3D ANATOMY-BASED PLANNING OPTIMIZATION FOR HDR BRACHYTHERAPY OF CERVIX CANCER

DR YASIR BAHADUR[1], DR CAMELIA CONSTANTINESCU[2], DR MOHAMAD EZZAT[2], MS NOOR GHASAL[2]

Department of Radiology, King Abdulaziz University Hospital, Jeddah, Saudi Arabia[1]
Department of Oncology, King Faisal Specialist Hospital & Research Center, Jeddah, Saudi Arabia[2]

Abstract:

Aim: To evaluate the dosimetric superiority of inverse planning optimization and isodose line manually optimization (both 3D planning methods) versus conventional treatment plan (point A planning method), using various dosimetric indices in HDR brachytherapy planning for cervical carcinoma.

Methods and materials: The data from 10 patients treated with HDR brachytherapy for cervical cancer using tandem and ovoids has been analyzed. Target and organ at risk volumes were defined using systematic guidelines. Dose distributions were created according to three different dose calculation protocols: point A, isodose line manually optimization, and inverse planning and dose–volume histograms from these plans were analyzed, and all plans were evaluated for V100%, V95%, the conformity index CI = V100%/VCTV, and the dose homogeneity index DHI = (V100% - V150%)/ V100% for target. For rectum D5cc, V50%, V70% and V100% of prescription dose were evaluated. For bladder D5cc, V50%, V80% and V100% of prescription dose were evaluated.

Results: Both 3D planning methods showed significant better target coverage compared with point A calculation: average 85.65% isodose manually shaping vs. 48.43% point A calculation ($p < 0.003$) and 90.33% inverse planning vs. 48.43% point A calculation ($p < 0.001$) for V7Gy. Dose homogeneity was better for both 3D planning protocols: average 0.33% isodose manually shaping vs. 0.39% point A calculation ($p < 0.008$) and 0.31% inverse planning vs. 0.39% point A calculation ($p < 0.031$) for DHI.
For organs at risk, point A calculation average was 4.29 Gy vs. 4.99 Gy isodose manually shaping ($p < 0.037$) and 4.29 Gy point A calculation vs. 5.14 Gy inverse planning ($p < 0.013$) for D5cc of rectum; and average 4.88 Gy point A calculation vs. 6.32 Gy isodose manually shaping ($p < 0.019$) and 4.88 Gy point A calculation vs. 5.78 Gy inverse planning ($p < 0.019$) for D5cc of bladder.

Conclusion: The 3D planning methods improve dose conformity and homogeneity of target coverage while minimizing dose to critical structures by chosen the appropriate priorities and allows for easy comparison between patients.

Keywords: Cancer cervix, inverse planning, Brachytherapy

Address for Correspondence:

Dr. Yasir Bahadur, Department of Radiology,
King Abdulaziz University Hospital, P.O. Box 6615, Jeddah 21452, Saudi Arabia
Fax: 0096626408047
E-mail: yasirbahadur@hotmail.com

Introduction:

Brachytherapy has been a standard component of radiation therapy for cervical cancer since shortly after the discovery of radium. Dose optimisation in brachytherapy is not a new concept and has been studied for more than 70 years. The reasons why this has only relatively recently become a topic for widespread study, is due to technological advances both in computing power and in imaging possibilities in 3D such as with CT and MRI.

In the particular case of cervix cancer, although there have been several different applicator systems and prescription methods, variations of the Manchester system have been the most commonly used. Dose prescription guidelines for this system are described in the ICRU report No. 38. Although these systems have provided a large body of well-documented clinical experience to support general prescription guidelines, there are limitations of these methods that likewise have been well documented [1, 2].

With the development of CT and MRI, compatible applicators, and computerized 3D treatment planning, it is now possible to obtain much more detailed information regarding tumor coverage and dose to nearby critical structures. Several authors have documented the underestimation of dose to bladder and rectum predicted by the Manchester system [3–6].

To address the inadequacies of traditional planning methods, three-dimensional treatment planning systems and anatomy-based planning optimization for brachytherapy are becoming available. Systematic guidelines for target delineation and dose constrictions have not yet been established for each disease site using anatomy-based planning systems.

