

Dose optimization in gynecological 3D image based interstitial brachytherapy using martinez universal perineal interstitial template (MUPIT) -an institutional experience

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ABSTRACT

The aim of this study was to evaluate the dose optimization in 3D image based gynecological interstitial brachytherapy using Martinez Universal Perineal Interstitial Template (MUPIT). Axial CT image data set of 20 patients of gynecological cancer who underwent external radiotherapy and high dose rate (HDR) interstitial brachytherapy using MUPIT was employed to delineate clinical target volume (CTV) and organs at risk (OARs). Geometrical and graphical optimization were done for optimum CTV coverage and sparing of OARs. Coverage Index (CI), dose homogeneity index (DHI), overdose index (OI), dose non-uniformity ratio (DNR), external volume index (EI), conformity index (COIN) and dose volume parameters recommended by GEC-ESTRO were evaluated. The mean CTV, bladder and rectum volume were 137 ± 47 cc, 106 ± 41 cc and 50 ± 25 cc, respectively. Mean CI, DHI and DNR were 0.86 ± 0.03 , 0.69 ± 0.11 and 0.31 ± 0.09 , while the mean OI, EI, and COIN were 0.08 ± 0.03 , 0.07 ± 0.05 and 0.79 ± 0.05 , respectively. The estimated mean CTV D90 was 76 ± 11 Gy and D100 was 63 ± 9 Gy. The different dosimetric parameters of bladder D2cc, D1cc and D0.1cc were 76 ± 11 Gy, 81 ± 14 Gy, and 98 ± 21 Gy and of rectum/recto-sigmoid were 80 ± 17 Gy, 85 ± 13 Gy, and 124 ± 37 Gy, respectively. Dose optimization yields superior coverage with optimal values of indices. Emerging data on 3D image based brachytherapy with reporting and clinical correlation of DVH parameters outcome is enterprizing and provides definite assistance in improving the quality of brachytherapy implants. DVH parameter for urethra in gynecological implants needs to be defined further.

Key words: Dose volume indices, dose volume parameters, image based interstitial brachytherapy, MUPIT, optimization

Introduction

Radiation therapy is the mainstay of treatment for locally advanced cancer of the uterine cervix, and is usually a combination of external beam radiotherapy (EBRT),

chemotherapy and brachytherapy. Intracavitary brachytherapy (ICBT) has certain limitations. It fails to deliver optimal dose in bulky primary disease, suboptimal and narrow vagina, parametrial and paravaginal involvement. Alternatively, interstitial brachytherapy (ISBT) has been utilized.^[1-3] Interstitial brachytherapy offers advantage over external radiation of delivering high dose to tumor volume and a rapid fall-off to the adjacent structures leading to improved local control and toxicities.^[4,5]

Conventional ISBT done using orthogonal or variable angle radiographs (2D planning) lacks adequate anatomical information for optimal treatment planning.^[6-8] Three-dimensional treatment planning uses computed tomography (CT)/magnetic resonance (MR) images that provide excellent soft tissue definition for better delineation of target volumes and organs at risk (OARs) with respect to the implanted needles and produce customized dose distributions to assess the accurate dose volume parameters/indices, both for the target and the OARs.

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High dose rate (HDR) brachytherapy uses a high activity miniature type single stepping source, which offers an advantage of varying dwell positions and dwell time for obtaining an appropriate dose distribution and isodose geometry.^[9] Graphical optimization, a software-planning tool may be used to manipulate the isodoses on screen to achieve a desired dose distribution. However, the associated hot and cold spots may be a cause of concern and hence an evaluation of dose volume parameters and dose volume indices is mandatory.

In 2005, GEC-ESTRO, published recommendations on image-guided brachytherapy (IGBT) for gynecological tumors that include guidelines on target volume delineation, reporting dose volume parameters and dose prescriptions.^[10] The objective was to standardize the terminology in reporting 3D MR image-based brachytherapy for reliable comparison of the clinical results on a global basis. The recommendations for 3D image-based brachytherapy have been successfully implemented among the European network.^[11]

The present study is aimed to document the various dose volume indices and parameters including those recommended by GEC-ESTRO for OARs to evaluate the dose optimization in 3D image-based gynecological HDR interstitial brachytherapy.

