

PHYSICS CONTRIBUTION

3D INVERSE TREATMENT PLANNING FOR THE TANDEM AND OVOID APPLICATOR IN CERVICAL CANCER

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Purpose: Three-dimensional treatment planning systems and inverse planning optimization for brachytherapy are becoming commercially available. Guidelines for target delineation and dose constrictions have not been established using this new software. In this study we describe a method of target delineation for the tandem and ovoids applicator. We then compare inverse planning dose distributions with the traditional methods of prescribing dose.

Methods and Materials: Target and organ-at-risk volumes were defined using systematic guidelines on 15 patients treated in our department with high-dose-rate brachytherapy for cervical cancer using tandem and ovoids. High-dose-rate distributions were created according to three different dose optimization protocols: inverse planning simulated annealing (IPSA), point A, and point A with a normalization of 2 cc of the bladder receiving 80% of the dose (bladder-sparing method). A uniform cost function for dose constraints was applied to all IPSA generated plans, and no manual optimization was allowed for any planning method.

Results: Guidelines for target and structure-at-risk volumes, as well as dose constraint cost functions, were established. Dose–volume histogram analysis showed that the IPSA algorithm indicated no difference in tumor coverage compared with point A optimization while decreasing dose to the bladder and rectum. The IPSA algorithm provided better target volume coverage compared with bladder-sparing method with equivalent doses to the bladder and rectum.

Conclusions: This study uses a systematic approach for delineating target and organ-at-risk volumes and a uniform cost function for generating IPSA plans for cervical cancer using tandem and ovoids. Compared with conventional dose prescription methods, IPSA provides a consistent method of optimization that maintains or improves target coverage while decreasing dose to normal structures. Image-guided brachytherapy and inverse planning improve brachytherapy dosimetry. © 2005 Elsevier Inc.

Cervical cancer, HDR brachytherapy, Tandem and ovoid, Anatomy-based planning, Inverse planning.

INTRODUCTION

Brachytherapy has been a standard component of definitive radiation therapy for cervical cancer since shortly after the discovery of radium. Although there have been several different applicator systems and prescription methods, variations of the Manchester system have been the most commonly used in the United States. 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 computed tomography (CT) and magnetic resonance imaging (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 (3–9).

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

In this study we describe a method of target and organ-at-risk delineation for the purpose of treatment planning and dose optimization for the tandem and ovoids applicator in cervical cancer. We then compare inverse planning dose distributions to target and organ-at-risk volumes with the

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Presented at the American Society for Therapeutic Radiology and Oncology Annual Meeting (ASTRO), Salt Lake City, UT, October 22, 2003.

Received Feb 12, 2004, and in revised form July 7, 2005. Accepted for publication July 11, 2005.

traditional methods of prescribing dose to determine whether inverse planning–simulated annealing (IPSA) can limit the dose to critical nearby structures without compromising target volume coverage.

METHODS AND MATERIALS

We retrospectively extracted the data from 15 patients treated in our department with high-dose-rate (HDR) brachytherapy for cervical cancer using CT-compatible tandem and ovoids. Target and organ-at-risk volumes were defined using systematic guidelines. The target volume included the ovoids as well as the cervix and the entire uterus. The lateral vaginal walls were included in the target volume, whereas the anterior and posterior vaginal walls were excluded to optimize the contribution from the ovoids without overdosing the vaginal mucosa (Fig. 1). Organ-at-risk volumes included the bladder, rectum, small bowel, and urethra. The rectum was contoured from the anus to the rectosigmoid flexure. All small

bowel surrounding the uterus and 2 cm above the fundus of the uterus was contoured.

High-dose-rate dose distributions were created according to three different dose optimization protocols: IPSA, point A, and point A with a normalization of 2 cc of the bladder receiving 80% of the dose (bladder-sparing method). This third optimization protocol was chosen to address clinically relevant dose limitations to the bladder that have been recommended by other authors (10–12) with 2 cc being a surrogate for a maximum point dose. By normalizing 2 cc of the bladder to receive 80% of the target dose, we ensured against a potentially dangerous hot spot in the bladder.