In clinical practice, dwell positions or/and time values are usually adjusted manually. These optimization methods are therefore highly operator dependent, and practical guidelines to determine the dwell positions or to optimize the dwell time of each dwell position have not been clearly established. Moreover, some available methods, such as geometric and dose-point optimization are based on the location of the active dwells, failing to use anatomic information. To address these inadequacies, different anatomy-based inverse planning algorithms have been developed, governed by prescribed dose constraints on each anatomic volume.

The purpose of this study is to retrospectively evaluate the dosimetric superiority of inverse planning optimization and isodose line manually optimization (both 3D planning methods) versus conventional treatment plan (point A planning method), using various dosimetric indices in HDR brachytherapy planning for cervical carcinoma.

In this study we describe and compare two methods of 3D dose optimization with the traditional method of prescribing dose for the tandem and ovoids applicator in cervical cancer. This comparison is made by analyzing dose distributions to target and organ at risk volumes, comprehensive constraint definitions, target coverage, dose homogeneity, and OAR sparing.

Methods and materials:

We retrospectively analysed the data from 10 patients treated in our radiation therapy unit with HDR brachytherapy for cervical cancer using tandem and ovoids. The patients have been randomly selected. Target and organ at risk volumes were defined using systematic guidelines [1, 2]. The FIGO staging of these ten patients were as follow; one case was stageIB2, 5 stages IIB, 1 stage IIIA, 2 stage IIIB and 1 stage VIA. All patients received External Beam Radiotherapy(EBRT) a dose of 45 Gy in 25 fractions over 5 weeks with concomitant weekly Cisplatin, followed by three fraction of 7 Gy weekly using Fletcher Suit Device (FSD).

Target delineation:

In this study, the clinical target volume included: the gross tumor volume, entire uterus, cervix, ovoids, and vaginal extent of the tumor. The entire uterus was chosen to safely encompass all tumours while reducing the risk of a geographic miss.

Organ at risk volumes included the bladder and rectum. The entire bladder was contoured and the rectum was contoured 2cm below the ovoid till the recto-sigmoid flexure. No walls have been contoured for the organs at risk.

CT based planning was performed on Varian Brachyvision planning system, version 8.0, for Varian HDR VariSource 200. The clinical target volume (CTV) and organs at risk (OAR) of bladder and rectum were delineated. For each patient, 3 plans were made. The prescription dose was 7 Gy.

Dose distributions were created according to three different dose calculation protocols: point A, isodose line manually optimization, and inverse planning.

Point A calculation protocol is the conventional treatment planning, prescribing the dose at point A and assuming equal times for all dwell positions.

Isodose line manually optimization was used as an alternative planning method; it is a 3D planning method and consists in manually shaping the isodose lines, using a free hand tool of the planning system. The treatment planning system automatically calculates the dwell times accordingly. The isodose lines shaping was performed by a physician.

Inverse planning identifies the combination of dwell times that best conforms to dose constraints of target volume and critical organs. After the volumes of interest are contoured, dose constraints are given to dose calculation within each volume. Once the volumes of interest are drawn and the dose constraints are set, the inverse planning algorithm is run to calculate the optimal dwell times that fulfil the dose constraints.

The dose constraints used in our study were:

- For CTV: 95% of the volume to receive 7 Gy and 100% of the volume to receive 6.65 Gy (95% of the prescribed dose) (as a minimum).
- For rectum: 5% of the volume to receive 4.9 Gy (70% of the prescribed dose) and 100% of the volume to receive 3.5 Gy (as a maximum).
- For bladder: 5% of the volume to receive 5.6 Gy (80% of the prescribed dose) and 100% of the volume to receive 4 Gy (as a maximum).

The constraints for the organs at risk were set to have 100% priority, while for the CTV were set with 50% priority. The dwell time constraints were set at 300 s

The algorithms used by both isodose line manually shaping and inverse planning protocol are beyond the scope of this study.

Dose distributions and dose–volume histograms from these plans were analyzed, and all plans were evaluated using following indices: the volume receiving 100% of prescription dose V100%, the volume receiving 95% of prescription dose V95%, the conformity index CI = V100%/ VCTV, and the dose homogeneity index DHI = (V100% - V150%)/ V100% for target. For rectum, the doses received by volume of 5 cm3 (D5cc) and volumes receiving 50% (V50%), 70% (V70%) and 100% (V100%) of prescription dose were evaluated, and for bladder, the doses received by volume of 5 cm3 (D5cc) and volumes receiving 50% (V50%), 80% (V80%) and 100% (V100%) of prescription dose were determined.

