

ESTRO project

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

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Abstract

The second part of the GYN GEC ESTRO working group recommendations is focused on 3D dose-volume parameters for brachytherapy of cervical carcinoma. Methods and parameters have been developed and validated from dosimetric, imaging and clinical experience from different institutions (University of Vienna, IGR Paris, University of Leuven).

Cumulative dose volume histograms (DVH) are recommended for evaluation of the complex dose heterogeneity. DVH parameters for GTV, HR CTV and IR CTV are the minimum dose delivered to 90 and 100% of the respective volume: D90, D100. The volume, which is enclosed by 150 or 200% of the prescribed dose (V150, V200), is recommended for overall assessment of high dose volumes. V100 is recommended for quality assessment only within a given treatment schedule. For Organs at Risk (OAR) the minimum dose in the most irradiated tissue volume is recommended for reporting: 0.1, 1, and 2 cm³; optional 5 and 10 cm³. Underlying assumptions are: full dose of external beam therapy in the volume of interest, identical location during fractionated brachytherapy, contiguous volumes and contouring of organ walls for >2 cm³. Dose values are reported as absorbed dose and also taking into account different dose rates. The linear-quadratic radiobiological model—equivalent dose (EQD₂)—is applied for brachytherapy and is also used for calculating dose from external beam therapy. This formalism allows systematic assessment within one patient, one centre and comparison between different centres with analysis of dose volume relations for GTV, CTV, and OAR.

Recommendations for the transition period from traditional to 3D image-based cervix cancer brachytherapy are formulated.

Supplementary data (available in the electronic version of this paper) deals with aspects of 3D imaging, radiation physics, radiation biology, dose at reference points and dimensions and volumes for the GTV and CTV (adding to [Haie-Meder C, Pötter R, Van Limbergen E et al. Recommendations from Gynaecological (GYN) GEC ESTRO Working Group (I): concepts and terms in 3D image-based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV. *Radiother Oncol* 2005;74:235-245]).

It is expected that the therapeutic ratio including target coverage and sparing of organs at risk can be significantly improved, if radiation dose is prescribed to a 3D image-based CTV taking into account dose volume constraints for OAR. However, prospective use of these recommendations in the clinical context is warranted, to further explore and develop the potential of 3D image-based cervix cancer brachytherapy.

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Keywords: Brachytherapy; Cervix cancer; Treatment planning; 3D imaging; Dose volume parameters; Recommendations

The concepts of GTV and CTV [16] need to be validated through prospective evaluation of clinical practice using 3D imaging for treatment planning and (at present) for recording and reporting.

Translating 3D image-based concepts fully into the clinical practice of brachytherapy requires several complex steps: anatomy [9,51], pathology [19,20,53], 3D imaging [11,13,37,44], physics [31,50], biology [1,4,5,6,10,26,33,41,43,47,49], clinical experience, and systematic application of dose volume parameters in the clinical setting.

Essentially, dose volume parameters are needed for GTV, HR CTV and IR CTV and the different OARs. It will be essential in the future to define them clearly, to understand and to use them in the clinical setting in order to make results in 3D gynaecologic brachytherapy comparable from the beginning, applying a common language. First evaluations within the GEC ESTRO working group based on 3D image-based intercomparison studies between three centres have shown their feasibility [25,34]. However, these dose volume parameters are recommended for use in larger patient cohorts and prospective clinical trials when evaluating 3D image-based treatment planning in cervix cancer brachytherapy.

A significant learning period is needed for fully understanding all the different aspects of this complex procedure. However, finally, 3D image-based brachytherapy is expected to become a practical clinical strategy comparable in its complexity with the most advanced external beam therapy techniques: intensity-modulated radiotherapy, stereotactic radiotherapy, and 4D-adaptive radiotherapy [14,18,24,27,54].

Dose volume parameters for GTV and HR/IR CTVs

Dose volume parameters are introduced and then demonstrated following the example of one patient with advanced disease: The series of figures includes diagnostic imaging and localisation imaging with applicator in place (Fig. 1a-h), a schematic diagram with GTV, HR/IR CTV and dose volume parameters (Fig. 2), a 3D MRI-based treatment

plan with display of GTV, HR/IR CTV contours and dose volume parameters (Fig. 3), and DVHs for GTV and HR/IR CTV (Fig. 4).

Dose prescription

Historically, dose prescription was based on certain systems with dedicated rules [12]. Recent developments such as computer assisted treatment planning have led to increased use of 'no system' or 'modified system'. It is, however, recommended to strictly follow the rules of a certain system with an enduring clinical tradition. Dose has been prescribed as milligram per hour of radium or TRAK and is currently mainly prescribed to specific well-defined points (e.g. point A) or to a reference volume. With the introduction of 3D imaging, more and more centres will prescribe to a target volume.