Inverse planning–simulated annealing is the HDR optimization tool that our team has developed at the University of California, San Francisco (13, 14). The program combines two parts: (1) a user-to-computer translator that gathers the anatomic dose constraints of the physician, and (2) an optimization engine that finds the best solution to fulfill the constraints. Target volumes and organs at risk are contoured on each slice of the scan used for CT-based planning. Dwell source positions are automatically de-

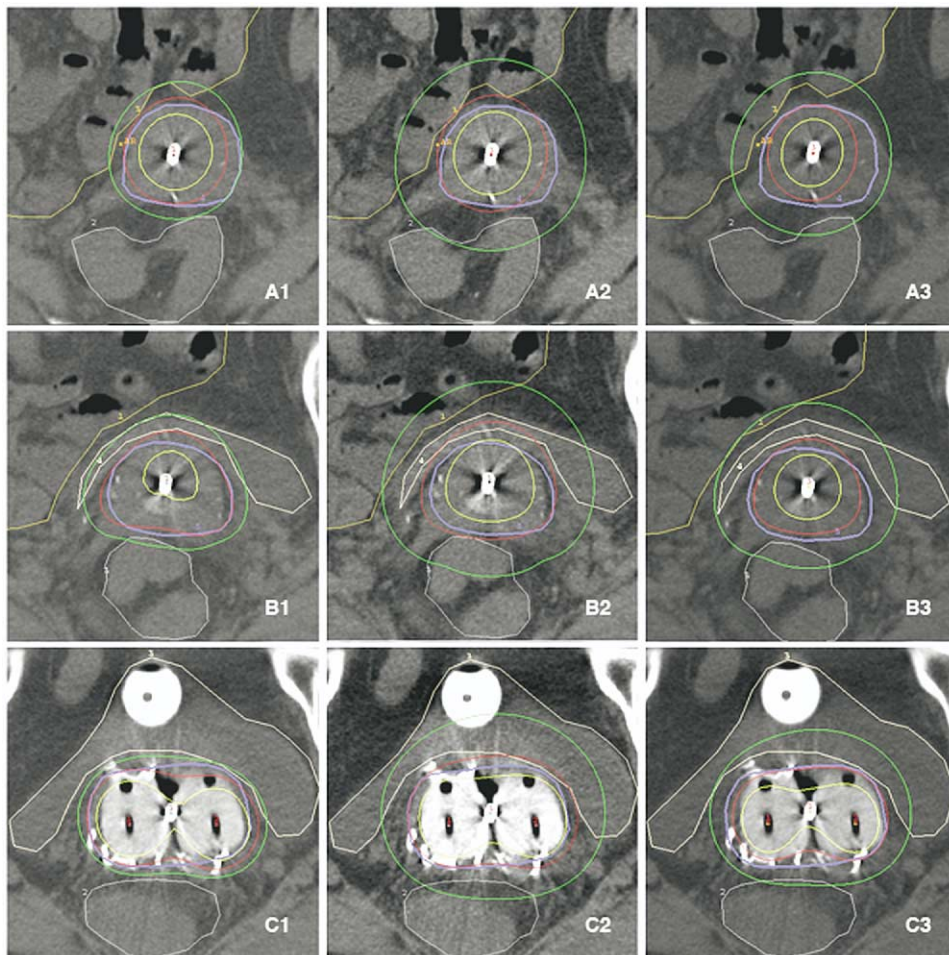


Fig. 1. Examples of target volume and dose distributions using three prescription methods. The target volume included the ovoids, cervix, and the entire uterus. Organ-at-risk volumes included the bladder, rectum, small bowel, and urethra. The lateral walls of the vagina were included in the target volume, whereas the anterior and posterior vaginal walls were excluded to optimize contribution from the ovoids without overdosing the vaginal mucosa. Panel A is at the level of the mid ovoids, Panel B is at the level cervical os, Panel C is at the level of point A. Method 1 is IPSA; method 2 is point A; method 3 is bladder sparing (2 cc of bladder limited to 80% of dose). The yellow line is the 150% isodose line, the red line is the 100% isodose line, and the green is the 50% isodose line.

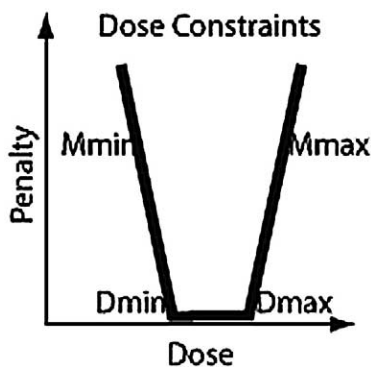


Fig. 2. A graphic illustration of the cost function. The cost function represents an allowable range of dose and an assigned penalty for violating that range. Dmin = minimum dose, Dmax = maximum dose, Mmin = slope of penalty function for violating minimum dose constraint, Mmax = slope of penalty function for violating maximum dose constraint. The slope ranges from 0 to 100. It allows the user to assign a relative weight to different portions of the curve. The cost function can be customized to each patient.

terminated based on the target and organ-at-risk contours, and dwell times are automatically optimized.

Inverse planning simulated annealing identifies the combination of dwell times that best conforms to dose constraints of target volumes and critical organs. After the volume of interest is contoured, dose constraints are given to dose calculation points within each volume. For each contoured volume, there are two types of dose calculation points. One set of dose calculation points is located near the surface of the contour, and the other set is located near the dwell positions. The adjustment dose to the first set of dose points controls the target coverage and conformality, and adjustment of dose to the second set of dose points controls the dose homogeneity. An example of dose constraints is described below and plotted in Fig. 2.

