Technical Note

Role of step size and max dwell time in anatomy based inverse optimization for prostate implants

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ABSTRACT

In high dose rate (HDR) brachytherapy, the source dwell times and dwell positions are vital parameters in achieving a desirable implant dose distribution. Inverse treatment planning requires an optimal choice of these parameters to achieve the desired target coverage with the lowest achievable dose to the organs at risk (OAR). This study was designed to evaluate the optimum source step size and maximum source dwell time for prostate brachytherapy implants using an Ir-192 source. In total, one hundred inverse treatment plans were generated for the four patients included in this study. Twenty-five treatment plans were created for each patient by varying the step size and maximum source dwell time during anatomy-based, inverse-planned optimization. Other relevant treatment planning parameters were kept constant, including the dose constraints and source dwell positions. Each plan was evaluated for target coverage, urethral and rectal dose sparing, treatment time, relative target dose homogeneity, and nonuniformity ratio. The plans with 0.5 cm step size were seen to have clinically acceptable tumor coverage, minimal normal structure doses, and minimum treatment time as compared with the other step sizes. The target coverage for this step size is 87% of the prescription dose, while the urethral and maximum rectal doses were 107.3 and 68.7%, respectively. No appreciable difference in plan quality was observed with variation in maximum source dwell time. The step size plays a significant role in plan optimization for prostate implants. Our study supports use of a 0.5 cm step size for prostate implants.

Key words: High dose rate brachytherapy, inverse optimization, adoptive volume optimization, step size, dwell time

Introduction

High dose rate (HDR) brachytherapy using a miniature Iridium-192 source plays a pivotal role in prostate radiotherapy. In this era of dose escalation and hypofractionation, when clinicians throughout the world are trying to exploit the unique radiobiological property of prostate cancer of having low α/β ratio, good HDR brachytherapy planning is becoming more and more important. Optimizing dwell time, dwell position, step size, and maximum dwell time using an inverse optimization technique; a wide range of treatment plans can be generated for a given implant and intensity optimized brachytherapy can be practiced in its true sense.

The challenge is to select the optimal values of dwell time, step size, and maximum dwell time for the unique clinical situation of each patient. The optimization tools presently used in treatment planning were developed at a time when secondary capture planar images were used for the treatment planning. That method tries to maximize the dose homogeneity within the tumor volume based on the catheter and source locations using the TG-43[1] recommendation, using a uniform tissue attenuation factor based on water and air measurements. Treatment planning systems based on this formalism do not incorporate the

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tissue attenuation based on measured Hounsfield units. Therefore, geometric coverage of the target volume by a specific isodose line may not reflect the true *in vivo* dose coverage. In the geometrical optimization technique, the dwell times need to be carefully adjusted after the optimization to improve the tumor dose coverage and reduce the dose delivered to the organs at risk (OARs).

Since anatomic information in axial computed tomography (CT) images (Hounsfield unit) is not considered in geometrical optimization, the treatment planning quality indices; such as coverage index, dose homogeneity index (DHI), overdose volume index, dose nonuniformity ratio (DNR), and OAR doses cannot be optimized. Manually adjusting several hundred dwell times through trial and error is a time consuming, labor intensive, and inaccurate process. Nonetheless, eventually a clinically acceptable treatment plan can be achieved.[2] Inverse optimization solves these issues using less planning time. Few authors have compared the superiority of inverse optimization with the other available optimization techniques.[2,3] This inverse optimization is accomplished using either anatomy-based inverse planning or inverse planning by stimulated annealing (IPSA).