Materials and Methods

The data set of 20 gynecological cancer patients, who underwent routine external radiotherapy and HDR interstitial brachytherapy boost using MUPIT template between September 2005 and October 2007 was selected for this dosimetric study. All patients received radical radiation therapy with/without concomitant cisplatin chemotherapy. The external radiation and brachytherapy doses were planned according to stage and as per institutional management protocol.^[12] The external radiation dose ranged between 45-50 Gy @ 1.8-2.0 Gy per fraction followed by 4-6 fractions of ISBT depending on the response to external radiation doses. A dose of 3.4-4 Gy per fraction with 2 fractions per day, 6 hours apart was delivered. Summation of EBRT and BT doses was performed by calculation of a biologically equivalent dose in 2 Gy per fraction (EQD2) using the linear-quadratic model with $\alpha/\beta = 10$ Gy for tumor effects and $\alpha/\beta = 3$ Gy for late normal tissue damage. The repair half-time was assumed to be 1.5 hours.^[13]

Brachytherapy procedure details

Before the brachytherapy procedure, a thorough pelvic examination was done under anesthesia to assess the normal pelvic anatomy, residual disease at vault, vagina, parametrium, and its relationship to the normal structures. To map the boundaries of the residual disease, silver

markers were inserted into the tissues. The urinary bladder was catheterized with 7 ml of urograffin pushed into its bulb. Cases, wherein IGBT was found to be suitable, the switch was done at the discretion of the operating physician.

After assessing the vaginal length, the vaginal cylinder with or without the guide needle was inserted. With the template held to the perineum and cylinder screwed into place, 18 gauge stainless steel needles with closed trocar tip were inserted depending on the area to be treated. Each needle was placed through the template under digital rectal examination guidance and trans-rectal ultrasound when required to avoid piercing the rectal mucosa. The needles were then secured to the template with the screws. These were then reinforced with the template cover and template secured to the perineum by four corner stitches. A rectal tube was inserted into the anorectum as per our institutional protocol. Patients were then taken for imaging and planning.

Dosimetry and optimization

Image acquisition for treatment planning was done on same day after the implant, for each patient, Axial CT scan of 5 mm slice thickness was taken on Somatom Emotion CT scanner (Siemens Medical Systems, Germany). The images were then transferred to Brachytherapy Planning System (PLATO-Sunrise v. 14.3, Nucletron B. V, Veenendaal, The NL) via local area network. The dose computation algorithm in our treatment planning system is based on TG-43 as recommended by the American Association of Physicists in Medicine (AAPM).^[14] The radiation oncologist delineated the clinical target volume (CTV) using pretreatment clinical extent, imaging (pretreatment and post EBRT), intra-operative findings and radio-opaque silver markers. Various OARs like rectum and bladder were delineated. Rectum was contoured from recto-sigmoid junction superiorly till ischial tuberosity inferiorly. The entire bladder was contoured. The GEC-ESTRO recommendations were also considered while delineation.^[10] Reconstruction of the implant geometry was carried out using multi-planar reconstruction (MPR). This algorithm enables the planner to track the catheters in axial, coronal and sagittal planes. A negative offset of 9 mm was given for each needle to compensate for the dead space (5.5 mm) and the source clearance (3.5 mm). The loading pattern of the source depends upon the geometry of the CTV. Dwell position in each catheter was loaded for adequate CTV coverage (95% of CTV volume to receive 95% of prescribed dose- as per our institution protocol). Basal dose prescription points were defined at the central axial plane of the implanted volume based on the rules of the Paris system. The dose was normalized on the dose points. The plans were then assessed for CTV coverage, and software plan optimization tools such as the geometrical/graphical optimization were used for improving the CTV coverage and sparing of the OARs.

Plan evaluation

Dosimetric outcome were compiled qualitatively and quantitatively by cumulative dose volume histogram (cDVH) for various dose volume indices and GEC-ESTRO DVH parameters.^[15] cDVH was calculated with 40 mm margins around the implanted volume in all directions with 100,000 calculation points randomly placed in the volume of interest. Volumetric quantifiers proposed by Van der Laarse and Baltas including coverage index (CI), dose homogeneity index (DHI), overdose volume index (OI), dose non-uniformity ratio (DNR), external volume index (EI) and conformity index (COIN) were estimated from the cDVH and differential dose volume histogram.^[16-18]

Coverage index (CI): Target volume ref/target volume

CI is the fraction of the target volume receiving a dose equal to or greater than the reference dose. This index helps us to understand how much of the target is covered by the 100% dose (Ideal CI = 1).

