

THE ROLE OF COMPUTED TOMOGRAPHY BASED TREATMENT PLANNING IN HIGH DOSE RATE (HDR) BRACHYTHERAPY IN CARCINOMA OF THE CERVIX

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Abstract:

Aim: To compare the high dose rate (HDR) brachytherapy treatment planning using standard orthogonal radiography and computerized tomography (CT) for carcinoma of the cervix.

Methods: Forty applications with orthogonal planning using the Brachy Vision treatment planning system version 7.3.10 were performed. Orthogonal and CT based planning in these applications were compared; the doses to point A, rectum and bladder were defined according to the American Brachytherapy Society (ABS) recommendation. Using CT planning, we calculated the dose volume histogram (DVH) for the CTV, rectum and bladder.

Results: Using orthogonal films to prescribe to point A, only 63.5% of CTV received the prescribed dose. The mean dose to the bladder point is 2.9 Gy and 17% of the bladder volume was encompassed by 2.9 Gy isodose line. The mean dose at the rectum point is 3.4 Gy and 21% of the rectum volume was encompassed by 3.4 Gy isodose line. The maximum dose to the rectum and the bladder derived from the CT is 1.7 and 2.6 times higher than the orthogonal reference points.

Conclusions: CT based treatment planning for HDR brachytherapy of cancer cervix is reliable and more accurate in definition and calculation of the dose to the target as well as the critical organs. It allows dose calculation based on the actual volume rather than points or bony landmarks.

Keywords: Cancer cervix, Brachytherapy, CT based planning HDR, 3-D treatment planning.

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Introduction:

The curative potential of radiation therapy in the management of cancer cervix is greatly enhanced by the use of brachytherapy^[1-4]. Success of brachytherapy requires delivery of a high radiation dose directly to the tumor while sparing, and reducing the dose to the surrounding normal tissues. Cervical carcinoma has traditionally been treated with low-dose rate (LDR) brachytherapy. High dose rate brachytherapy (HDR) was developed to overcome the potential disadvantage of LDR; including radiation exposure to medical staff, prolonged treatment time, mandatory hospitalization and applicator movement^[5-7]. The primary disadvantage of HDR is the potential late toxicity of large dose per fraction; as with external beam radiation therapy (EBRT), which also delivered at high dose rates.

These radiobiological disadvantages can be overcome through adequate fractionation and better delineation of organs at risk. Additionally, in HDR brachytherapy complications might be minimized more effectively than in LDR, because of low possibility of normal tissue displacement (the bladder anteriorly, and the rectum posteriorly in short treatment time and with the use of retraction devices in some applications^[8,9].

Several studies (including randomized, non randomized, prospective trials and meta analysis) have compared LDR with HDR brachytherapy in the management of cervical cancer. It shows that both modalities have comparable local control, survival, and morbidity^[10-22]. Some even showed lower rectal morbidity with the use of HDR^[14, 17, 18].

Modern approach in the treatment planning of cancer cervix is based on series of transverse computed tomography (CT) sections and on three dimensional (3-D) dose computations. This allows evaluating dose distributions in different volumes as regards the gross tumor volume (GTV), clinical target volume (CTV) and organs at risk. When these techniques are not available, dose calculation was based on orthogonal radiographs which provide the position of the applicator relative to bony structures, this allow dose calculation at defined fixed points related to bony structures. Point A and B representatives to the tumor and pelvic side wall respectively and other reference points considered representative for the organs at risk (bladder and rectum)^[23].

In order to correlate information obtained with these two approaches, we compared the two treatment planning methods (radiographs and CT planning methods) in this study of 40 applications.

Material and methods:

Between January 2007 and May 2008, 40 applications of HDR remote afterloading using Ir192 were done for 14 patients of cancer cervix following external beam radiotherapy (EBRT); with individualized treatment dose and schedules. CT was done for all applications. Patients were treated based on the orthogonal calculation, and another calculation was performed based on the CT information, and both methods data were compared.