Dmin and Dmax represent the lower and the upper range of acceptable doses. If the dose goes below or above the range, the penalty increases at rates Mmin and Mmax, respectively. Adjustment of Mmin and Mmax sets the relative importance between structures. Once the dose constraints are set, IPSA finds the dwell time combination with the least amount of penalty using the simulated annealing algorithm.

Once the target volumes are drawn and the cost function dose constraints are set, the inverse planning routine is run to determine which dwell positions are active and calculates dwell times to fulfill the dose constraints. No manual optimization was allowed

for any planning method. Dose–volume histograms from these plans were analyzed, and data were compared using the Wilcoxon matched pairs test.

RESULTS

Guidelines for target and structure-at-risk volumes, as well as dose constraint cost functions, were established that adequately accommodated all 15 patient plans with no manual optimization. Dose–volume histogram analysis showed that the IPSA algorithm indicated no difference in clinical tumor volume prescription dose coverage compared with point A optimization (medians, 87% [IPSA] vs. 82% [point A]; $p = 0.36$) (Fig. 3A) while simultaneously decreasing dose to the bladder and rectum ($p = 0.04$ and $p = 0.05$, respectively) (Fig. 3B, 3C). The IPSA algorithm provided better clinical tumor volume prescription coverage compared with bladder-sparing method (medians, 87% [IPSA] vs. 75% [bladder at 80%]; $p = 0.05$) (Fig. 3A) with equivalent dose to the bladder and rectum ($p = 0.39$ and $p = 0.24$, respectively) (Fig. 3B, 3C). All planning methods provided an equivalently low dose to the urethra and small bowel and were clinically negligible in all cases. IPSA provided a mean of 87% of the prescribed dose at point A compared to the other two planning methods that delivered, by definition of the normalization point, 100% of the dose at point A.

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. Several studies have shown ICRU prescription

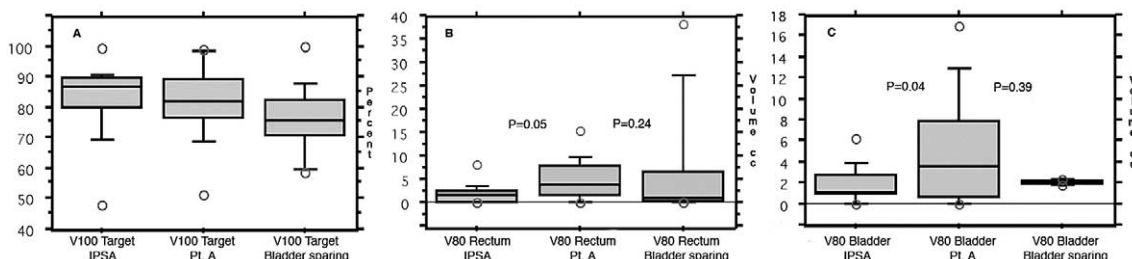


Fig. 3. Box plot diagrams of dose–volume histogram analyses of three prescription methods. (A) P100 target = percent of target receiving 100% of the prescribed dose. (B) V80 rectum = volume of rectum receiving 80% of the prescribed dose. (C) V80 bladder = volume of bladder receiving 80% of the prescribed dose.

points to be underestimations of bladder and rectal maximum doses. Additionally, ICRU does not account for dose to the small bowel.

In a review of 28 patients treated with tandem and ovoids, Fellner *et al.* (3) superimposed dose distributions obtained by traditional point A prescribing methods on CT scans to derive dose–volume histograms of the target and critical structures. In this study, the target was described as the cervix, gross tumor, and parametrial extension if identifiable, as well as the cervix and central part of the uterine corpus if the images did not reveal a gross tumor. Results from comparison showed that 9 cc of the rectum and 16 cc of the bladder were receiving doses above the ICRU maximum doses. On average, the maximum doses to these organs were found to be 1.5 times higher for rectum and 1.4 times higher for bladder compared with the ICRU points. Less than 25% of the time was the ICRU point an accurate estimation of Dmax for bladder. Other authors have also shown ICRU points to be an underestimation of the bladder Dmax (5–8, 15–17).

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. Although manual optimization is always an option, a systematic method of dose prescription is important for quality assurance, reproducibility, and respect of time restrictions. The IPSA routine provides a reliable method of reducing critically high overdosing of sensitive structures in less than 1 min and allows for easy comparison between patients. Ultimately, this allows for less reliance on the experience of the dosimetrist and treating physician.