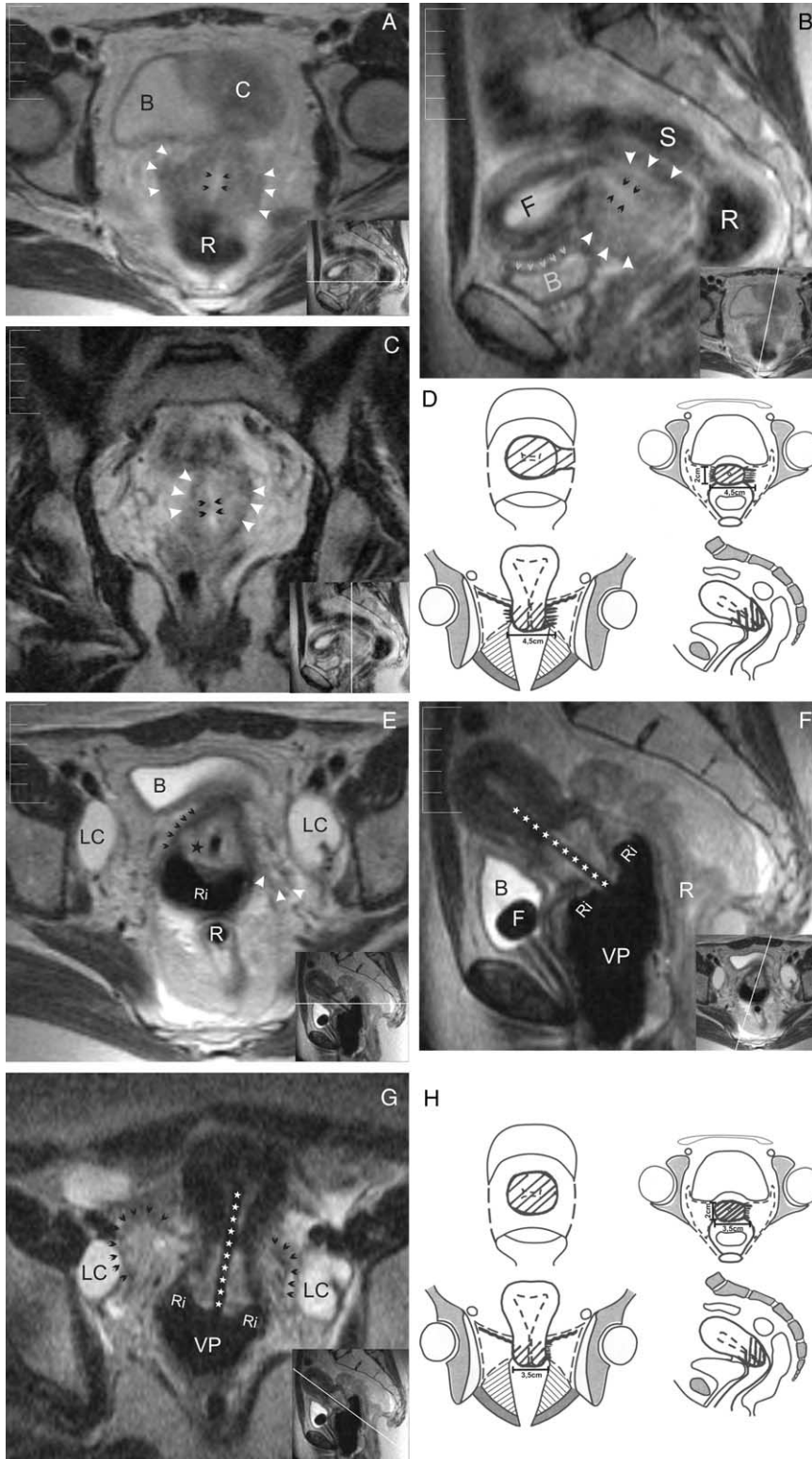
When prescribing to a target, the prescription dose is the planned dose to cover this target as completely as possible.

Dose prescription point(s) and dose normalisation point(s) are not necessarily the same. It is possible to use new user-defined points for normalisation and optimisation, while the dose at point A is used for reporting the prescription dose. On the other hand, if prescription is not based on point A (but e.g. on a target volume), it is still possible to normalise to point A by changing the normalisation value until the prescribed isodose reaches a certain dimension.

Image-guided brachytherapy allows more consistency in regard to the target (and organs at risk). The prescribed dose is always related to the target, while the actual coverage can be evaluated with the use of DVH parameters. Normalisation and reference dose points are a tool for treatment planning and allow the achievement of reproducible dwell time weightings and isodose distributions.

When considering adapting the dose prescription to an image-based CTV, the following procedure is recommended, at least for a significant transition period: patients are investigated with 3D images and the CTV is delineated on the images as described recently [16]. The traditional dose prescription system is also applied. Correlations are investigated between traditional dose prescriptions (e.g. at point A or for 60 Gy reference volume) and the image-based target coverage [2,3,8,28,29]. In the next phase, dose

Fig. 1. Fifty-year-old patient with cervical cancer FIGO stage IIB. TSE T2-weighted axial, sagittal and coronal images at diagnosis (a, b, c) and at time of brachytherapy after combined radiochemotherapy (e, f, g). Small images placed on the right lower corner indicate the slice orientation. Adapted anatomical schemes in three orientations (axial, coronal, sagittal) and additional direct speculum view, indicate clinical findings at diagnosis (d) and at time of brachytherapy (h). (a) High density tumour mass with invasion of both parametria (white arrowheads). Cervical rim is completely replaced. Fluid in the cervical canal produces contrast to the surrounding tumour. Impression of the bladder by the anteflexed uterine corpus. (b) Tumour (white arrowheads) is limited to the cervix without invading the uterine corpus. Bladder impression by the anteflexed uterus (grey arrowheads). (c) On the coronal view tumour growth to the medial third of both parametria (white arrowheads). (d) Clinical examination prior to therapy revealed invasion of both parametria (left > right), as seen on axial and coronal drawings. Direct speculum view indicated involvement of the left fornix. (e) Intracervical high signal intensity residual tumour mass (black star). Cervical rim is partly reconstituted (black arrowheads). Residual pathologic tissue within the proximal part of left parametrium (white arrowheads). (f) On para-sagittal view tandem and ring of the applicator are displayed with low signal intensity. Major parts of visible high signal intensity tumour mass are surrounded by reconstituted low signal intensity cervical rim. (g) Black arrowheads are indicating parametrial borders. (h) At time of brachytherapy, there is only slight invasion of the left parametrium on clinical examination. Bladder (B), uterine corpus (C), rectum (R), fluid in the uterine corpus (F), sigmoid colon (S), cervical canal (black arrowheads), lymphocele after lymph node staging (LC), applicator: ring (Ri), balloon of foley catheter (F), vaginal packing (VP), tandem (white stars).



coverage of the target can be improved starting from the standard dose prescription system as applied before and careful adaptation of loading pattern and dwell times. Finally, dose can be prescribed to an image-based target. In order to facilitate comparison, dose reporting should refer to the prescribed dose to the image-based target

(dose coverage parameters, see below) and to the traditional system [23].