The IPSA method uses an objective function equal to a weighted sum of penalty costs at dose calculation points, given the dwell times. In the IPSA framework, the mathematically optimal solution is the solution of dwell times that globally minimizes the objective function. IPSA's single objective function assumes that the clinician has specified desirable dose penalty costs and generates a single dwell time's solution, in contrast to multiobjective optimization formulations that consider the weights as variables and generate a Pareto front of solutions.[4]

The anatomy-based inverse planning was tested with different theories and algorithms.[5-9] One of such method is adoptive volume optimization (AVOL). AVOL commercially available with Ecilpse BrachyVision software (Varian Medical System Inc, Palo Alto, CA) uses a dose volume histogram (DVH) and dwell time optimization to find an optimal dwell time and dwell positions. The main limitation of such optimizer engines is the requirement of selecting the optimal input parameters such as step size and maximum dwell time before starting a new plan with inverse optimization by the treatment planner. These input parameters are the initial solutions to start the iterations process. An experience treatment planner put the input values from the clinical experience, however these values are arbitrary. The final solutions, that is, calculated source dwell time and dwell positions of the completed treatment planning are likely to be contingent by the initial solution. Different selections of step size and maximum dwell time will result in different dose distributions. Although it is a day-to-day problem for the treatment planner to choose an appropriate input parameter; however, no significant literature is found that tests these parameters for prostate implants. Therefore, this study was designed to find the optimal step size and maximum dwell time for planning prostate implants using the Eclipse BrachyVision software.

Materials and Methods

Mathematical formulation for AVOL

BrachyVision 8.0 uses an AVOL. The optimization program attempts to match the user-defined dose volume histogram (DVH) limits with the structure DVH, while creating smoother dwell times and less hot spots (HSs).[10] The AVOL optimizer works to solve the weighted, quadratic (parabolic; $Y = x^2 + x$) set of simultaneous equations to find the vector t of dwell times to minimize the sum of the DVH error (Δ_{DVH}; Equation i), HS error (Δ_{HS}; Equation ii) and dwell time (DT) error (Δ_{DT}; Equation iii). Δ_{DVH} is the sum of the total DVH error for all organs at risk is given as:

$$\Delta_{DVH} = \sum_{g=1}^{p} w_g \times (Z_g^2 + Z_g) \quad \text{..... (i)}$$

Where π is the total number of DVH constraints for all surface/volume constraints across all structures. Z_γ is the percentage by which constraint γ is not satisfied. Z_γ reduces to zero if all constraints are satisfied. w_γ is the weight/priority of constraints. In the graphical user interface (GUI), w_γ is specified in the range (0,100); however at the final stage of optimization it is renormalized to (0, 1) range.

Total HS error Δ_{HS} is formulated as:

$$\Delta_{HS} = \frac{^{w}HS}{H} \times \sum_{h=1}^{H} (N_h^2 + 0.5 \times N_h) \quad \text{.....(ii)}$$

w_{HS} is weight/priority of the HS constraints, normalized over total number of HSs H. In GUI, w_{HS} specified in the range (0,100) then normalized to (0,1) at the final stage of optimization. N_h is the percentage by which a HS dose is above the allowed limit (0 if ≤ limit).

Total Dwell time error is formulated as:

$$\Delta_{DT} = w_{DT} \times \sum_{d=1}^{D} 1(T_{d-1}, T_d) \times \left(\frac{|T_{d-1} - T_d|}{T_{d-1} + T_d} \times 10 \right)^{\alpha} \quad \text{..... (iii)}$$

Where, w_{DT} is the weight/priority of the dwell-time constraints specified in the range 0,1. α is the "smooth" power and specified in the GUI in the range of (0, 300), and finally scale down to (0,3) range. D is the number of dwell positions. T is a vector of D dwell times. T_d is the dwell time at dwell index d. $1(T_{d-1}, T_d)$ is an indicator function returning 1 if T_{d-1}, T_d are adjacent and $T_{d-1} + T_d > 0$. The

dwell time error is very sensitive to small dwell times, for example, adjacent dwell times of (0,0) contribute an error of 0 while adjacent dwell times of ($0,10^{-7}$) contribute an error of 10α (the maximum error). AVOL also has a maximum dwell time limit and it is assumed that the optimizer obey this limit. Conclusively, to get an optimal individual treatment plan based on the anatomy-based AVOL; a set of simultaneous equations (i, ii, and iii) of degree two (parabolic) need to be solved against the dwell time and dwell index (position). However, this mathematical formulation is attributed to the optimization process which is contingent by the input parameters. Therefore, it is required to specify the most appropriate input parameters for achieving the clinically most appropriate treatment plan with desirable tumor coverage and fewer doses to organ at risk. For testing the software in clinical setting and to find the most appropriate input values of maximum dwell time and step size, four patients with carcinoma of the prostate were chosen for investigation purposes, each of these patient had been previously treated earlier in our clinic using geometrical optimization. New treatment plans were generated using the treatment planning system and the inverse optimization technique, this time considering the anatomical structures.

