporting

All that is reported in Level 2 plus:

1. Detailed DVH parameters for target or OAR biological endpoints

2. NTPC and TPC calculations, with the model explicitly stated

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Dose and Volume Parameters for Prescribing, Recording, and Reporting Brachytherapy, Alone and Combined with External-Beam Radiotherapy

## **Recommendations for reporting**

Level 1: Minimum standard for reporting

Dose reporting

- TRAK
- Point A dose
- Recto-vaginal reference point dose
- $D_{0.1 {
  m cm}^3}$ ,  $D_{2 {
  m cm}^3}$  for the bladder, rectum

Level 2: Advanced standard for reporting All that is reported in level 1 plus

Dose reporting for defined volumes

- $D_{98~\%}, D_{90~\%}, D_{50~\%}$  for the  $\mathrm{CTV}_{\mathrm{HR}}$
- (D<sub>98 %</sub>, D<sub>90 %</sub> for the CTV<sub>IR</sub> if used for prescription)
- D<sub>98 %</sub> for GTV<sub>res</sub>
- $D_{98~\%}$  for pathological lymph nodes

Dose reporting OARs

- Bladder reference-point dose
- D<sub>0.1cm<sup>3</sup></sub>, D<sub>2cm<sup>3</sup></sub> for the sigmoid
- D<sub>cm<sup>3</sup></sub> for the bowel
- Intermediate- and low-dose parameters for the bladder, rectum, sigmoid, and bowel (e.g.,  $V_{15 \text{ Gy}}$ ,  $V_{25 \text{ Gy}}$ ,  $V_{35 \text{ Gy}}$ ,  $V_{45 \text{ Gy}}$  or  $D_{98 \text{ \%}}$ ,  $D_{50 \text{ \%}}$ ,  $D_{2 \text{ \%}}$ )
- Vaginal point doses at level of sources (lateral at 5 mm)<sup>a</sup>
- Lower and mid-vagina doses (PIBS, PIBS  $\pm 2 \text{ cm}$ )<sup>a</sup>

Level 3: Research-oriented reporting All that is reported in Level 1 and 2 plus

Absorbed-dose reporting for the tumor:

- $D_{98~\%}, D_{90~\%}$  for the  $\mathrm{CTV_{IR}}$  even if not used for prescription
- D<sub>90 %</sub> for the GTV<sub>res</sub>
- · DVH parameters for the PTV
- $D_{50\%}$  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., trigonum 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 OARs

- Dose-volume and DSH parameters for additional OARs and sub-volumes
- Vaginal dose profiles, dose-volume, and DSHs
- Length of treated vagina

Isodose surface volumes

- 85 Gy EQD2 volume
- 60 Gy EQD2 volume

## GEC - ESTRO RECOMMENDATIONS Dose Volume Parameters for Targets & OAR's



### D100, D90 for GTV, HR CTV, IR CTV

### D0.1cc, D1cc, D2cc for OARs

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### Dose prescription according to risk large variations in initial/adaptive volumes and doses



### Dose prescription protocol in cervix cancer DVH parameters for adaptive BT

	D90 CTV <sub>HR</sub> EQD2 <sub>1</sub>	D98 CTV <sub>HR</sub> EQD2 <sub>10</sub>	D98 GTV EQD2 <sub>10</sub>	D98 CTV <sub>R</sub> EQD2 <sub>10</sub>	Point A EQD2 <sub>10</sub>
Plannin g Aims	>90 Gy <95 Gy	>75 Gy	>95 Gy	>60 Gy	>65 Gy
Limits for Prescr ib <sup>67/01/2018</sup>	>85 Gy	– ICRU 89, Misbah Han SKIMS, Sr	>90 Gy id for ICRO-2018, magar	MRI guided adaptive	brachytherapy (IGABT)

### Dose prescription protocol in cervix cancer OAR dose volume constraints for adaptive BT

	Bladd	Rectum D <sub>2cm<sup>3</sup></sub>	Recto-	Sigmoid/
	er	EQD2 <sub>3</sub>	vaginal	Bowel D <sub>2cm<sup>3</sup></sub>
	D <sub>2cm<sup>3</sup></sub>		point EQD2 <sub>3</sub>	EQD2 <sub>3</sub>
	EQD2 <sub>3</sub>			
Planning	< 80	<65 Gy	<65 Gy	<70 Gy*
Aims	Gy			
Limits for	< 90	<75 Gy	<75 Gy	<75 Gy*
Prescri	Gy			
bed		Small Bowe	MRI guided adaptive	brachytherapy (IGABT)
Dose		Rectum		70% 50% D <sub>2cm</sub> = 61Gy (< 70Gy)
07/01/2018	ŀ	CRU 89, Missay Hangid for ICRO-2	018,	Bladder D <sub>2cm</sub> = 76Gy (< 80Gy)