The statistical analysis was done using the Wilcoxon matched pairs test and a p value of < 0.05 was considered significant.

Results:

Dose distributions and dose–volume histograms were generated for the target and organs at risk for all patients and all calculation protocols, as shown in ***Fig. 1.-3***.

The mean values with standard deviation for all dosimetric indices are given in ***(Table 1)***, as well as the p value generated by Wilcoxon matched pairs test. The point A calculation protocol has been considered as baseline of reference. Comparison of dose optimization methods in HDR brachytherapy for cervix cancer ***(table1)*** with 50 % priorities to CVT versus 100 % for the OAR

Dose–volume histogram analysis showed that both 3D planning methods indicated significant difference in clinical tumor volume prescription dose coverage compared with point A calculation: average 85.65% isodose manually shaping vs. 48.43% point A calculation ($p < 0.003$) and 90.33% inverse planning vs. 48.43% point A calculation ($p < 0.001$) for V7Gy. Also, the dose homogeneity was better for both 3D planning protocols: average 0.33% isodose manually shaping vs. 0.39% point A calculation ($p < 0.008$) and 0.31% inverse planning vs. 0.39% point A calculation ($p < 0.031$) for DHI. No statistical significance was found between isodose manually shaping and inverse planning

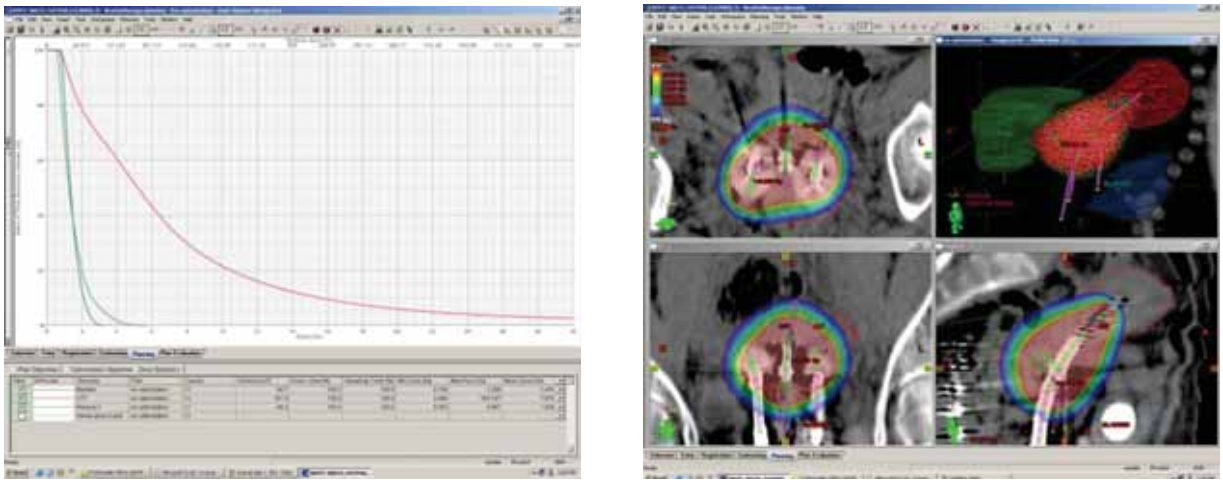

FIG. 1. POINT A CALCULATION PROTOCOL

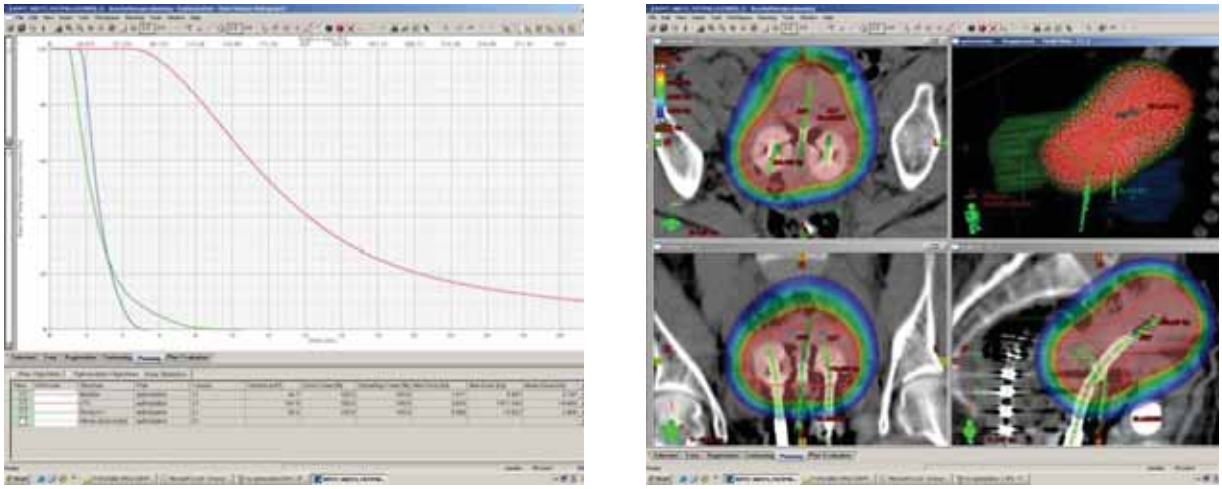

FIG. 2. ISODOSE LINE MANUALLY SHAPING

regarding the dose homogeneity index ($p < 0.546$).