Brachytherapy source loading catheters were implanted in the patient using transrectal ultrasound (TRUS) imaging, followed by reconstructed axial CT slices for treatment planning with Eclipse BrachyVision.

The urethra was defined using a Foley catheter. Rectum, bladder, and target volume were delineated by the clinician on the CT images. The goal of inverse planning was set to be more than 85% target coverage with maximum urethra dose not to exceed 120%. The 85% target coverage was selected to restrict the dose to the anterior rectal wall as the clinical target volumes (CTV) included the anterior rectal wall. Thus, some portion of CTV needed to be underdosed. The rectal dose was limited to 65% of the prescribed dose.

The study was designed to evaluate the impact of two variables: The maximum source dwell time and the step size in clinical treatment planning subject to the relative dose volume constraints for individual patients. All combinations ($^5C_1 \times {}^5C_1$) of different step sizes 1, 3, 5, 7, and 10 mm and maximum dwell times 20, 40, 60, 80, and 100 s were checked; generating 25 treatment plans for every patient and total 100 treatment plans for four patients. All the treatment plans were evaluated for target coverage, normal structure doses, treatment time, and other quality indices as defined here below.

Relative DHI

This is defined as the ratio of the target volume which receives a dose in the range from 100 to 150% of the reference dose to the volume of the target that receives a dose equal to or greater than the reference dose.[8]

$$DHI = [TV_{Dref} - TV_{1.5Dref}]/TV_{Dref}$$

Where, TV_{Dref} is the total treatment volume enclosed by the prescribed treatment dose rate (D_{ref}) and $TV_{1.5Dref}$ indicates the volume enclosed by high dose rate, which is 1.5 times higher than reference dose rate ($1.5 \times D_{ref}$).

Dose nonuniformity ratio

This is the ratio of the target volume receiving a dose equal to or greater than 150% of reference dose to the volume of the target which receives a dose equal to or greater than the reference dose.[8]

$$DNR = TV_{1.5Dref}/TV_{Dref}$$

Notations have their usual meaning as specified in case of DHI.

Results

On analyzing a total of 100 treatment plans, we found a mean target volume of 58.2 cm^3. A minimum of 16 and maximum of 18 catheters were used to achieve target coverage with prescribed dose. Minimum 16 and maximum 18 catheters were used for obtaining required dose coverage to target. Source loading length in craniocaudal direction varied between 5.0 and 6.5 cm for all patients. The minimum and maximum target volumes were covered by prescription dose of 74.8 and 92.5%, respectively; with standard deviation (SD) of 4.4%. Thirty-eight percent of treatment plans fulfilled our criteria for clinical acceptability, achieving the target volume coverage by at least 85% of the prescribed dose.

Step sizes of 1 and 10 mm were used in the eight plans with a ratio of 3:5, respectively. Table 1 shows the variation of target coverage with step sizes. The amount of planning target volume (PTV) receiving 200% of the prescribed isodose (V_{200}) varied from 1 to 10% was noted as a function of the step size and the maximum dwell time. Detailed analysis shows that step sizes of 1 and 10 mm produced plans with higher V_{200} values, as compared to other step sizes. Approximately 85% of plans with 1 mm step size and 75% of plans with 10 mm step size produced V_{200} of more than 3% of volume. The maximum variation in V_{200} for the variation in step size was noted as 11% and a minimum V_{200} value, of 1% was noted with 5 mm step size.

Mean SD of V_{200} for different step sizes varied from 0.16 to 1.26. Variation of V_{200} with step size for a given dwell time is presented in Figure 1a. The variation in V_{200} with the variation in maximum dwell time constraint was insignificant, as compared to the variation with step size.