nint = 64G



Figure 8.5. Sagittal view showing the volumes related to  $D_{0.1 \text{cm}^3}$ ,  $D_{2\text{cm}^3}$ , and a  $D_V$  with  $V > 5 \text{ cm}^3$ . Note that if the dose to large volumes should be evaluated, delineation of an organ wall is needed, while small volumes will be located mainly within the wall, even with whole-organ contouring. The location of the bladder and recto-vaginal reference points are also shown. For the vagina, heavily irradiated volumes of approximately 2 cm<sup>3</sup> and smaller are located adjacent to the lateral parts of the applicator not visible in this cross-sectional view (see Figures 8.12 and 10.1).

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Figure 8.12. Sagittal views showing the vagina at the time of EBRT and at brachytherapy with an intracavitary applicator in place. At the level of the vaginal source, dose points lateral to the rings or ovoids can be defined at 0 mm and 5 mm from the applicator surface. The additional points are defined along the central axis of the vagina in the cranio-caudal direction. The PIBS vaginal-dose point was defined a composterior from the posterior-inferior border of the pubic symphysis and for brachytherapy at the point of this line where it crosses to applicator tandem. From there, two additional points 2 cm up and down along the vaginal axis are defined with PIBS+2 representing the introitus level [from Westerveld *et al.* (2013)].
Physics Aspects of Three-Dimensional Volumetric Dose Assessment

- Co-registration and fusion as applied to EBRTand brachytherapy still have major unresolved problems.
- Besides spatial fusion, temporal fusion is also essential, as fractionated treatments are applied to anatomy that changes with time.
- Various types of uncertainties arising from spatial fusion (3D) and temporal fusion (4D) are systematically addressed and classified as intrafraction, inter-fraction, and inter-application uncertainties.

#### Uncertainties in cervix cancer brachytherapy:

Uncertainty (SD) for intracavitary brachytherapy

	Target (HR CTV D90)	OARs (D <sub>2cm3</sub> )
Source strength	2%	2%
Dose and DVH calculation	3%	3%
Dwell position uncertainty (reconstruction	4%	4%
and source positioning)		
DVH addition across fractions (previously	NA	1%*-?%
called "worst case assumption")		
Contouring (inter-observer)	9%	5-11%
Intra- and inter-fraction (intra-application)	11%	20-25%
uncertainties <sup>**</sup> (5)		
Total <sup>***</sup>	12%	21-26%
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 The major thrust of this report concerns the concepts of 3D volumetric and 4D assessment and representation of volumes/dimensions and doses, including the application of biological models.

- The same biological models as used in 3D volumetric situations can be applied for reference points as defined on radiographs.
- Therefore, specific attention is given in Section 10 to define these points for 3D radiographbased practice in limited resource settings for the tumor-related target specification, for OAR, and for lymph nodes.

 Some of the recommended reference points are taken from the previous ICRU Report 38 (ICRU, 1985) (bladder, rectum, pelvic wall, lymphatic trapezoid) and some additional points are specified (vagina).

- Essential to this report is the adoption of Point A as a major reference point with a straightforward definition related to the applicator for absorbed dose specification:
- for the planning aim (optional),
- for prescribing (optional), and
- for reporting (mandatory) in the volumetric image-based approach as well.

 This geometrical definition is recommended in order to provide a clear distinction with the anatomically defined target dose–volume definition that has been introduced here as a new concept.







Figure 12.2. Examples of Point A-based standard loading patterns delivering the same absorbed dose to Point A, but using widely different vaginal and tandem loading. The image on the left shows an absorbed-dose distribution without vaginal loading, the middle image relates to a dose-point optimization along tandem-and-vaginal applicator, and the absorbed-dose distribution on the right is based on the same number of dwell positions with equal dwell times in the vaginal applicator and the tandem. The width of the Point A isodose volume is illustrated by the maximum width of the light blue isodose.