Dose heterogeneity within target volumes

The GTV and CTV in intracavitary brachytherapy are close to the sources, usually within 15-40 mm, and are dependent

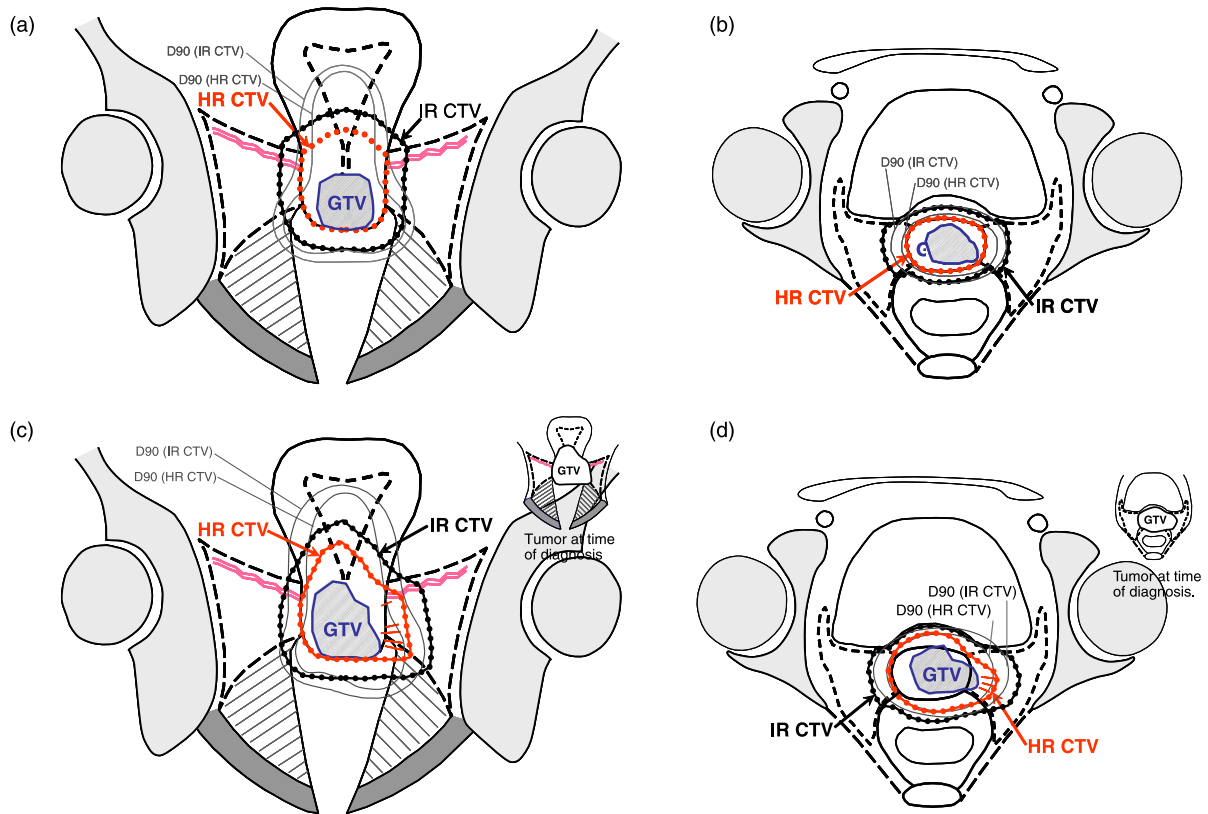


Fig. 2. Schematic diagram for cervix cancer with coronal (a, c) and transverse (b, d) sections of an optimised treatment plan for limited (a, b) and advanced (c, d) disease with partial remission after EBT (grey zones in left parametrium on MRI) (compare Figs. 5 and 7 in [16]). GTV, HR CTV and IR CTV and isodose lines for D90 of HR CTV and IR CTV are indicated. For advanced disease the extension at diagnosis is also indicated.

on the position of the applicator, size and location of the tumour, cervix and on the method applied for CTV determination (HR CTV/IR CTV). Due to the steep dose fall-off close to the sources, there is a significant change in dose and dose-rate throughout the target volumes. The closer to the source, the more pronounced this effect: the dose along an axis perpendicular to the intrauterine source at the level of point A decreases from approximately 200 to 100% of the dose to point A when going from 10 to 20 mm from the source, whereas dose decreases from 100% to approximately 60% from 20 to 30 mm. As not only dose but also dose rate follows the gradient effect, one should be aware that the gradient is even steeper in terms of biologically equivalent dose. This dose inhomogeneity is certainly of major importance for the biological effect of intracavitary brachytherapy (see biology chapter in Supplementary data).

Definition of dose volume parameters

Dose volume parameters for target volumes can be derived from cumulative dose volume histogram (DVH) analysis. DVHs for the GTV and the CTV in intracavitary brachytherapy have a plateau, which indicates 100% dose coverage of the volume of interest. This plateau goes down smoothly indicating decreasing percentage of dose coverage with increasing dose (see Fig. 4). Certain dose coverage values can be defined to describe the specific shape of such a DVH, e.g. D100 and D90, defining the minimum dose delivered to 100 and 90% of the volume of interest, respectively.