Patient selection:

This feasibility study included 14 patients; 10 were stage IIB, 3 stage IB, and one stage IIIA. Nine patients had squamous cell carcinoma, four patients with adenocarcinoma, and one patient reported as poorly differentiated carcinoma.

All patients' undergone examination under anesthesia (EUA), cystoscopy, proctoscopy and CT or MRI of the abdomen and pelvis before the start of EBRT. EUA was repeated in selected patients before brachytherapy. CT or MRI was repeated before brachytherapy to assess the response and to help for insertion of the applicator.

Treatment scheme:

Treatment consists of combination of external beam therapy and high dose rate (HDR) brachytherapy; External beam therapy was delivered at a dose of 45 Gy with daily dose of 1.8 Gy over 5 weeks, 5 fractions/week, using a linear accelerator of 18 MV, applying the four fields "Box technique" with no midline shielding. Three patients received concomitant chemotherapy in the form of weekly Cisplatin 30-40 mg/m².

All patients received brachytherapy after the end of the EBRT. HDR brachytherapy with Ir192 source was performed in 3-4 fractions, one fraction per week, depending on the department load and the anesthesia schedule; using dose range between 6-7 Gy per fraction for most of the patients.

External beam radiotherapy (EBRT) technique:

All the patients received pelvic irradiation, with 4 fields (Box technique); Anterior-Posterior (AP), Posterior-Anterior (PA), and 2 lateral fields.

The upper border of the AP and the PA field was at the interspaces of lumbar vertebrae 4-5; with the lower border 3 cm below the gross tumor, usually at the level of the ischeal tuborsity. The lateral borders were 1.5 cm from the lateral pelvic brim. For the lateral fields, the upper and lower borders were the same as the AP, PA fields, while the anterior border was at the tip of the symphysis pubis and the posterior border is 2 cm behinds the posterior extension of the tumor.

Brachytherapy technique:

Fractionated afterloading HDR brachytherapy was performed, using the Fletcher Suit Delclos applicator (FSD) or Henschke applicator, within one week of completing EBRT using the uterine tandem of 20 to 50 mm length with 2 medium or large sized ovoids according to the anatomical variations.

Packing was done anterior and posterior to the applicator to displace the bladder and the rectum. Foleys' catheter was inserted into the bladder and the balloon was inflated with diluted 7 cc of iodinated contrast, and pulled downwards so that it lies at the trigone (neck) of the bladder. Rectal catheter for insertion of diluted barium into the rectum with rectal marker also was inserted.

Two orthogonal films; one anterior-posterior (fig. 2) and one lateral (Fig. 3) were taken to determine the prescription,

bladder and rectum points. The dose was prescribed to point A (point H) using the American Brachytherapy Society (ABS) recommendation for HDR for cancer cervix (fig.1)^[24]. These points were specified as per the International Commission for Radiation Units (ICRU) in report 38^[23]. In this report; the bladder point in the anterior film lies in the center of the catheter balloon, while in the lateral film it lies on the most posterior surface of the balloon. The point selected corresponds to the maximum dose on the surface of this balloon; this point may not be the posterior aspect of the bladder as it may be situated either to one side or significantly superior or inferior to the vaginal applicator.

The rectal point is defined on the lateral film as 0.5 cm posterior to the posterior vaginal wall, or the nearest rectal point to the vaginal ovoids and this point is reflected in the anterior film guided by the rectal marker. Alternatively the anterior rectal wall may be visualized by injecting a diluted solution of contrast (50 % barium : 50 % saline) with some air contrast in the rectum.

The patients were treated based on the orthogonal film calculation. Starting with digitization of films using the Vedar system, the position of the applicator (the tandem and ovoids), rectal and bladder reference points as well as A and B points were digitized in the anterior-posterior film and verified in the lateral films; to ensure the same position in relation to the anatomy of the patients. Computerized planning was then done with determination of the dwell time and position of the source using the Brachy Vision

V 7.3.10 planning system, with source strength (activity) ranged from 4.4 to 6.8 Ci (mean value of 5.7 Ci). Normalization of the dose was done to point A and the relative dose to the bladder and rectum reference points and point B were then calculated.

