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The Effect of Needle Number on the Quality of High-dose-rate Prostate Brachytherapy Implants

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Abstract The aim of this study is to evaluate the effect of the number of needles on the quality of dose distributions in high-dose-rate (HDR) prostate implants regarding target coverage, dose homogeneity and dose to organs at risk. Treatment plans of 174 implants were evaluated using cumulative dose-volume histograms. The plans were divided into three groups according to the number of implanted needles: <15: LNG (low number group), 15–17: MNG (medium number group) and >17: HNG (high number group). Treatment planning was based on transrectal ultrasound imaging. Dose-volume parameters for target (V90, V100, V150, V200, D90, D_{min}) and quality indices (DNR, DHI, CI, COIN) were calculated. Maximal dose in reference points and high dose volumes were determined for rectum and urethra. Nonparametric analysis of variance and correlation was used with regard to needle numbers. Between the groups differences were found only in the following parameters: V_p was larger when more needles were used with the values of 22.8 cm^3, 28.0 cm^3 and 30.9 cm^3 for the three groups, and more needles were used when the central cross-section of the prostate was larger. V200 in MNG was lower than in LNG (12%, 14%). Dose to rectum was higher in MNG than in LNG (D_2: 51%, 47%). Doses to the urethra were higher in HNG than in MNG (D1: 142%, 137%, and $D_{0.1}$: 128%, 125%). There was no significant difference in other parameters. Different number of needles results significant differences in treatment plans. However, the optimal needle number depends on not only the size of the prostate, but also the individual anatomy of the patient. Based on our results, in most cases the use of 15–17 needles seems to provide a dosimetrically acceptable treatment plan in HDR prostate implants.

Keywords Dose-volume analysis · High-dose-rate · Prostate brachytherapy · Number of needles · Organs at risk · Treatment planning

Abbreviations

3D-CRT	three dimensional conformal radiotherapy
BT	brachytherapy
CI	coverage index
COIN	conformal index
CTV	clinical target volume
DHI	dose homogeneity index
DNR	dose nonuniformity ratio
DVH	dose volume histogram
EAU	European Association of Urologists
GEC/ESTRO	Groupe Européen de Curiethérapie/ European Society for Therapeutic Radiology and Oncology
HDR	high-dose-rate
OAR	organ at risk
PDR	pulsed-dose-rate
PTV	planning target volume
RD	reference dose
RT	radiotherapy
US	ultrasound

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Introduction

Interstitial brachytherapy (BT) using temporary high-dose-rate (HDR) implants is widely accepted for the management of localized prostate cancer. Therefore, several clinical and dosimetric parameters were evaluated in detail [1–8], and the relations between them have been also investigated recently [9–11]. The role of the number of needles on the quality of implants, however has been rarely investigated [12].

The treatment protocol for intermediate- and high-risk, clinically non-metastatic prostate cancer at our institution includes the combination of teletherapy (3D conformal radiotherapy; 3D-CRT) and BT boost using HDR afterloading technique. For risk group definition the D'Amico criteria were used [13]. The radiation source is Iridium (^{192}Ir) with initial activity of 370 GBq.

The purpose of the present study is to evaluate the effect of the number of needles on the quality of dose distributions of prostate HDR BT implants, which can be a basis for further studies in order to establish correlations between the needle number and treatment outcome including local control and side effects.

Materials and Methods

In the Department of Radiotherapy of the National Institute of Oncology (NIO), Budapest 174 clinically localized intermediate- or high-risk patients with prostate cancer were treated with the combination of 3D-CRT and HDR BT boost treatment between October 2005 and January 2009. Brachytherapy treatment plans of these patients were selected for this study.

Teletherapy

Teletherapy was performed with 18 MV photon beams, using 3D-CRT with a four-field box technique. The prescribed teletherapy dose to the whole pelvis (clinical target volume 1; CTV1) was 44–46 Gy (with 2 Gy/day fractions), then the prostate and the vesicle seminals (CTV2) were treated up to a total dose of 60 Gy using shrinking fields. For high-risk patients, CTV2 included the prostate and the whole seminal vesicles, or if there was no vesicle seminal infiltration, the basal 2 cm of seminal vesicles only. In intermediate risk patients, only the prostate and the basal 1 cm of the vesicles were treated. The CTVs to planning target volumes (PTVs) margin was 1 cm in all directions.