Dose homogeneity index (DHI): $1 - V_{1.5 \text{ ref/target volume ref}}$

DHI is the fraction of the target volume receiving a dose in the range of 1.0 to 1.5 times of the reference dose to the volume of the target that receives a dose equal to or greater than the reference dose (Ideal DHI = 1).

Overdose volume index (OI): $V_{2 \text{ ref/target volume ref}}$

This is the fraction of the target volume which receives a dose equal to or more than 2.0 times of the reference dose to the volume of the target that receives a dose equal to or greater than the reference dose (Ideal OI = 0).

Dose non uniformity ratio (DNR): $V_{1.5 \text{ ref/target volume ref}}$

This is the fraction of the target volume which receives a dose equal to or greater than 1.5 times of the reference dose to the volume of the target which receives a dose equal to or greater than the reference dose (Ideal DNR = 0).

External volume index (EI): $1 - \text{target volume ref}/V_{\text{ref}}$

It is the amount of normal tissue volume outside the target volume that receives a dose equal to or greater than the reference dose (Ideal EI = 0).

Conformity Index (COIN): $c1 \times c2$

($c1 = \text{Target Volume ref}/\text{Target Volume}$ and $c2 = \text{Target Volume ref}/V_{\text{ref}}$)

COIN describes how well the reference dose encompasses the target volume and excludes non-target structures.

The fraction of the target volume, which is covered by the reference dose, is described by $c1$ and the fraction of the total volume covered by the reference dose that belongs to the target volume by $c2$ (Ideal COIN = 1).

GEC-ESTRO DVH parameters for the doses delivered to 90% and 100% of the CTV i. e. D90, D100 were calculated. For OAR's the D2cc, D1cc, and D0.1cc i. e. minimum dose to the most exposed 2cc, 1cc and 0.1cc of bladder, rectum/recto-sigmoid and urethra were compiled. All the doses mentioned henceforth are in EQD2 values with alpha/beta ratio of 10 Gy and 3 Gy for tumor tissue and late reacting normal tissues, respectively.

Results

All 20 applications were evaluable for the dosimetric evaluation. The target included significant parametrial tissues and the average number of implanted needles was 20 ± 5 to ensure complete coverage. All the plans were optimized such that CTV receives the maximum dose with optimal sparing of OARs. Geometrical and graphical optimization software tools were used for adequate CTV coverage and optimal sparing of OARs. The dose distribution of a representative patient is shown in Figure 1. The mean volume of CTV was 137 ± 47 cc (range: 68-204 cc).

Dose volume indices

Figure 2 shows the various dose volume indices derived from cDVH. CI of 0.86 ± 0.03 (range: 0.79-0.92). Mean DHI of the implant was found to be 0.69 ± 0.11 (range: 0.51-0.87). Mean V150 and V200 was lesser than 73.8cc (mean 36.3 ± 16.2) and 23.7cc (mean 11.5 ± 4.8), respectively. Mean DNR was 0.31 ± 0.09 (range: 0.11-0.43) which reveals that implanted volume dose was heterogeneous. Mean OI, was observed to be 0.08 ± 0.03 (range: 0.03-0.15). Mean EI and COIN were found to be 0.07 ± 0.05 (range: 0.01-0.16) and 0.79 ± 0.05 (range: 0.71-0.85), respectively. Also dose volume parameters for CTV and OARs were evaluated and tabulated as per GEC-ESTRO guidelines [Tables 1 and 2].