CT based planning brachytherapy technique:

At the time of calculation for orthogonal films, CT scanning was done for all patients with 0.25-0.5 cm interspaces. Data from CT were read into the planning system via a line connection. The 3-D data set and the dose grid of the position of the applicator is identified; using the same dwell position of the source used in the orthogonal film.

Point A was identified to be more accurately close to point A in the orthogonal film. In the CT images; the CTV, bladder and rectum were contoured; delineation of the GTV was performed based on the CT information at the time of the brachytherapy and supported by the clinical findings. The macroscopic tumor was delineated as appropriate as possible.

We added safety margin (usually one cm in the 3 dimensions) to create the CTV. Additional margin was added to CTV to create the PTV. In principal, the cervix, which could be defined on the CT, was included. If the parametrium structures had also to be included, the depth and the width of infiltration were estimated. If the images showed a normal configuration of the corpus uteri only the central part of the corpus was enclosed, and if there was an involvement of the fornices or proximal vagina, these were included.

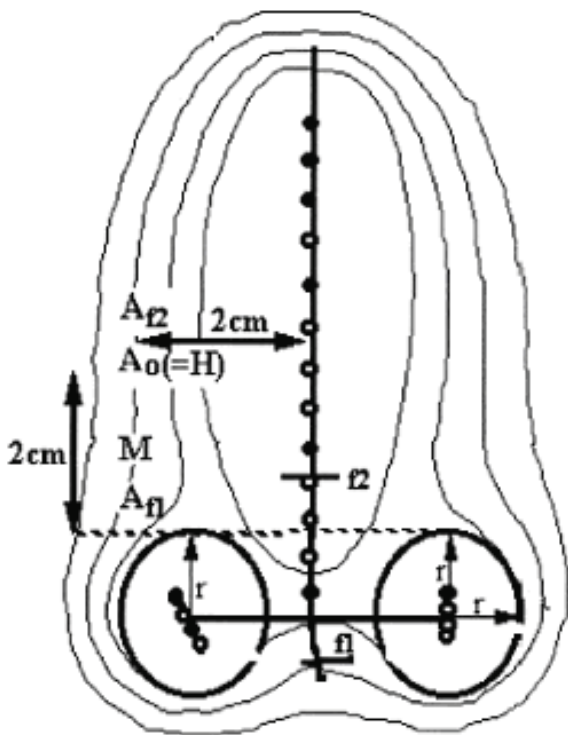


Fig. 1: An illustration relevant for intracavitary dosimetry for a tandem and ovoids application.

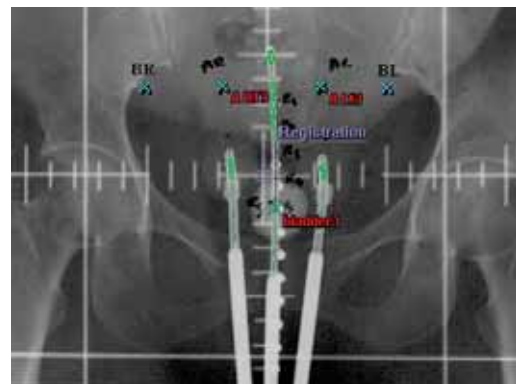


Fig. 2: Antero-posterior (AP) orthogonal film



Fig. 3: Lateral orthogonal film

Delineation of rectum and bladder was done along the outer contour. The rectum was contoured from about 2 cm below the lowest point of the ovoids up to the recto-sigmoid junction. The whole bladder was contoured. Anatomical dose volume histogram was calculated for the CTV, bladder and rectum. These data were compared with data derived from the orthogonal films. (Fig.6, 7)

Radiography based treatment planning:

The mean dose to point A was 6.6 Gy ranged between 6 to 8 Gy, the dose to point B was ranged between 20 to 25% of the dose to point A. The mean dose to bladder and rectum points according to the ICRU definition were 2.9 and 3.4 Gy respectively with a range of 1.2:4.2 Gy for the bladder, and 0.5:4.8 Gy for the rectum.