For the organs at risk considered in this study, point A calculation method showed to provide better sparing then both 3D planning methods: average 4.29 Gy point A calculation vs. 4.99 Gy isodose manually shaping ($p < 0.037$) and 4.29 Gy point A calculation vs. 5.14 Gy inverse planning ($p < 0.013$) for D5cc of rectum; and average 4.88 Gy point A calculation vs. 6.32 Gy isodose manually shaping ($p < 0.019$) and 4.88 Gy point A calculation vs. 5.78 Gy inverse planning ($p < 0.019$) for D5cc of bladder. Again, the difference between isodose manually shaping and inverse planning regarding the sparing of organs at risk was not statistically significant ($p < 0.165$ for D5cc of rectum and $p < 0.919$ for D5cc of bladder).

Discussion:

Brachytherapy has been a standard component of therapy for carcinoma of the cervix for over 100 years. Although the Manchester system of prescribing to point A has been widely used for treatments with tandem and ovoids, several authors have questioned the accuracy of this planning method in terms of target coverage and dose to critical nearby structures [3, 5, 8, 9]. In particular, the method described in ICRU report No. 38 dictates dose distributions based on the visualization of the applicator and bony landmarks rather than coverage of the tumor and critical structures [3]. With the advent of CT-based treatment planning systems, these controversial issues can be quantitatively addressed.

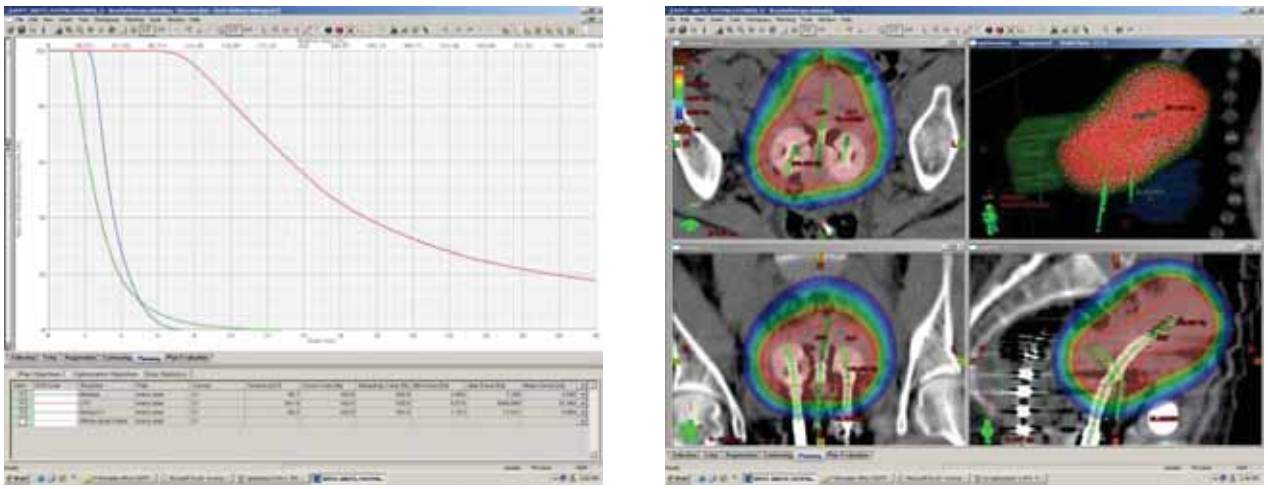

Fig. 3. Inverse planning

Table 1. Comparison of dose optimization methods in HDR brachytherapy for cervix cancer