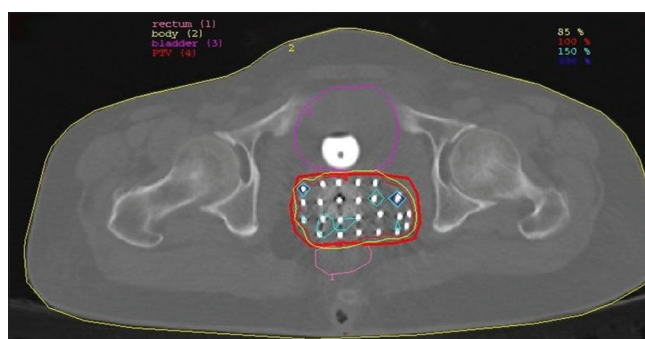


Figure 1: Planning axial CT Image showing dose distribution and OARs

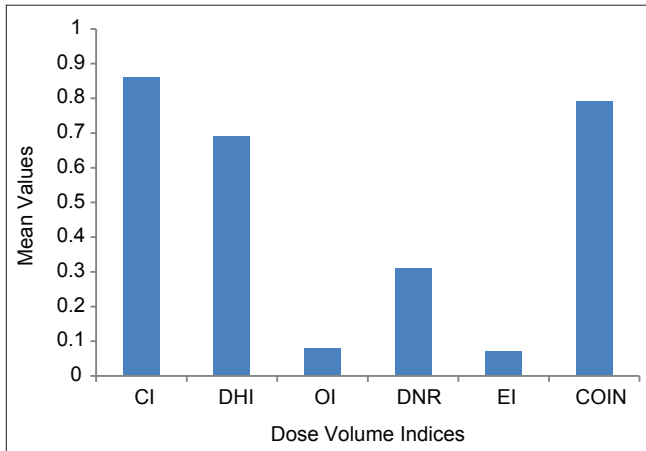


Figure 2: Bar diagram for various indices

Table 1: GEC-ESTRO DVH Parameters for CTV

CTV	Dose/fraction BT	Dose/fraction EQD2	Total dose BT	Total dose EXRT+BT
D_{90} (Gy)	3.8 ± 0.2	4.4 ± 0.4	26 ± 5	76 ± 11
	2.1 ± 0.2	2.2 ± 0.5	13 ± 4	63 ± 9

CTV: Clinical target volume, DVH: Dose volume histogram, EQD2: Equivalent dose in 2

Table 2: GEC-ESTRO DVH Parameters for CTV

Organ/Vol. (cc)	EQD2 dose	D2cc (Gy)	D1cc (Gy)	
Rectum 50±25	BT	26±9	31±12	48±11
	EBRT+BT	80±17	85±13	124±37
Bladder 106±41	Dose BT/Fr	3±1	4±1	5±2
	BT	30±6	35±7	74±21
Urethra 2.4±0.8	EBRT+BT	76±11	81±14	98±21
	Dose BT/Fr	1.3±1	2.6±0.8	3.6±1.3
	BT	5±2	14±4	22±6
		55±10	64±11	72±14

BT: Brachytherapy, BT/Fr: Brachytherapy per fraction, EBRT+BT: External beam radiotherapy+Brachytherapy, EQD2: Biologically equivalent dose @ 2 Gy per fraction

Discussion

Martinez Universal Perineal Interstitial Template (MUPIT) was first devised by Martinez for brachytherapy in prostate, cervix, vagina, female urethra, perineum and anorectal region to allow better control of the needle geometry and reliable placement of active source positions within the tumor volume.^[19] It provides a therapeutic window to reduce doses to OARs without compromising the CTV doses.

3D image-based brachytherapy is being widely practiced with flexible software optimization tools such as graphical optimization. However, the question of adequate optimization needs to be answered to generate an optimal

plan. Currently available optimization methods, such as geometric and dose point optimization, are based only on the location of the active dwell positions. The objective of these methods is to improve the dose homogeneity over the target volume. However, both these optimization methods fail to consider geometrical irregularities, coverage of CTV and sparing of OARs. Graphical optimization is a rapid operator-dependent method, which mends the dose distribution pattern related to geometrical irregularities. Use of graphical optimization in generating an optimal plan may result in an unconventional plan with undesirable hot and cold spots in the implanted volume and OARs. Reports are now available that confirm the contribution of dose optimization to an improvement in local control and morbidity thus having a favourable impact on cancer specific survival and overall survival. Reporting of dose volume parameters as per GEC/ESTRO recommendations can help to correlate with clinical outcome and to further explore and develop the potential of 3D image-based brachytherapy. In accordance, we hereby report our institutional dosimetric results in this interstitial brachytherapy study for documentation purpose.