#### 10.5 Recommendations for Reporting

Level 1: Minimum standard for reporting

Dose reporting:

- TRAK
- Point A dose
- Recto-vaginal reference point dose
- Bladder reference point dose

Level 2: Advanced standard for reporting All that is reported in level 1 plus

Dose reporting for defined volumes:

- Estimated dose in the CTV<sub>HR</sub>(according to estimated maximum width and thickness) (in the CTV<sub>IR</sub> if used for prescription)
- Pelvic wall point (optional)
- Lymphatic trapezoid (optional)
- Dose reporting for OARs:
- Vaginal point doses at level of sources (lateral at 5 mm) Lower- and mid-vagina doses (PIBS, PIBS ±2 cm)

Level 3: Research oriented reporting All that is reported in Level 1 and 2 plus

OAR volumes, points:

- Additional bladder and rectum points
- Sigmoid point
- Anal-canal point (e.g., low-vagina point)
- Vulva point (e.g., low-vagina point)
- Other points of interest
- OAR-dose reporting:
- Length of treated vagina
- Isodose surface volumes:
- 85 Gy EQD2 volume
- 60 Gy EQDW volume

#### Sources and Dose Calculation

- physical background for dose calculation.
- The source strength is specified in units of reference air-kerma rate (RAKR) at 1 m.
- The total reference air kerma (TRAK) is defined as the integral of RAKR over the whole treatment duration summed for all sources.

#### Sources and Dose Calculation

 For absorbed-dose calculation, the American Association of Physicists in Medicine (AAPM) Task Group 43 (Nath et al., 1995) formalism with recent improvements is recommended.

### **Recommendations for Reporting**

- Reporting of all cases should include:
- (1) The radionuclide and source models used.
- (2) The modality used [HDR, LDR, pulsed dose rate (PDR)].
- (3) The TRAK.
- (4) The geometric pattern of source-strength distribution (in RAKR or air-kerma strength) and treatment duration for LDR applications, or dwell-time pattern and source strength (in RAKR or airkermastrength)forHDRandPDRapplications.
- (5) The algorithm used for the absorbed-dose determination.

#### **Treatment Planning**

- the complete treatment-planning process for imageguided adaptive brachytherapy, incorporating the concepts and methods outlined in this report, is described.
- Treatment planning includes the decisions related to the use of radiotherapy (EBRT, brachytherapy) and chemotherapy, the planning aims, results of the medical examinations, definition of applicator geometry (pre-planning), imaging information, targetvolume determination, OAR contouring, dosimetricplan optimization, and integration of biological models into the treatment-planning process.

### **Treatment Planning**

- The final plan evaluation includes a complete assessment of the various dose-point and dose-volume parameters.
- The plan selected and prescribed is the most appropriate one that meets the needs of the clinical situation.

#### **Clinical Examples**

 Nine clinical examples describing in detail the various clinical, imaging, technical, and biological scenarios with respect to the FIGO stage of disease with and without nodes, the various EBRT techniques (3D conformal radiotherapy, IMRT), the different application techniques (tandem-ovoids/tandemring/tandem-mold, with and without interstitial needles), different absorbed dose rates (HDR/PDR/LDR), various physical and biological doses and dose rates, fractionation schedules, treatment planning based on the radiographic (adaptive) approach or the volume-image adaptive approach, and various combinations of these.

# **Clinical Examples**

- The major recommendations as outlined in this ICRU report are applied and specified in these examples.
- These examples are given in a common format to show how the different steps for treatment planning, for final treatment prescription, and for treatment delivery can be reported.

- Case 8: Large Cervical Cancer Stage IIIB with No Nodes, Treated with 3D Conformal Box with Concomitant Chemotherapy and MRI-Based Intracavitary and Interstitial HDR Brachytherapy with Tandem/Ring Applicator and Needles
- Thirty-five-year-old female with a squamous cell carcinoma of the cervix FIGO IIIB, T3N0M0



-> Needle positions

Figure A.8.4. Residual GTV and residual pathological tissue at the time of first brachytherapy: Clinical drawings (upper) and corresponding MRI images (lower) at the time of brachytherapy with applicator in place.

			Planning aim (Gy)	Prescribed dose (Gy)
CTV <sub>HR</sub>	$D_{90}$	EQD2 <sub>10</sub>	$\geq 85$	96.2
Bladder	$D_{2cm^3}$	EQD2 <sub>3</sub>	<b>≤90</b>	82.9
Rectum	$D_{2cm^3}$	EQD2 <sub>3</sub>	$\leq$ 70	68.3
Sigmoid	$D_{2\text{cm}^3}$	EQD2 <sub>3</sub>	$\leq 75$	67.4

Table A.8.3. Treatment planning aim and prescribed dose.