Recent data from Cheng *et al.* have suggested that a proximal rectal dose, defined as the anterior rectal wall at the rectosigmoid junction, is a better estimation of Dmax than the ICRU rectal point. Clinical outcomes were found to correlate with this finding, because patients with \geq Grade 2 rectal complications were found to have a higher proximal rectal dose, whereas this outcome did not correlate with the ICRU rectal point (18).

Although it is possible that systematic modifications of the ICRU prescription methods, such as using the proximal rectal dose or limiting the Dmax to 2 cc of the bladder or rectum, could guard against dangerously high doses to critical structures, our study shows that doing this is likely to compromise coverage of the target volume. Dosimetric analysis using 3D treatment planning is critical to know the effects of various modifications on tumor and nearby structure doses. IPSA provides a systematic method of assuring target coverage while simultaneously limiting dose to nearby structures. IPSA also leads to optimization not achievable by humans, because of the number of variables posed by too many structures and dwell positions in the setting of time constraints.

Target delineation

Delineation of target volume is another issue of debate that is addressed in this study. Previously, the standard method of dose prescription has been to ICRU points based

on bony landmarks and applicator position. With the advent of image-based treatment planning, we are now posed with defining what appropriate target and critical structure volumes should be.

In our study we included the entire uterus, the cervix, the ovoids, and the lateral walls of the vagina in the target volume. The lateral walls of the vagina were included to increase contribution from the ovoids, thus more effectively treating the parametrium without overdosing the bladder and rectum. The entire uterus was chosen to safely encompass all tumor while reducing the risk of a geographic miss.

Other authors have suggested more conformal fields based on image-guided tumor delineation with MRI. In a study by Wachter-Gerstner *et al.*, MRI was found to be superior to CT in delineating accurate tumor volumes. Target delineation was defined as the whole uterine cervix and tumor extension into the uterine corpus. No margin was added to the target volume. By using MRI images to delineate tumor volume, the investigators were able to escalate dose to the target without increasing dose to the bladder and rectum beyond tolerance levels (12). In the study by Fellner *et al.*, CT images were used to delineate target volumes. If possible, the macroscopic tumor was delineated and a margin added. However, if the corpus uteri appeared normal on CT, only the central portion of the corpus was enclosed (3).

At this point, we do not have the clinical outcomes data to support the use of one target delineation method over another. However, it seems prudent to avoid being overly conformal in the absence of reliable imaging methods to define precise tumor volume. MRI-based treatment planning, as described in the study by Wachter-Gerstner *et al.*, may obviate the need for conservative tumor delineation, allowing us to make the next step toward increasing conformality (12). The IPSA planning routine has allowed us to be generous in our choice of a target and closely resemble the ICRU 38 guidelines while reducing the dose to critical nearby structures. Whether this concept of adequate dose distribution can be abandoned for more conformal targeting remains to be seen.

Cost function

The IPSA treatment planning system finds an optimal solution by processing cost functions with boundary conditions. The cost function, therefore, defines these boundaries for each structure and assigns penalties for violating these boundaries. The dose constraints are defined for the target or organ surface as well as points within these structures. This allows for definition of underdosing and overdosing constraints. It is in the designation of these boundaries and penalties that the physician controls the treatment planning. The IPSA dose optimization system has previously been shown to provide brachytherapy plans that allow for higher doses to tumor without overdosing nearby critical structures in both prostate and interstitial gynecologic implants (13, 14, 19, 20).

One goal of this study was to define a uniform cost function that provided an adequate dose distribution for

all 15 patients without manual optimization. In doing so, we devised a single cost function that worked well for 13 of the 15 patients in our study. There were 2 patients for which this cost function resulted in a poor coverage of the tumor, explaining the outliers in the graph. While no optimization system can overcome poor geometry, in clinical practice at our institution we do not adhere strictly to this single-cost function. Penalties for dosing different structures are manually relaxed or heightened to achieve an adequate dose distribution for all patients. The cost function presented in our study provides a reliable starting point applicable to all tandem and ovoid treatments with minimal manual optimization.

CONCLUSION

As the use of anatomy-based treatment planning for tandem and ovoid brachytherapy applicators becomes

more widely used in both academic and community settings, the need for a set of guidelines regarding target and critical structure delineation, as well as dose prescriptions, increases. This study defines systematic guidelines for delineating target and organ-at-risk volumes and establishes a uniform cost function for generating IPSA plans for cervical cancer using tandem and ovoids. IPSA provides a method of optimizing target coverage while minimizing dose to critical structures. Compared with conventional dose prescription methods, IPSA maintains or improves target coverage while decreasing dose to normal structures. This study provides practical guidelines for use of this recently available planning software for treatment of cervical cancer with tandem and ovoids and gives data to suggest its advantage over traditional prescription methods in reducing the risk of long-term severe side effects.

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