Also parameters describing a volume (with regard to the GTV or CTV) receiving a certain biologically weighted equivalent dose EQD_2 can be defined, either as an absolute number (e.g. $V(85 Gy_{EQD_2})$, $V(60 Gy_{EQD_2})$) or as percentage (e.g. $V100$) (for EQD_2 dose see biology in Supplementary data).

Potential and limitations of dose volume parameters

There are some specific considerations concerning dose-volume analysis of intracavitary brachytherapy. The minimum target dose D100 bears at least one practical limitation in accuracy as the reported dose value is extremely dependent on target delineation. Due to the steep dose gradient, small spikes in the contour cause large deviations in D100. D90 is less sensitive to these influences and is therefore considered to be a more 'stable' parameter [23]. Although their clinical relevance has not been proven yet, D100 and D90 are both highly recommended for reporting: they can easily be calculated from a DVH and converted to biologically weighted EQD_2 doses, which makes them suitable for correct plan comparison of all dose rate techniques.

V100 describes how closely the intended treatment could be achieved in terms of target coverage, providing information indirectly on the proportion of the underdosed area. However, V100 is based on the prescribed physical dose and is consequently only relevant within a specific dose rate and fractionation schedule. Hence, it cannot be used for

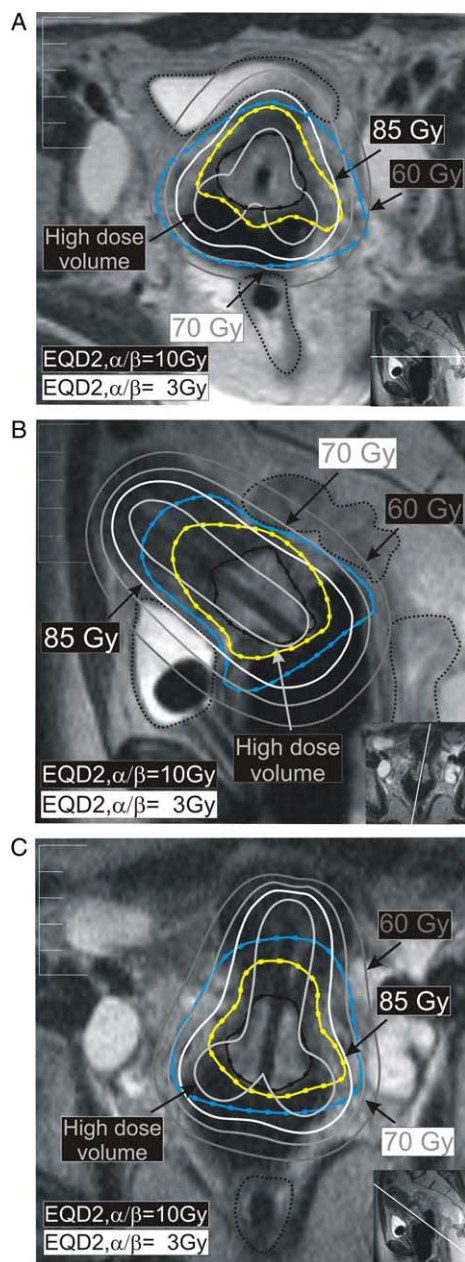


Fig. 3. MRI based 3D treatment plan with relevant dose volume parameters for GTV, HR/IR CTV and OAR (at time of brachytherapy (patient, Fig. 1)). Pelvic MRI at time of brachytherapy and treatment plan in (a) transverse, (b) parasagittal, and (c) paracoronal orientation with MRI compatible applicator in place (vaginal packing with diluted gadolinium (1:1), rectal tube, bladder balloon with diluted gadolinium (1:10) and defined bladder filling (50 cm³)). Tumour and cervix have shrunk significantly (for details compare Fig. 1) after combined radiochemotherapy (5 weeks) with a residual tumour mass (high signal intensity) of 2.5 cm width \times 3.5 cm height \times 3 cm thickness (\sim 12 cm³) and some grey zones in the left proximal parametrium corresponding to findings from clinical examination. After laparoscopic lymph node sampling there are lymphoceles in both obturator regions. GTV, HR CTV, IR CTV, and OAR (bladder, rectum, sigmoid) are contoured. Isodose lines are given for the total dose of 84 Gy_{EQD2} ($\alpha/\beta = 10$ Gy), the prescribed dose (100%) for the HR CTV, for 70 Gy_{EQD2} ($\alpha/\beta = 3$ Gy) as a significant dose for rectum and sigma, for 60 Gy_{EQD2} ($\alpha/\beta = 10$ Gy) related to the IR CTV and for 200% of the brachytherapy dose representing the high dose volume.

intercomparison purposes. Therefore, V100 should be applied solely for intra-patient plan comparison or in a series of patients treated with the same dose (rate) and fractionation.

The intercomparison problem is avoided when biologically equivalent doses are used, e.g. V(60 Gy_{EQD2}), V(85 Gy_{EQD2}). For fractionated treatment, however, this type of parameter is only usable for evaluation after the last fraction, as it uses summed doses of all fractions. Although correlation with clinical outcome needs to be further investigated, we expect this type of parameter to play an important role in the future. V(60 Gy_{EQD2}) can play a role for evaluation of the IR CTV as an equivalent for the more general 60 Gy reference volume previously defined for LDR. V(85 Gy_{EQD2}) reports a dose which represents more closely the prescription dose to the HR CTV [25].

High dose volumes

There is no consensus on how to report high dose volumes for intracavitary brachytherapy at present, although this is regarded as important. For a direct investigation of high dose volumes, one relevant parameter is the volume receiving at least a fixed biologically weighted EQD₂ dose level (e.g. 100 Gy) for the whole treatment (V(100 Gy_{EQD2})). Other parameters of interest are the minimum biologically weighted EQD₂ doses to specified percentages of the targets (e.g. D50, D30, etc.).