Doses are given in EQD2 using  $\alpha/\beta = 10$  Gy for target and  $\alpha/\beta = 3$  Gy for organs at risk. (No dose constraints were applied for the vagina.)



Figure A.8.5. Equipment used for brachytherapy.







#### A.8.6 Treatment Planning and Reporting Brachytherapy and EBRT

	First application	Second application
Nominal tandem length	60 mm	60 mm
Nominal ring diameter	26 mm	26 mm
Number of active needles	12	12
60 Gy volume	$290 \text{ cm}^{3}$	$280 \text{ cm}^{3}$
75 Gy volume	$175 \text{ cm}^3$	$165 \text{ cm}^3$
85 Gy volume	$70 \text{ cm}^3$	$60 \text{ cm}^3$
TRAK	$2 \times 5 \text{ mGy}$	$2 \times 4.8 \text{ mGy}$

Table A.8.4. Applicators and EQD2<sub>10</sub> isodose surface volumes.

	First application		Second application		Total dose	
	BT1 (Gy)	BT2 (Gy)	BT3 (Gy)	BT4 (Gy)	EBRT + BT (EQD2 Gy)	
Point						
Α						
Right	x <sup>a</sup>	x <sup>a</sup>	x <sup>a</sup>	x <sup>a</sup>	x <sup>a</sup>	
0	(Needle)					
Left	5.0	5.0	6.0	6.0	72.8	
Pelvic wall						
Point						
Right	4.0	4.0	4.2	4.2	63.5	
Left	1.5	1.5	1.6	1.6	50.2	
Bladder						
ICRU						
Point	5.5	5.5	5.7	5.7	81.7	
Recto-vagin	al					
ICRU						
Point	4.7	4.7	4.9	4.9	73.2	
Vagina						
$5 \mathrm{mm}$						
Right	13.0	13.0	7.6	7.6	158.6	
Left	6.2	6.2	7.2	7.2	95.4	
PIBS <sup>b</sup>						
+2  cm	6.5	6.5	6.3	6.3	91.3	
0 cm	2.1 <sub>ICRU 8</sub>	9, <b>P</b> iisbah Ha	mid for ICRO	-2018,	50.4	
-2  cm	1.1	1.3KIMS, 9	SriQaZar	0.7	4.6	

#### Table A.8.5a. Point-based absorbed dose reporting.

	First application		Second application		Total dose	
	BT1 (Gy)	BT2 (Gy)	BT3 (Gy)	BT4 (Gy)	EBRT + BT (EQD2 Gy)	
GTV <sub>res</sub>						
$D_{98.\%}$	10.4	10.4	10.5	10.5	115.5	
$D_{90\%}$	11.6	11.6	11.2	11.2	125.6	
CTV <sub>HR</sub>						
$D_{98.\%}$	7.3	7.3	7.0	7.0	85.1	
$D_{90\%}$	8.6	8.6	8.3	8.3	96.2	
$D_{50\%}$	12.3	12.3	12.6	12.6	137.4	
CTV <sub>IR</sub>						
$D_{98\ \%}$	4.1	4.1	3.8	3.8	62.6	
$D_{90\%}$	5.7	5.7	5.5	5.5	73.4	
$D_{50\%}$	10.1	10.1	9.5	9.5	109.0	
Bladder						
$D_{0.1  {\rm cm}^3}$	7.1	7.1	6.5	6.5	96.6	
$D_{2 \text{ cm}^3}$	5.9	5.9	5.5	5.5	82.9	
Rectum						
$D_{0.1  {\rm cm}^3}$	6.2	6.2	5.6	5.6	85.3	
$D_{2 \text{ cm}^3}$	4.4	4.4	4.2	4.2	68.3	
Sigmoid						
$D_{0.1{\rm cm}^3}$	5.6	5.6	5.2	5.2	79.5	
$D_{2{ m cm}^3}$	4.3	4.3	4.1	4.1	67.4	

Table A.8.5b. DVH-based absorbed dose reporting (Level II).

Total doses in EQD2 were calculated using  $\alpha/\beta = 10$  Gy for target and  $\alpha/\beta = 3$  Gy for normal tissue volumes. The dose considered to be delivered at the same location by EBRT was 44.3 Gy EQD2<sub>10</sub> for target and 43.2 Gy EQD2<sub>3</sub> for OARs.

# **Electronic Spreadsheet**

• On the website

http://icru.org/content/reports/ prescribingrecording-and-reporting-brachytherapyforcancer-of-the-cervix-report-no-89, spreadsheets for calculating EQD2 doses for HDR and PDR schedules are provided.