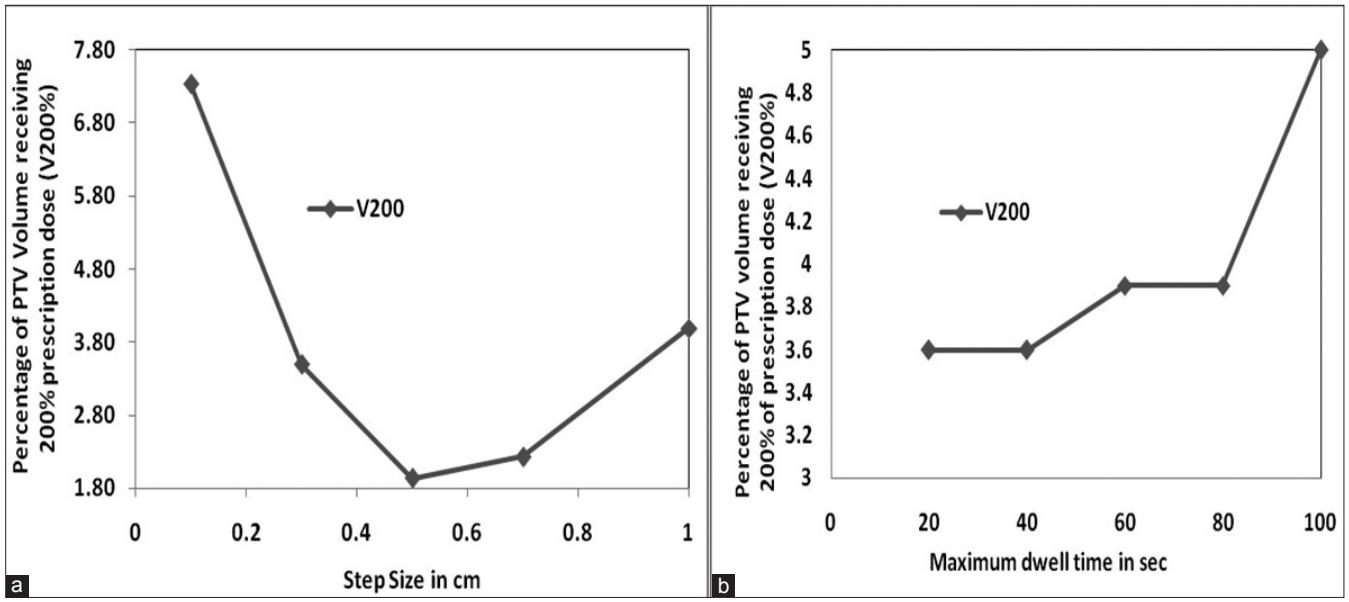

Figure 1: (a) Variation of planning target volume receiving 200% of prescription dose with maximum dwell time. (b) Variation of percentage PTV receiving 200% of prescription dose with maximum dwell time

V_{200} shows a variation of 3.5-5% with the maximum dwell time variation. The treatment plan using a 40 s dwell time had a lower V_{200} value of 3.5%. In addition, the minimum value of mean SD of V_{200} was 2.3% for 40 s plans, while other plans had more than 2.6% SD. It reached the value 3.1% when the maximum dwell time was set to be 100 s. The variation of V_{200} and its with respect to maximum dwell time is represented in Figure 1b.

The variation of SD with respect to maximum dwell time was found between 2.6 and 3.

Among the normal structures, the variation in maximum urethra dose was from 83 to 236% [Figure 2] as the step size was varied. In 30% of all the generated treatment plans, the optimizer failed to achieve intended constraint of a mean urethral dose less than 120%. Higher urethra dose was observed for the plans having step size 1 or 10 mm, with 21 out of 30 plans producing such results.

The plans with step sizes of 3 and 7 mm, were seen to spare the urethra better than those with 1 and 10 mm step size. Only four out of 30 treatment plans generated using 3 and 7 mm step size and only one plan with step size 5 mm delivered a urethral dose of more than 120% of the prescription dose. The mean SD of urethra doses varied from 2.3 to 15.8% with the median of 3.3%. The step size 1 mm resulted in the maximum SD. This observation is attributed for all individual dwell times tested as parameter.