CT based treatment planning:

The mean absolute volume of CTV for the 10 applications was 85cm³ (ranged from 60.9 to 132 cm³). The mean percentage volume was 63.5 % (ranged from 38 to 77.25 %) that received the prescribed dose to point A; in another words 63.5% of the CTV received the prescribed dose to point A.

The mean dose to bladder point from the orthogonal film, which was 2.9 Gy, corresponded to the 21% of bladder volume in CT (mean 25 cc). Range between 3.5: 58 cc. While the mean dose to the rectum point in orthogonal film (3.4 Gy) was corresponded to 17% of the volume of the rectum in CT (with a mean of 9 cc) range between 0.5-28 cc. This means that 3.4 and 2.9 Gy isodose lines correspond to the 17% and 21% of rectum and bladder volume in CT respectively.

By comparison the maximum dose to bladder and rectum derived from the CT is 2.6 and 1.7 times higher than orthogonal reference points.

The relation between percentage of the CT volume (25, 50, 75, 100%) of the CTV, rectum and bladder with the mean dose in Gy prescribed to point A and corresponding percentage to this volume revealed that: with the mean prescribed dose to point A is 6.6 Gy, an average of about 25-30 % of the CTV not received this dose. while about 25% of the rectal and bladder volume received 40% of the dose to point A, and 12-14 % of the volume of the rectum and the bladder received 100 % of the dose to point A (Table 1).

Discussion:

With radiography, the calculation of dose distribution is based on visualization of the applicator relative to bony structures. Reference volume, doses at point A and B and doses to other points like the ICRU 38 reference points can be derived [24]. This method does not allow the evaluation as to what extent the treated volume encompasses the CTV. In contrast, CT-based planning allows the delineation in each slice, the CTV and organs at risk and from there the dose-volume relations can be calculated [25]. Modern treatment planning in brachytherapy allows combining (a) dose-volume histogram calculation based on CT sections (b) point dose calculation based on orthogonal radiography [26,27].

In this study, data from both methods were compared and correlated. In addition, we attempted to apply the concept of CTV definition, as recommended in ICRU 50 report for external beam therapy to brachytherapy [28]. The ICRU 38 [24] was developed for dose and volume specification and for reporting intracavitary therapy in gynecology. Volumes like targets, treatment, references and irradiated volume were already defined. The use of ICRU 38 in clinical practice is part of a common quality assurance program and contributes reaching consensus between different centers [29]. ICRU reference points are used in only a few groups who calculated and reported the dose to these points [30,31,32].

Our data showed that The ICRU reference point dose to the bladder and rectum was 2.9 and 3.4 Gy respectively. This dose corresponds to 21% (25cc) and 17% (9cc) of the bladder and rectum volume calculated from CT. This was less than reported with Fellner et al [25] in a similar study using HDR with corresponding mean dose to the rectum and bladder at the ICRU reference point were 4.3 and 5.8 Gy respectively; with related volume of the rectum and bladder that received this dose were 12% (9cc) and 8% (16cc) respectively. Other investigators using LDR reported similar data [30–31]. About 50% of the rectal and bladder volume in our study received dose below the corresponding doses calculated at the ICRU point from the orthogonal film. This agreed with the data reported by others [25, 33, 34].

The maximum dose to the organs at risk was calculated from dose volume histograms. Based on 3D calculations, the maximum dose compared to the ICRU point was found to be 2.7 and 1.6 times higher than the orthogonal reference points for the bladder and rectum respectively. Similar results was reported by Fellner et al [25], with maximum dose to the rectum 1.5 times higher than ICRU reference point while the maximum dose to the bladder is 1.4 times higher than its corresponding ICRU point calculation.

Deshpande et al [35] investigated points other than the ICRU rectum reference points to estimate the maximum dose in 182 application. It was concluded that several points along the rectal wall should be considered. Hunter et al [36] found that the ratio of maximum bladder dose (calculated from CT images) to the ICRU reference dose (calculated with radiographs) varied from 1.01 to 3.59 times. Barillot et al [37] found that the maximum dose in bladder (calculated from ultrasonography) were on average 2.7 times higher than dose at ICRU reference points (calculated with radiographs). Schoepel et al [34] found a ratio on average of 2.3 for the bladder and 1.3 for the rectum, which is similar to our study results.