Since the intrauterine tandem is placed within or near the macroscopic tumour, the dose to the GTV is higher than the dose to the CTV. Therefore, the D100 and D90 for the GTV consequently imply relevant information about the high dose regions within the HR and the IR CTV.

Parameters such as V150/V200, the volume receiving at least 1.5/2 times the prescribed physical dose are recommended, but should be used with caution: a multiplying factor of the prescribed physical dose is applied, therefore, the dose and the biologically weighted values of the reported high dose volumes are only applicable for intercomparison for a specific dose prescription and within a specific dose rate and fractionation schedule. They cannot be used for intercomparison of different treatment concepts. However, these parameters are of significant importance, as they indicate the relative amount of CTV, in percent, treated with a significantly higher dose (50 or 100%), which is rather unique in radiation therapy.

Applicator volume

When analysing DVH parameters, some part of the target volumes evaluated consist of applicator volume. The volume of the applicator does not influence the evaluated parameters too much as long as large volumes compared to the applicator volume are investigated. Dose volume parameters for which small volumes are considered, such as e.g. D30 (30% of target volume), may include too much of the applicator volume to be a meaningful parameter. Currently, it is not clear if and how the applicator volume should be taken into account. This issue needs further investigation. However, when reporting DVH parameters it should be always mentioned if the applicator is included in the considered volume or not.

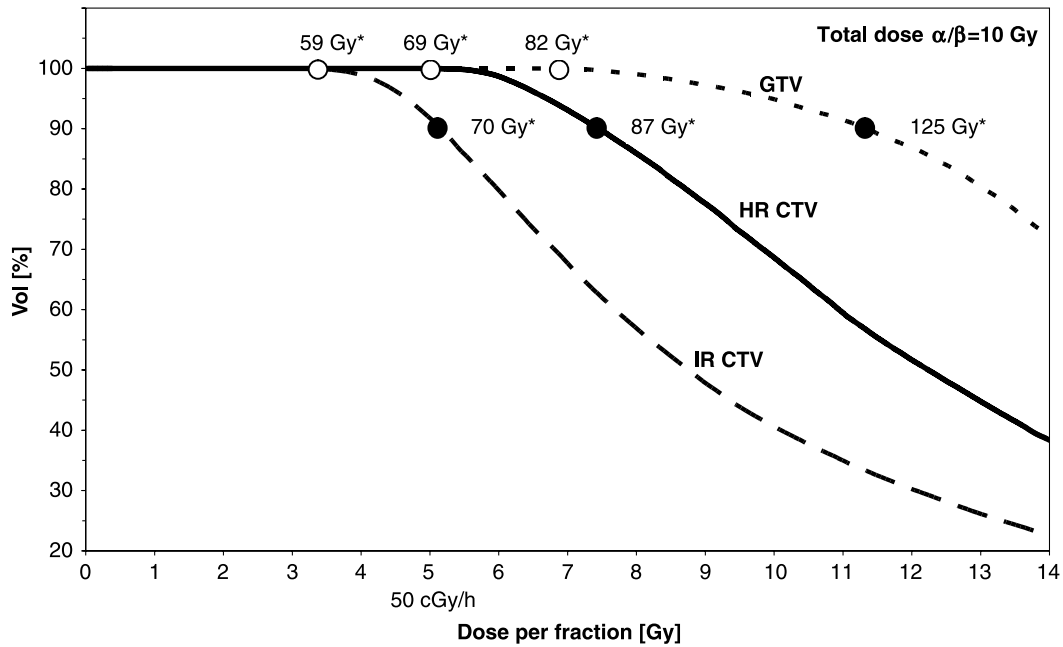


Fig. 4. Dose volume histograms of GTV, HR CTV, and IR CTV for one fraction of HDR intracavitary brachytherapy (patients Figs. 1, 3, 5 and 6). Prescribed dose is 25×1.8 Gy external beam therapy to ICRU point plus $40 \text{ Gy}_{\text{EQD2}}$ (4×7 Gy) brachytherapy to HR CTV, which gives a total of $84 \text{ Gy}_{\text{EQD2}}$ ($\alpha/\beta = 10$ Gy). *Total EQD2 values are given based on four identical fractions. In general, similar DVH curves are obtained for LDR or PDR treatments, but with different total EQD2 doses, e.g. 48 h LDR treatment with 50 cGy/h for D90 of IR CTV gives $69 \text{ Gy}_{\text{EQD2}}$, but $83 \text{ Gy}_{\text{EQD2}}$ (74 cGy/h) for D90 of HR CTV and $110 \text{ Gy}_{\text{EQD2}}$ (113 cGy/h) for D90 of GTV.

Reference volume for applicator systems

The reference volume is the volume encompassed by the reference isodose, selected and specified in terms of dimensions and absolute volume to compare treatments performed in different centres using different techniques [22]. In ICRU Report 38, a reference dose level of 60 Gy delivered at the classical low dose rate (50 cGy/h) is recommended. This is the dose appropriate to cure microscopic disease in cervix cancer corresponding to the Intermediate Risk CTV in definitive treatment. The dose currently employed to cure macroscopic disease corresponding to the High Risk CTV ranges between 75 and 90 Gy_{EQD2} (and above). Therefore, in addition to the 60 Gy reference volume, higher reference dose levels (e.g. 85 Gy_{EQD2}) have been proposed recently [38]. Dose levels for reporting reference volumes have to be biologically weighted according to differences in dose-rate and fractionation schedules as described in the Supplementary data using the LQ model and EQD_2 dose values.