We found little urethral dose variation as a function of dwell time varied with all step size considered as parameter. The variation was from 116 to 123% of the prescription. As in the previous case, the 40 s dwell time had the smallest value of 117% among the other dwell times averaged over all step sizes. The rectum dose was found to increase with the increase in step size for all dwell times. Its values were different than the urethral doses. It had a minimum value of 56.7% and maximum of 88% of the prescription. The smaller rectal doses were found in lower step sizes for all dwell times. No plan using 1 and 3 mm step sizes crossed the rectal dose of 70% of the prescription. The plans produced rectal doses of 75, 55, and 35% for the step sizes 5, 7, and 10 mm, respectively for all dwell times. For the variation in maximum dwell time, the rectal dose showed little variation for all step sizes. The quality indices, as defined, were calculated and analyzed. Their variation was found to be similar.

The Eclipse BrachyVision generally calculates the treatment time for a 10 Ci source and the necessary decay is applied in the treatment console in accordance with the activity at the time of treatment. The decay factors are generally provided by the manufacturer. The treatment time for the variation of step size and maximum dwell time for 10 Ci source was analyzed and shown in Figure 3. When step size was varied for experiment, the mean values over all the dwell time was considered and vice versa.

Discussion

AVOL technique based on the complex mathematical formulation, tries to match the user-defined DVH by minimizing the total DVH error, HS error, and maximum dwell time error. The optimizer efficiency is limited by input parameters like maximum dwell time and step size and final optimization result is biased by them. Therefore, it is required to find the optimum input parameter to achieve

the best quality treatment plan. As per the protocol of this study, all 100 plans were analyzed to get an appropriate step size and maximum dwell time which would result in the optimum target coverage with acceptable quality indices and lower OAR doses. The target coverage first increased and after reaching saturation started decreasing on variation of step size. According to this, 5 mm as well as 7 mm, each are nearly produce good target coverage's. When target coverage alone considered, neglecting all other tested parameters, 7 mm step size is preferable over 5 mm because of its higher target coverage. Since target coverage and normal structures constrains both are considered for a clinically acceptable plan, a 7 mm step size will not be considered superior over 5 mm. The mean V_{200} is less for a 5 mm step size as compared to 7 mm step size (1.9 and 2.4%, respectively). Even then, the variation seems to be small enough as to have no practical importance. All other step sizes resulted in larger V_{200}, leading to them being rejected on comparison with these sizes. The variation in urethral and rectal dose was more prominent on variation of dwell position than that of dwell time. This is because of the dimensions of urethra and rectum. The urethra has a smaller volume, while the rectum is present throughout most of the treatment volume. Therefore, if dwell positions are densely placed, then the dose to the urethra is greater and dose to rectum is less. This is because of volume averaging of the dose over smaller (urethra) and higher (rectum) volume. Minimum rectum dose was observed for 1 mm step size. Minimum urethra dose was observed for 5 mm step size and 40 s maximum dwell time when normalized over all step sizes and dwell times, respectively.

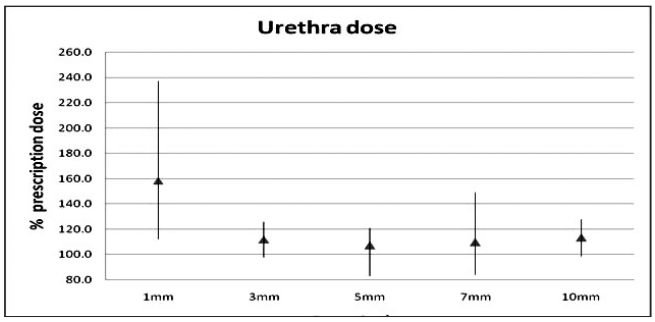

Figure 2: Variation of urethra dose with step size

The urethra doses also favors a 5 mm step size, with less mean dose of 107.3% when all other step sizes resulted in