### TAKE HOME POINTS.....!!

- Image-guided adaptive brachytherapy is based on tumor regression obtained during 5–6 weeks of EBRT.
- Adaptive brachytherapy should therefore be applied toward the end, or shortly after completion, of EBRT.
- However, the overall treatment time including brachytherapy should not exceed 7–8 weeks.

### TAKE HOME POINTS.....!!

- Forward planning is the current standard of care, retaining a classical pear-shaped isodose distribution with a high central absorbed dose as far as possible.
- The optimization process should therefore preferably originate from a well-known and accepted standard loading of the given applicator.

#### TAKE HOME POINTS.....!!

- The levels of reporting should follow a common language globally for
  - Volumes GTV/CTV & OAR's
  - Equi-effective doses
  - Dose –volume parameters 3D/4D
  - Planning aims to prescription
  - Dose point parameters -2D

Level 1: Minimum standard for reporting

Volumetric-imaging approximation based on:

- Comprehensive clinical gynecologic examination
- Volumetric imaging (MR, CT, US, PET-CT) at the time of diagnosis and brachytherapy

#### FIGO/TNM stage

Baseline morbidity and QoL assessment

Schematic 3D documentation on a clinical diagram indicating dimensions (width, thickness, height) and volumes for:

- GTV<sub>init</sub> (the GTV at diagnosis)
- GTV<sub>res</sub> (the GTV at brachytherapy)
- CTV<sub>HR</sub> [the GTV<sub>res</sub> (if present) plus residual pathologic tissue (if present) plus whole cervix]
- (CTV<sub>IR</sub>: area of GTV<sub>init</sub> and/or CTV<sub>HR</sub> plus safety margin if used for prescription)

Dose reporting:

- TRAK
- Point A dose
- Recto-vaginal reference-point dose
- D<sub>0.1cm<sup>3</sup></sub> and D<sub>2cm<sup>3</sup></sub> for the bladder and rectum

Dose delivery pattern:

- Absorbed-dose rate/dose per fraction
- Number of fractions
- Time between fractions
- · (Pulse number, size, time, if PDR)
- Overall treatment time
- Total EQD2 dose

ource and dose calculation:

- Radionuclide and source model
- Source strength

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Dose calculation algorithm

Radiographic approximation based on:

- · Comprehensive clinical gynecologic examination
- Radiographic imaging (plus additional volumetric 3D imaging if available)

#### F.GO/TNM stage

Baseline morbidity and QoL assessment

Schematic 3D documentation on a clinical diagram indicating dimensions [width, thickness, (height)] and volumes for:

- GTV<sub>init</sub> (the GTV at diagnosis)
- GTV<sub>res</sub> (the GTV at brachytherapy)
- CTV<sub>HR</sub> [the GTV<sub>res</sub> (if present) plus residual pathologic tissue (if present) plus whole cervix]
- (CTV<sub>IR</sub>: area of GTV<sub>init</sub> and/or CTV<sub>HR</sub> plus safety margin if used for prescription)

Dose reporting:

- TRAK
- Point A dose
- Recto-vaginal reference-point dose
- Bladder reference-point dose

Dose delivery pattern:

- Absorbed-dose rate/dose per fraction
- Number of fractions
- Time between fractions
- (Pulse number, size, time, if PDR)
- Overall treatment time
- Total EQD2 dose

Source and dose calculation:

- · Radionuclide and source model
- Source strength
- Dose-calculation algorithm

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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):

- GTV<sub>res</sub>
- CTV<sub>HR</sub>
- (CTV<sub>IR</sub> if used for prescription)
- · With maximum width, height, thickness, and with volume

Dose reporting for defined volumes:

- $D_{98~\%}, D_{90~\%}, D_{50~\%}$  for the  $\mathrm{CTV}_{\mathrm{HR}}$
- +  $(D_{98\%}, D_{90\%}$  for the  $\mathrm{CTV_{IR}}$  if used for prescription)
- D<sub>98 %</sub> for GTV<sub>res</sub>
- $D_{98\%}$  for pathological lymph nodes

Dose reporting OARs:

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- Bladder reference point dose
- $D_{0.1 \text{cm}^3}, D_{2 \text{cm}^3}$  for sigmoid<sup>a</sup>
- $D_{2 \text{cm}^3}$  bowel
- Intermediate- and low-dose parameters in bladder, rectum, sigmoid, bowel

(e.g.,  $V_{15 \text{ Gy}}, V_{25 \text{ Gy}}, V_{35 \text{ Gy}}, V_{45 \text{ Gy}}$  or  $D_{98 \%}, D_{50 \%}, D_{2 \%}$ )

- Vaginal point doses at level of sources (lateral at 5 mm)<sup>a</sup>
- + Lower- and mid-vagina doses (PIBS, PIBS  $\pm 2 \text{ cm}$ )<sup>a</sup>

<sup>a</sup>Surrogate points for volumetric vaginal dose assessment.