It has to be emphasized that there is no direct relation between the reference volume and the target-orientated dose volume parameters as introduced above. Therefore, the reference volume in the context of 3D image-based cervix cancer brachytherapy is recommended to be only used to describe the dimensions of its width, thickness and height which can be covered by a certain dose (60, 85 Gy_{EQD2}) with a certain applicator and a certain typical loading pattern [12].

Dose volume parameters for organs at risk

In cervical cancer, the location of organs at risk close to the brachytherapy sources (rectum, sigmoid, bladder)

significantly influences the treatment planning process and the dose that can be prescribed. The vagina should be taken into consideration. Other parts of bowel may also receive a significant dose.

Dose volume parameters for OAR are introduced and demonstrated following the same example for one patient as above (Figs. 1, 3 and 4). In addition, a schematic diagram indicates the dose volume parameters (Fig. 6), and a dose volume histogram the evaluation of a treatment plan for different OARs (Fig. 5).

Point doses versus dose volume parameters

So far, in gynaecologic brachytherapy correlation between the radiation dose and the normal tissue effects have been assessed using point doses. Since 1985, these points have been defined using the standardized dose specification points proposed in the ICRU 38 report [36]. There is general agreement that correlation of radiation point doses and dose volume effects is inferior to correlation of dose volume relations and dose volume effects in any given organ. However, for gynaecologic brachytherapy, this correlation could hardly be investigated until now, as conventional orthogonal film-based treatment planning for brachytherapy was based on point doses and not on dose volume relations. A comprehensive assessment has only recently become feasible when introducing cross sectional image-based treatment planning for brachytherapy using CT or MRI [2,8,12,17,23,25,28,34,52].

Dose heterogeneity in organs at risk

With external beam therapy, it is presumed that a homogeneous dose is delivered to the organs at risk with a sharp dose gradient at the field edges. With intracavitary

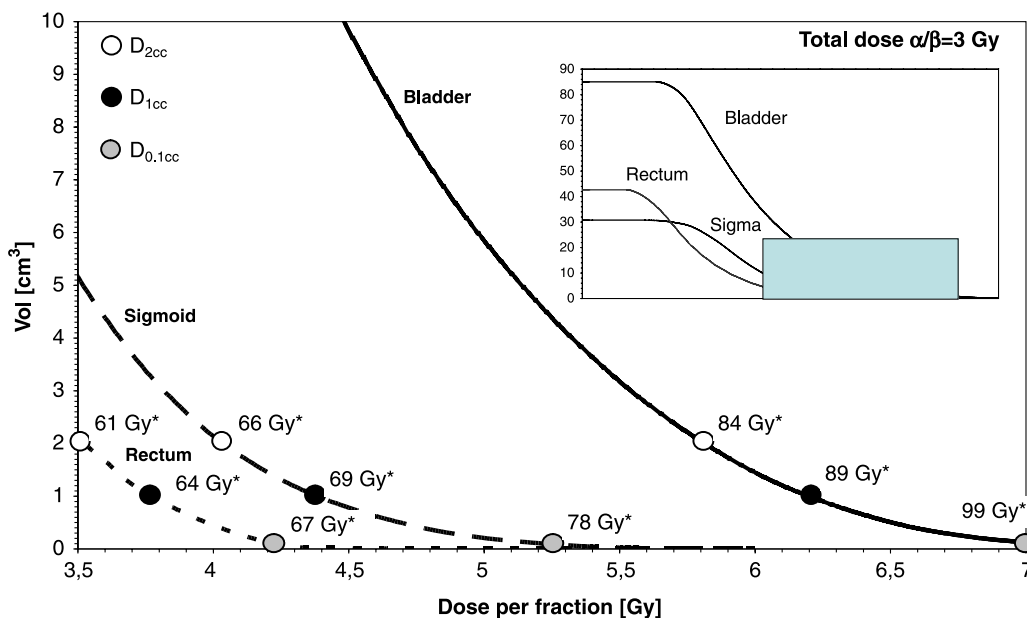


Fig. 5. Cumulative dose volume histograms of bladder, rectum and sigmoid (patient, Figs. 1, 3, 4 and 6) based on organ contouring indicating the minimum dose in the most irradiated tissue volume adjacent to the applicator ($D_{0.1cc}$, D_{1cc} , D_{2cc} for 0.1, 1, and 2 cm^3). *Total EQD2 dose values for these OAR are given assuming four identical HDR fractions with an α/β of 3 Gy. Treatment planning, for this example, was based on dose constraints for D_{2cc} (bladder: 90 Gy_{EQD2} ; rectum, sigma: 70 Gy_{EQD2}). 90 Gy_{EQD2} is reached with four HDR fractions of 6.3 Gy (25.2 Gy), which is corresponding to 48 PDR pulses with 77 cGy/puls, 1 puls/h (37 Gy) and to LDR with 77 cGy/h in 48 h (37 Gy). For 70 Gy_{EQD2} the dose per HDR fraction is 4.5 Gy (18 Gy). The same dose is reached with 48 PDR pulses with 54 cGy/puls, 1 puls/h (26 Gy), and LDR with 54 cGy/h in 48 h (26 Gy).

brachytherapy, there is an inhomogeneous dose distribution, especially in the tissues adjacent to the sources (Fig. 3). The adjacent organs at risk are hollow, with the typical organ wall consisting of mucosal, submucosal, and muscular layers. The configuration and thickness of the different organ walls (variation from 2-3 up to 6-8 mm) is dependent on the degree of filling, the impact of which is most pronounced in the bladder, rectosigmoid, and vagina.