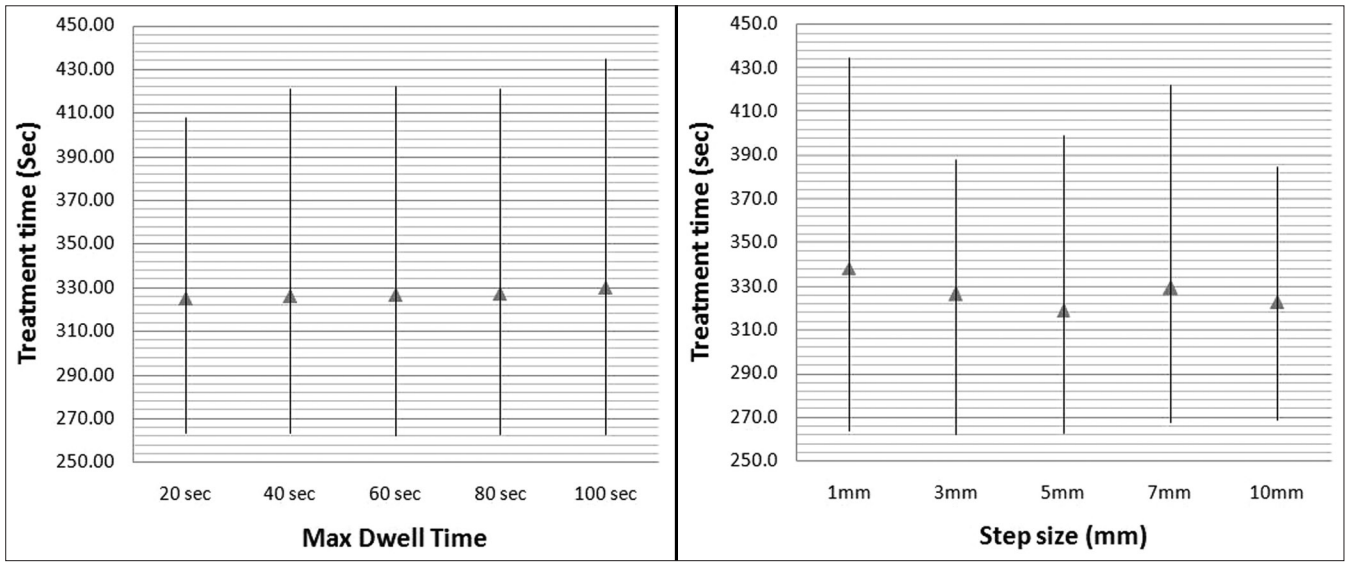

Figure 3: Variation of treatment time with step size and dwell time

Table 1: Mean values of the different analyzed parameters. For a particular step size, maximum dwell time variations were averaged; and for a maximum dwell time the step sizes were averaged

	Step sizes					*Maximum dwell time*				
	0.1 cm	*0.3 cm*	*0.5 cm*	*0.7 cm*	*1 cm*	*20 s*	*40 s*	*60 s*	*80 s*	*100 s*
Target coverage (%)	83.3	84.6	87.0	87.2	85.4	85.16	85.54	84.88	84.63	85.39
V_{200} (%)	7.3	3.5	1.9	2.2	4.0	3.6	3.6	3.9	3.9	5.0
Urethra (%)	156.8	112.0	107.3	109.7	113.5	119.1	117.0	120.0	123.3	120.0
Rectum (%)	63.1	65.0	68.7	69.3	71.1	67.2	67.3	67.2	67.1	68.1
Treatment time (s)	338.2	326.2	318.8	329.0	322.9	325.2	325.9	326.66	327.32	329.98
DHI	0.67	0.76	0.87	0.87	0.84	0.81	0.81	0.80	0.80	0.80
DNR	0.33	0.24	0.13	0.13	0.16	0.19	0.19	0.20	0.20	0.20

DHI: Dose homogeneity index, DNI: Dose nonhomogeneity index, DNR: Dose nonuniformity ratio

more than 109% of the prescription. As shown in Figure 2, the urethral dose has less variation about the mean for step size of 5 mm which was not noted in the other step sizes. The maximum urethra dose even reached 158% in some plans. Only one plan with 5 mm step size exceeded the limit of 120% of the prescription. Though the 5 mm step size has an advantage over other step sizes in term of target coverage and V_{200}, the rectum dose was higher, as compared with 1 and 3 mm step sizes. This may not be significant because the mean SD in rectal doses reaches its maximum at 2.7% for the step size 1 mm in comparison with the minimum of 0.6% for the 5 mm step size. Although smaller step sizes resulted in less rectal dose, they did not produce good target coverage. These smaller step sizes gave lower urethral doses, as previously explained. They also produced a large V_{200}.