According to literature it is evident that the ICRU reference points [23] underestimate dose in the maximum dose in the rectum and bladder. However, the published data vary within a broad range. These differences could be due to the fact that several methods (radiography, ultrasound, CT) were used and that the individual patients anatomy varies significantly. In our study a complete 3-D assessment of organs was included whereas most of the publications deal with points. The present study demonstrates

that for dose estimation; the 3-D assessment of the organ should be considered, not only points.

The mean dose calculated at point A is 6.7 Gy with about 63.5 % of the CTV volume derived from CT covered by this isodose line. This means that using the ICRU reference point (Point A) for calculation may under dose the target volume. Similar data reported by Fellner et al [25] with an average 83% of the CT derived CTV covered by the prescribed isodose line.

Special attention was paid to organs at risk (rectum and bladder)^[23] and the encompassed volumes by these doses were calculated in order to translate accepted reference points into volumes. Also the maximum doses in these organs were calculated. It is obvious that 3-D imaging based treatment planning is more comprehensive and more adequate for volume assessment of critical organs. This makes its use, as substitute to the orthogonal film calculation, more logic. Also, in further studies these dose volume relations have to be correlated with data of clinical outcome, side effects and tumor control.

Conclusion:

The aim of this study was to compare two different planning methods of calculations for HDR brachytherapy, the point dose which is based on orthogonal radiographs and the volume methods which is based on sectional images. We conclude that for valid and reliable dose estimation in CTV and in organs at risk, a 3-D imaging based treatment planning is superior compared to treatment planning based on points in radiographs.

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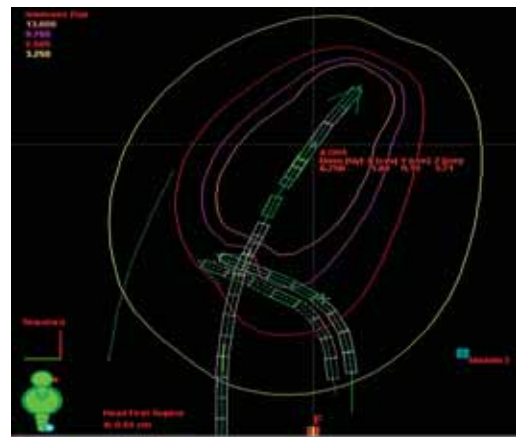


Fig. 5: Isodose distribution on lateral view

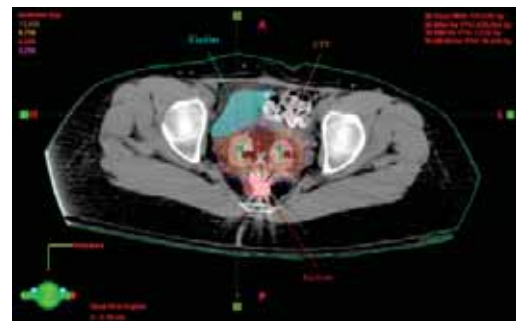


Fig. 6: Transverse CT cut showing target volume, bladder, rectum and isodose distribution



Fig. 4: Isodose distribution on AP view

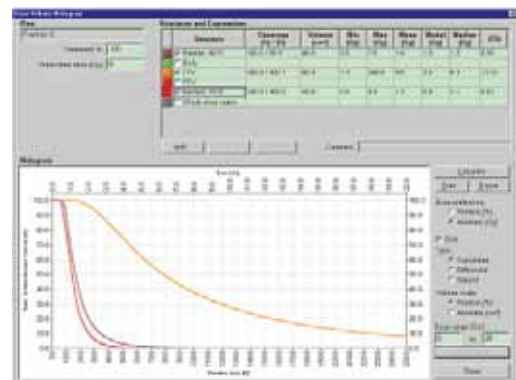


Fig. 7: Dose Volume Histogram (DVH) for target volume, bladder and rectum

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