	Isodose manually shaping (b)	Inverse planning (c)	p (a-b)	p (a-c)	p (b-c)
CTV					
V_{7Gy} (%)	85.65 ± 8.25	90.33 ± 7.97	0.003	0.001	0.275
$V_{95\%}$ (%)	88.2 ± 7.6	91.61 ± 7.21	0.003	0.001	0.556
CI (%)	0.85 ± 0.08	0.90 ± 0.07	0.003	0.001	0.275
DHI (%)	0.33 ± 0.09	0.31 ± 0.11	0.008	0.031	0.546
Rectum					
D_{5cc} (Gy)	4.99 ± 1.05	5.14 ± 7.97	0.037	0.013	0.919
$V_{50\%}$ (%)	34.91 ± 14.09	38.16 ± 7.21	0.027	0.011	0.244
$V_{70\%}$ (%)	11.67 ± 7.93	12.96 ± 19.04	0.004	0.009	0.431
$V_{80\%}$ (%)	4.44 ± 4.56	6.26 ± 2.31	0.013	0.013	0.184
$V_{100\%}$ (%)	1.22 ± 0.98	1.87 ± 7.73	0.652	0.148	0.695
Bladder					
D_{5cc} (Gy)	6.32 ± 4.19	5.78 ± 3.17	0.019	0.019	0.232
$V_{50\%}$ (%)	49.77 ± 28.23	51.76 ± 13.63	0.013	0.013	0.198
$V_{80\%}$ (%)	15.88 ± 20.32	11.01 ± 24.28	0.006	0.012	0.155
$V_{100\%}$ (%)	7.04 ± 17.96	3.79 ± 12.51	0.078	0.954	0.148

The important next step to these studies documenting the inadequacies of the ICRU prescription method is to determine whether something can be done to improve on it.
As the use of anatomy-based treatment planning for HDR brachytherapy of the cervical carcinoma becomes more widely used, a systematic method of dose optimization is important for quality assurance, reproducibility, and respect of time restrictions.
Currently available optimization schemes, such as geometric and dose point optimization, fail to use the anatomic information. Because these optimizations are based only on the location of the active dwells, these methods necessarily result in an approximation of the shape of the anatomy. Reducing the clinical target volume to a geometric representation without regard to anatomic relationships can result in a poor coverage of the target and an overdosage of normal tissues. To maintain complete coverage of the tumor and simultaneously reduce the dose to normal organs at risk of radiation injury, the dose distribution should be as conformal as possible to the relevant anatomy.
Alternatively, dose distribution can be manually obtained by adjusting relative dwell time values until an acceptable solution is found; computer is used only to calculate the dose distribution once the plan has been decided by the dosimetrist. This approach, or the combination of this approach with geometric optimization, requires more time and skill. A better and more efficient planning system would mean replacing manual planning with a computer optimization program that integrates scan based anatomic information. The current commercial planning systems cannot be truly anatomy based without a genuinely anatomy-based optimization. An important distinction must be made between a planning system where doses are optimized based on anatomic structures vs. a geometrically optimized planning system where doses are optimized based on location of the active dwells. Employment of anatomy-based optimization is the final step toward truly anatomy-based planning. This approach brings the planning process nearest to the real clinical issues.
In this study we described and compared two methods of 3D dose optimization (isodose line manually shaping and inverse planning) with the traditional method of prescribing dose for the tandem and ovoids applicator in cervical cancer (point A planning method), by retrospectively analyzing dose distributions to target and organ at risk volumes, using various dosimetric indices. Both 3D planning methods proved to provide superior dosimetric target coverage than conventional treatment plan (point A planning method). However, this improvement in target coverage was associated with slightly more dose to organ at risk
Kelly et al showed that inverse planning simulated annealing (IPSA) did not improve clinical tumour coverage (CTV) as compared with point A method of calculation with optimization (median 87 % Vs 82 %, p=0.36) dose to bladder and rectum were less, p=0.04 and P= 0.05 respectively. Our study did not show a similar improvement in the sparing of rectum and bladder doses which could be due to their definition of target volume which excluded the anterior and posterior vaginal walls, while in our study the target volume include all vaginal walls and this explain why in our study the inverse planning has little effect in sparing the OAR. .
Also, because the 3D planning methods are independent of the dosimetrist experience, and the anatomic dose prescription does not change, plans are produced that are consistent between patients, allowing comparisons between them.
With these dose 3D optimization methods, physicians have more control of the treatment. The ability to balance the target dose coverage against the dose homogeneity and the protection of organs at risk is improved and the focus becomes the physician's prescription to the target and the adjustments required to limit injury to normal structure, adapted to individual clinical circumstances.
However, a note of caution must be added: in the case of isodose line manually shaping method, enabling isodoses to conform to the specific topography of the target may involve wide variations in dwell times, resulting in hot spots within the implant and the clinical consequences must be considered carefully. There are no clearly defined rules for treatment plan optimization in brachytherapy, and the exact limits of variations between dwell times are yet unknown. In this regard, software tools performing automatic optimization of the dose distribution should be used with caution. This is not the case of inverse planning method, where constraints for the dwell times can be easily set, resulting in more homogeneous dwell times and making this method to appear safer.(this means that although there is no statistically significant between the isodose manual shaping and in verse planning; the inverse planning is better and reliable
The total treatment planning time for a case (including CT, contouring, dosimetry, analysis, and approval) is around 60 min for 3D planning protocols and about 45 min for point A calculation method.