The organ walls adjacent to the applicator (sources), like the anterior rectal and sigmoid walls, inferior-posterior bladder wall, or the vaginal wall adjacent to the cervix, are irradiated by the brachytherapy sources with a high inhomogeneous dose (>20-40 Gy), whereas the organ walls further away, like the posterior rectosigmoid walls, the superior-anterior bladder wall, or the inferior vagina, are irradiated with much lower doses (<5-10 Gy). With definitive irradiation, this inhomogeneous dose delivered with brachytherapy to different parts of the organ walls, is combined with the dose from external beam applied to large parts of the organ walls (e.g. 45-50 Gy to 75-95% of rectum and sigmoid, to 60-90% of bladder [15], and to 50-90% of vagina). These parts irradiated by external beam also include portions of the wall, which are irradiated with a lower more homogenous dose from brachytherapy (e.g. posterior rectal wall).

Assumptions when combining external beam therapy and several brachytherapy fraction doses

In order to be able to match dose volume relations from both external beam and brachytherapy, it is necessary to match each tissue volume element (voxel) irradiated by external beam with the corresponding voxel irradiated by brachytherapy. These systematic image matching procedures

require complex calculations based on image-based dose volume assessments and applies in principle also for GTV and CTV assessment. For these calculations, some assumptions have to be introduced, which apply for most clinical situations. From clinical experience, it can be concluded that the organ walls adjacent to the applicator receiving a high inhomogeneous dose are always irradiated with the full dose of external beam therapy [35]. As these areas are located near the ICRU reference point, inaccuracies should not be larger than $\pm 5\%$ for the dose of external beam therapy. Such an assumption is not necessarily valid for the parts of organ walls at a larger distance from the applicator, as this value depends on the external beam technique as well as the amount of change in topography due to tumour remission and due to introduction of the applicator.

Furthermore, in fractionated brachytherapy, the location of the high dose region from brachytherapy may not be identical for each fraction. As tumours shrink during the course of radiation, there is a change in tumour volume and configuration over time [16] and consequently a change in normal tissue topography over time (4D) [17,21,46]. In addition, the brachytherapy applicator changes normal tissue topography significantly, each time it is inserted. When adding dose volume relations, however, it has to be assumed, that the location of the region of interest is identical each time [35]. In particular, in case of dose volume relations exceeding dose volume constraints, such 'worst case assumption' must be carefully checked.

Finally, due to the shape of a given organ wall, a high dose region may be contiguous or non-contiguous. Non-contiguous high dose volumes are typically seen in the bladder wall, due to the filled lateral recessus (horns) [32].

Definition of dose volume parameters

The method of analysing the 3D dose distribution in an organ at risk has been based on the hypothesis that clinically useful information has to include volume information obtained with cumulative dose volume histogram (DVH) analysis. Two main approaches have been described for DVH analysis, one referring to relative organ (wall) volumes (widely applied in EBT), and the other referring to absolute organ (wall) volumes. Typical adverse effects from brachytherapy such as local inflammation, fibrosis, telangiectasias, ulceration, necrosis and fistulas occur mainly in limited volumes adjacent to the applicator irradiated with high doses (> 70-80 Gy), whereas whole organ side effects like overall organ inflammation, fibrosis or telangiectasia occur mainly after whole organ irradiation with intermediate or high doses (60-70+ Gy).

As these organs of interest are hollow, the filling status of the respective organ should be clearly stated, especially for the brachytherapy component. The most constant filling status possible is advised for valid and reliable data collection, especially for the bladder, as this may change within short time periods [52].

When assessing late effects from brachytherapy, small organ (wall) volumes irradiated to a high dose seem to be of major interest. As there is rapid dose fall-off near the sources, in particular in adjacent small organ (wall) volumes, the dose assessment has to refer to one (or more) defined dose point(s) in these limited volumes. The minimum dose in the most irradiated tissue volume adjacent to the applicator (0.1, 1, 2 and 5 cm³) is recommended for recording and reporting, as has been proposed by several authors previously (Figs. 5 and 6) [2,8,23,38,40,42,48,52]. When assuming a wall thickness of 5 mm these volumes correspond to 'wall planes' of 5 mm × 4 mm (0.1 cm³), 1.4 cm × 1.4 cm (1 cm³), 2 cm × 2 cm (2 cm³), and 3.3 cm × 3.3 cm (5 cm³). Furthermore, it is assumed that these volumes are contiguous. In order to indicate the dose range in these small volumes, it is recommended to report at least two values which should be 1 and 2 cm³. This value has been called, e.g. 'maximum dose to a 2 cm³ tissue' [30], which is obviously not correct, if the DVH as demonstrated in Fig. 6 is analysed [39].

A maximum dose value for recording and reporting, as described by several authors and partly derived from experience with orthogonal film-based treatment planning [45], seems to not be appropriate due to uncertainties in the calculations (calculation algorithm is not reliable for voxels) and due to less clinical relevance to be expected when correlating such point doses to biological end points ('voxel necrosis' does not exist in clinical practice). Instead, it is recommended to indicate the dose to a very limited volume (0.1 cm³), which is still appropriate for dose calculation and probably still bears clinical relevance (e.g. microulceration).