Treatment time, which is the another important factor in our analysis, clearly showed that the optimizer produces treatment plans with larger treatment time for step sizes other than 5 mm. Nonetheless, larger treatment time did not help the plans to achieve results compatible with 5 mm step size. Still all the plans with step size other than 5 mm have inferior target coverage and higher OAR doses. The variation of treatment time with step sizes is shown in Figure 3. When the variation of step size is presented, dwell time is averaged over all step sizes and vice versa. Since, in BrachyVision all the plans are calculated for a 10 Ci source, even a difference of 1 second in treatment time results in over dose. Here in our study, the plans with different step sizes in comparison with 5 mm step size show a minimum of 4 s to maximum of 20 s difference in dwell time. These longer times show the inability of those step sizes to achieve a plan similar to 5 mm step size plan. Even then, the quality indices were not appreciably different. The mean SD of quality indices about their mean make some considerable differences in the SD among the plans in their plan quality. This is given in Table 1.

Even then, the percentage variation among the plans is small. It is evident from the quality index results given in Table 1 that 5 mm step size gives good target coverage and lower OAR doses with good quality indices. The same type of analysis was also done for the variation in maximum dwell time. There was no notable difference in target coverage with respect to dwell times. But there is variation in the mean SD in target coverage. The minimum value of SD for the target coverage is obtained for maximum dwell time constraint of 40 s. Analogues result was obtained with urethra dose also. The minimum value of urethra dose (117%) was attributed to maximum dwell time constraints of 40 s. Other tested dwell time constrains resulted in more than 119% mean urethra dose. But the variation in dwell time did not result in equal variation as in urethra dose variation with step sizes. Maximum dwell time of 40 s constrain yield lesser dose to rectum. The quality indices, like DHI and dose nonhomogeneity index (DNI), does not show any significant variation with respect to maximum dwell time constrains for all tested step sizes.

Analysis of these results supports the use of a 40 s dwell time. A summary of the different plans are given in the Table 1. All the above analysis with 100 plans gives the impression that the factors which need to be given at the beginning of the inverse planning process should be selective. A random selection of these parameters wastes time, and time is the prime aspect of brachytherapy planning. It may be argued that lower step sizes (e.g., 1 mm) will give the planner higher degree of freedom to optimize the treatment plan. The disadvantage of smaller step sizes is the overlapping regions in the source length. The miniature Ir-192 brachytherapy source having active length of 3.9 mm, achieving a better treatment plan for 5 mm step size indicate the preference of discreet source geometry over the continuous. This is because step size less than or equal to 3.6 mm will give a source overlap region and a larger HS; hence, optimizer need to work hard to reduce the HS error (Equation ii). Moreover these HSs will deteriorate the DHI and DNI. By single minded analogy overlap, source active lengths will give a higher OAR dose also.

Similarly, an increase of the dwell time will increase the HS, hence the dose homogeneity. Nevertheless, minimum dwell time may not lead to a best clinically acceptable plan. Therefore, there is an optimum value for the maximum dwell time. The clinically best maximum dwell time is recorded in study as 40 s, as optimum value for maximum dwell time.

Geometrical optimization seem to produce good results, but at the cost of time. Achieving the necessary OAR doses is more difficult in inverse planning than in geometrical optimization. The issue that bothers planner doing inverse planning is the selection of these parameters. Once they are selected appropriately, the planning will require less time as compared to geometrical optimization, and with better clinical outcome. The classic idea of keeping the step size at 5 mm was found in our study to be an ideal step size for brachytherapy planning.

Conclusion

The performance of AVOL method strongly depends on the initial input parameters like step size and maximum dwell time. Our clinical study on prostate implants identified the step size of 0.5 cm and the maximum dwell time of 40 s as the optimum values. We recommend these parameters for prostate HDR implants for BrachyVision users.

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