One of the important parameters for the assessment of implant quality is the adequate coverage of the target volume with the prescription dose. The mean CI of the CTV in our study was 0.86 (range: 0.79-0.92). Review of literature showed that CI of 0.91 has been achieved for breast implant, while 0.95 has been accepted for cervical and oropharyngeal implants.^[20,21] Major *et al.*, reported that for an ideal implant, the target volume coverage CI should be 0.95.^[22] To improve the suboptimal coverage, Kestin *et al.* proposed an optimization algorithm and have shown that an increase in dwell times at one to three dwell positions can lead to an increase in the proportion of the CTV receiving the prescription dose.^[23] Although attempts were made to improve the CI in the present study, we found that the CI was improving at the cost of homogeneity. Hence, a balance was maintained between CI and DHI as the DHI is the measure of high dose region within the implanted volume. It was not very clear that what should be the threshold value of DHI such that further graphical optimization should be stopped to achieve an optimal plan in terms of CI and DHI. Major *et al.*, in their study have reported that in an ideal implant geometry using a stepping source and conformal dosimetry system, a DHI of 0.68 was achieved and a dosimetric study on HDR prostate implants from Tata Memorial Hospital has reported mean values of DHI in the range (0.65-0.81).^[22,24] On extrapolation of this to our study, MUPIT template also has a fixed geometry so a threshold value of DHI of 0.68 was set for our implants. The mean value of DHI in the present study was 0.69 (range: 0.51-0.87). Similarly, threshold values were set for various indices such that optimal plan can be obtained while using the graphical optimization (OI = 0.08, COIN = 0.75, EI = 0.1). These

values may not be generic as they may depend on the implant site and institution specific. Institutional protocol can be made regarding the acceptability criteria of indices such that the use of optimization can be made uniform among the users within the institution. Hence, these values may not be conclusive; however, this study suggests that indices do represent the quality of the implant in terms of optimal target coverage, sparing of OARs with acceptable hotspot within the implanted volume. Most of these DVI have been used to define the target volume coverage. One of the limitations of these indices is non-availability of any parameters to evaluate OARs with respect to target coverage.

The collection of data of dose volume parameters recommended by GEC ESTRO, may yield accurate information regarding the normal tissue tolerance, and establish the dose response. The DVH parameters have been defined for both CTV and the OARs. The DVH parameters achieved in our study seems to be inferior in terms of both CTV and OAR doses with the literature.^[15] Our CTV D90 doses of 76 Gy seem to be lower than that reported by Kirisits *et al.*, (HR-CTV of 96Gy) for the combined intracavitary and interstitial brachytherapy plans. Also, for OARs the bladder 2 cc doses of 76 Gy are comparable while the rectal/recto sigmoid doses of 80 Gy are higher. The uterosacral ligaments (at least medial half) lie close to rectum and form part of the CTV. So the needles tend to be closer to rectum and D2cc and 0.1cc doses are highly sensitive to relatively close proximity to the source positions in interstitial implants. This could possibly explain high doses to rectum/recto sigmoid. There are no DVH parameters reported for urethra in gynecological interstitial implants. There is lot of literature on urethral dose constrains and tolerance levels defined for prostatic urethra in permanent and temporary implants for prostatic cancers.^[25] In the present times, there are several optimization methods available for use with multichannel applicators; in a study inverse planning by simulated annealing (IPSA), dose point optimization and graphical optimization have been compared for HDR brachytherapy.^[26]

Dose volume indices and dose volume parameters of the CTV and the OARs during interstitial gynecological brachytherapy are useful in maintaining the uniformity of optimization among the users and may yield more accurate information regarding normal tissue tolerance and to establish dose response relationship in the future. Emerging data on image-based brachytherapy with reporting and clinical correlation of DVH parameters outcome is enterprising. Our dosimetric study reports the implementation of various dose volume parameters during interstitial gynecological brachytherapy plan evaluation. This study was undertaken as a part of good clinical practice, where the paradigm shift to 3D brachytherapy treatment planning and optimization is gaining popularity.

Conclusion

3D image-based dosimetry with CT based planning using MUPIT for gynecological brachytherapy implants is feasible. Plan evaluation and documentation using various indices and parameters recommended by GEC-ESTRO assist in objective evaluation and reproducibility. Emerging data on 3D image-based brachytherapy with reporting and clinical correlation of DVH parameters outcome is enterprising and provides definite assistance in improving the quality of brachytherapy implants. DVH parameter for urethra in gynecological implants needs to be defined further.

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