Organ contouring

When using organ wall volumes for recording and reporting, the organ walls have to be delineated slice by slice. However, major practical difficulties have to be overcome because of the very small dimensions and the

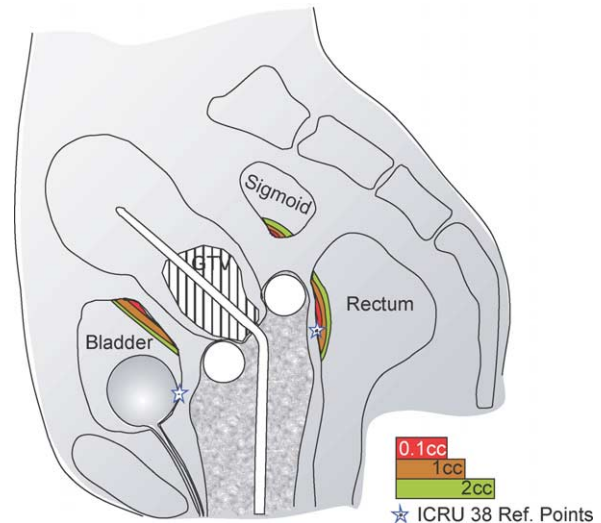


Fig. 6. Schematic anatomical diagram (sagittal view) indicating the most irradiated tissue volumes adjacent to the applicator for rectum, sigmoid and bladder: 0.1, 1, and 2 cm³ (identical patient as in Figs. 1 and 2, dose volume parameters for this schematic patient example can be taken from Fig. 5).

inability to have automatically generated second contours at selected distances by the treatment planning system. These factors represent major uncertainties and may lead to major inaccuracies. For practical reasons, it should, therefore, be taken into consideration, that for organ wall volumes up to 2-3 cm³, organ and organ wall contouring lead to almost identical numerical results [52], which allows for organ contouring only. If larger organ wall volumes are considered, organ wall contouring has to be performed.

The choice of the most appropriate 3D imaging system for delineation is of major importance because variations in delineation within a few millimetres lead to significant variation of dose due to the inverse square law. Whereas there is no doubt that MRI is superior to CT for the discrimination of GTV and adjacent normal (uterine) tissue, CT and MRI provide basically similar quality for discrimination of the bladder, rectum, sigmoid, bowel and vagina. However, in practice delineation seems to be more accurate when using MRI: delineation of organs at risk in relation to the MRI compatible applicator was excellent in one study in more than 90% of cases [7].

Radiobiological modelling of doses

When applying 3D dose volume assessments, each fraction has to be evaluated and a biologically weighted dose (EQD2 or 50 cGy/h) has to be calculated (see biology chapter in Supplementary data). The different fractions can then be added arriving at a cumulative biologically weighted dose. This cumulative value from brachytherapy is to be added to the dose from external beam therapy, also biologically weighted. This sum then represents the total biologically weighted dose (for dose rate/dose per fraction) which was applied to the volume of interest, e.g. the minimum in 2 cm³ rectum, in the GTV or in the HR CTV.

Integration of new parameters

Three-dimensional tools for dose volume assessment should be prospectively used for short and long term evaluation, in order to establish valuable clinical information correlated to 3D dose volume relations [39]. Appropriate methods for morbidity assessment have to be integrated for different organ systems (French-Italian Glossary, LENT SOMA, CTCAE 3.0).

These 3D tools should be used (in a transition period) in parallel with film-based reference points as proposed by ICRU 38 and some further points as proposed in the literature in the past (maximum bladder point, mean and maximum rectum point, etc. [23]).

When assessing these dose volume relations based on traditional performance of brachytherapy, dose volume constraints can be expected to be generated which are more valid and reliable and thus clinically relevant [39] than those in the past based only on points doses and ICRU reference volumes. However, these new dose volume constraints should be discussed in the frame of traditional experience. For sigmoid (small bowel, ovary) meaningful dose volume constraints are expected to be generated.

Recommendations for reporting

Parameters to be reported for image-based brachytherapy of cervical carcinoma are listed in Table 1. Dose values of single fractions should be reported in absorbed dose (optional in addition in biologically weighted form). For the whole treatment, total dose values should be reported as

Table 1
Recommendations for recording and reporting 3D gynaecological brachytherapy

Complete description of clinical situation including anatomy and pathology and imaging examination dimensions and volume of GTV at diagnosis and at time of brachytherapy
dimensions and volumes of HR CTV and IR CTV, respectively
Complete description of 3D sectional imaging technique and contouring procedure
Complete description of brachytherapy technique radionuclide; source type (wire, stepping source); source strength; applicator type; type of afterloading (manual or remote); description of additional interstitial needles if any
Treatment prescription and treatment planning applicator reconstruction technique, standard loading pattern, dose specification method; optimisation method, if applied
Prescribed dose
Total Reference Air Kerma (TRAK)
Dose at point A (right, left, mean)
D100, D90 for GTV and HR CTV and IR CTV, respectively
Dose to bladder and rectum for ICRU reference points
$D_{0.1cc}$, D_{1cc} , D_{2cc} for organs at risk (e.g. rectum, sigmoid, bladder) (vagina ^a)
D_{5cc} , D_{10cc} for organs at risk if contouring of organ walls is performed
Complete description of time-dose pattern: physical and biologically weighted doses ($\alpha/\beta = 10$ Gy for GTV and CTV; $\alpha/\beta = 3$ Gy for OAR; $T_{1/2} = 1.5$ h for GTV, CTV and OAR)

^a For vagina dose volume parameters still need to be defined.

physical dose, indicating the fractionation and dose rate, and in addition as biologically weighted dose (EQD2).

As only few studies have evaluated 3D dose volume parameters in correlation with outcome, the significance of the defined parameters needs to be clinically verified. Pilot studies in dedicated centres have shown so far the usefulness and feasibility of the defined reporting concept [16,23,25,34]. Here, it is recommended to report the presented data set for 3D image-based cervix cancer brachytherapy as a minimum requirement to determine which parameters provide clinically useful information. Following institutional traditions, additional parameters may also be reported.

Acknowledgements

The GYN GEC ESTRO working group has been supported by an unrestricted grant from VARIAN to ESTRO. The working group would like to thank Daniel Berger, MSc, from the Department of Radiotherapy and Radiobiology, Medical University of Vienna, who assisted in preparing images and drawings for this manuscript.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.radonc.2005.11.014](https://doi.org/10.1016/j.radonc.2005.11.014)

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Received 10 June 2005; received in revised form 28 October 2005; accepted 10 November 2005

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