Radiographic approximation based on:

Topography for volumes (on isodose plan with applicator/on radiographs with applicator)

- GTV<sub>res</sub>
- CTV<sub>HR</sub>
- CTV<sub>IR</sub> (if used for prescription)
- With maximum width, thickness, standard height, and with volume

Dose reporting for defined volumes:

- Estimated dose to  $CTV_{HR}$
- · (according to estimated maximum width and thickness)
- · Pelvic wall point (optional)
- Lymphatic trapezoid (optional)

Dose reporting OARs:

- Vaginal point doses at level of sources (lateral at 5 mm)
- + Lower- and mid-vagina doses (PIBS, PIBS  $\pm~2~{\rm cm})$

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Level 3: Research-oriented reporting All that is reported in Level 1 and 2 plus:	
<ul> <li>Volumetric-imaging approximation based on: Tumor-related volumes:</li> <li>(1) GTV, CTV<sub>HR</sub> sub-volumes based on functional imaging idiagnosis, during treatment, and at brachytherapy)</li> <li>(2) PTV</li> <li>Jsodose surface volumes: For example</li> <li>85 Gy EQD2 volume</li> <li>60 Gy EQD2 volume</li> <li>Dose reporting for tumor:</li> <li>(1) Dos a and Doo a for the CTV re even if not used for prescription</li> </ul>	Radiographic approximation based on: Isodose surface volumes: For example • 85 Gy EQD2 volume • 60 Gy EQD2 volume
<ul> <li>(2) D<sub>90 %</sub> for the GTV<sub>res</sub></li> <li>(3) DVH parameters for the PTV</li> <li>(4) D<sub>50 %</sub> for pathological lymph nodes</li> <li>(5) DVH parameters for non-involved nodes (ext/int iliac, common liac)</li> </ul>	
<ul> <li>OAR volumes and points:</li> <li>(1) Additional bladder and rectum reference points</li> <li>(2) OAR sub-volumes (e.g., trigonum or bladder neck, sphinctermuscles)</li> <li>(3) Vagina (upper, middle, lower)</li> <li>(4) Anal canal (sphincter)</li> <li>(5) Vulva (labia, clitoris)</li> <li>(6) Other volumes/sub-volumes of interest (e.g., ureter)</li> <li>Dose-volume reporting for OAR:</li> <li>(1) Dose-volume and dose-surface histogram parameters for additional OARs and sub-volumes</li> <li>(2) Vaginal dose profiles, dose-volume, and dose-surface histograms</li> <li>(3) Length of treated vagina</li> </ul>	<ul> <li>OAR volumes, points:</li> <li>(1) Additional bladder and rectum points</li> <li>(2) Sigmoid point</li> <li>(3) Anal-canal point (e.g., low vagina point)</li> <li>(4) Vulva point (e.g., low vagina point)</li> <li>(5) Other points of interest</li> <li>OAR dose reporting:</li> <li>Length of treated vagina</li> </ul>

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Table 13.1 General principles for assessment and reporting of absorbed and equieffective EBRT and brachytherapy dose (all reporting levels).

Reporting of dose for relevant targets, OARs, and dose points:

- Planning-aim dose
- Prescribed dose
- Delivered dose

Absorbed dose and number of fractions assessed for target, OARs, dose points:

- Brachytherapy
- EBRT

Total equieffective dose (EQD2) calculated according to the linear-quadratic model through the following steps:

- (1) Brachytherapy EQD2 for each fraction
- (2) Total brachytherapy EQD2
- (3) Total EBRT EQD2

(4) Accumulated total EBRT + brachytherapy EQD2 (based on current assumptions outlined in Sections 7.6, 8.5, 9.5.3)

Reporting of radiobiological parameters:

•  $\alpha/\beta$  values for tumor and OARs; In addition,  $T_{1/2}$  and recovery model for LDR and PDR treatments(At present:  $\alpha/\beta = 3$  Gy for late effects in the OAR and 10 Gy for Ph2 tumor, and  $T_{1/2} = 1.5$  h)

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# Thank You .....for your kind attention

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