Conclusion:

As the use of anatomy-based treatment planning for HDR brachytherapy of the cervix becomes more widely used, a systematic method of dose optimization is important for quality assurance, reproducibility, and respect of time restrictions.
Although manually adjusting relative dwell time values is always an option, the 3D planning methods (isodose line manually optimization, and inverse planning) provide a reliable, fast and automatic solutions for the optimization of dose distribution by improving dose conformity and homogeneity of target coverage while minimizing dose to critical structures by chosen the appropriate priorities and allows for easy comparison between patients. The dosimetric gain achieved by inverse planning may reflect in patient treatment outcome significantly.

REFERECES:

1. Richard Potter et al., 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, Radiotherapy and Oncology, Vol. 78, 67–77, 2006.

2. Haie-Meder C. 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, Radiotherapy and Oncology, Vol. 74, 235–245, 2005.

3. Kelly D. DeWitt et al., 3D Inverse treatment planning for the tandem and ovoid applicator in cervical cancer, Int. J. Radiation Oncology Biol. Phys., Vol. 63, No. 4, 1270–1274, 2005.

4. Etienne Lessard et al., Inverse planning for interstitial gynaecologic template: truly anatomy-based planning, Int. J. Radiation Oncology Biol. Phys., Vol. 54, No. 4, 1243–1251, 2002.

5. G. K. Rath et al., Comparison of inverse planning optimization with classical optimization methods in HDR interstitial template Brachytherapy planning for cervical carcinoma, Int. J. Radiation Oncology Biol. Phys., Vol. 69, No. 3, 2007.

6. D. Baltas, Optimisation - inverse optimisation and inverse planning in brachytherapy: almost a common approach to external beam, Int. J. Radiation Oncology Biol. Phys., Vol. 58, No. 4, 2002.

7. Dietmar Georg et al., Image-guided radiotherapy for cervix cancer: high-tech external beam therapy versus high-tech brachytherapy, Int. J. Radiation Oncology Biol. Phys., Vol. 71, No. 4, pp. 1272–1278, 2008.

8. Nag S., Cardenes H., et al. Proposed guidelines for image-based intracavitary brachytherapy for cervical carcinoma: report from image-guided brachytherapy working group, Int. J. Radiat. Oncology Biol. Phys., Vol. 60, No. 4, 2004.

9. Enrique Chajon et al., Inverse planning approach for 3-D MRI-based pulse-dose rate intracavitary brachytherapy in cervix cancer, Int. J. Radiation Oncology Biol. Phys., Vol. 69, No. 3, pp. 955–961, 2007 .