Brachytherapy Implantation Technique

The single fraction of HDR BT boost was performed during the first four weeks of teletherapy. Metal needles were implanted into the prostate in spinal anaesthesia with transrectal ultrasound (US)-guidance. Transversal US images were acquired with a 5 mm step size for treatment planning. The reference plane was selected at the largest cross-section of the prostate. Anterior-posterior and lateral verification X-ray images were taken, visualising the needles and the bladder balloon catheter (Foley-catheter) filled with contrast medium. The PLATO Brachytherapy Planning System v14.2.6 (Nucletron, Veenendaal, The Netherlands) was used for treatment planning, and the patients were treated with a microSelectron V2 afterloading machine (Nucletron, Veenendaal, The Netherlands).

Brachytherapy Treatment Planning

The contoured PTV was the whole prostate gland without safety margin. The prescribed dose was 10 Gy (reference dose; RD: 100%) to the surface of the prostate (Fig. 1a, b). Treatment plan was acceptable if at least 95% of prostate volume received the RD. The rectum and urethra were contoured as organs at risk (OARs). On each axial image the rectum reference point was placed at 0.5 cm from the outer surface of the US probe in anterior direction (Fig. 1a). The urethra reference points were placed into the centre of the urethral catheter in each US slice (Fig. 1a). The maximum reference point doses were limited to 80% and 120% of the reference dose, respectively. The rectum volume was defined as a shell with 5 mm thickness following the curvature of the US probe (Fig. 1b), and the urethra contour was outlined around the Foley-catheter with 1 mm margin in each intraprostatic slice representing the outer surface of the urethral wall (Fig. 1b).

During treatment planning geometrical optimization was used followed by graphical optimization in order to achieve an acceptable dose distribution (Fig. 1a).

Dosimetric Evaluation

The dose plans were quantitatively evaluated using cumulative dose-volume histograms (DVHs). Volume and dose parameters and quality indices (coverage, conformality and homogeneity) were calculated for all treatment plans.

The following parameters were used for quantitative evaluation of the dose distributions:

Volume and dose parameters:

V_p	volume of the prostate
A	central cross-section of prostate approximated by the smallest rectangle which includes the prostate contour
V90, V100, V150, V200	volume of the PTV in percentage receiving 90, 100, 150 and 200% of the RD

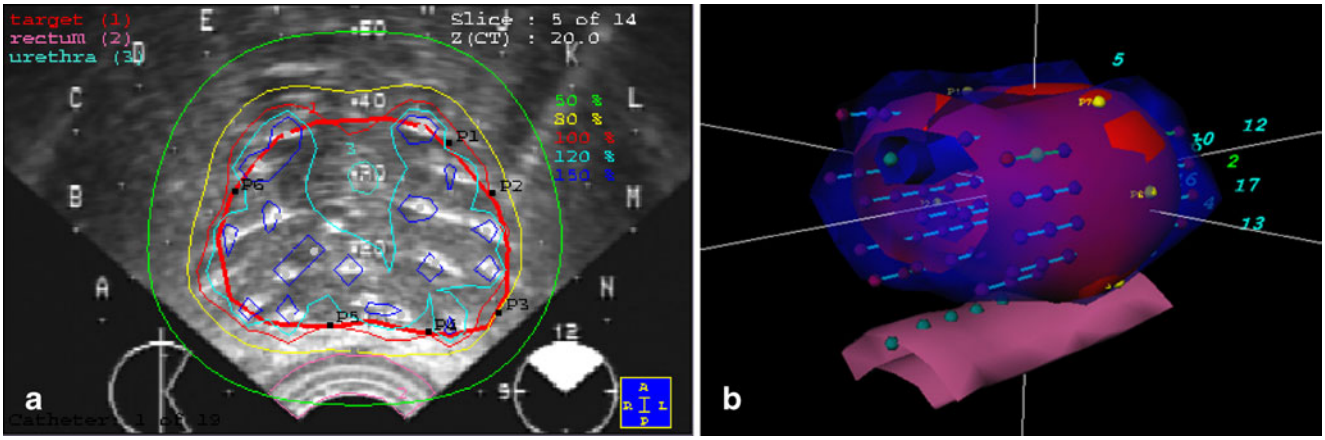

Fig. 1 **a**. Relative dose distribution in the reference plane: the thick red line is the contour of the prostate with the black reference points defined for dose normalization. **b**. 3D reconstruction of an implant with surfaces of prostate (red), rectum (rose), urethra (dark blue), reference isodose (translucent blue), and reference points (bluish grey) and source dwell positions (red)

D90	minimum dose in percentage delivered to 90% of the PTV volume
D_{min}	minimum dose in the PTV in percentage

Indices:

DNR	Dose Nonuniformity Ratio, $DNR = V_{150}/V_{100}$

where V_{100} *and* V_{150} is the absolute volume in cm^3 irradiated by 100 and 150% of the RD.

DHI	Dose Homogeneity Index, *DHI= (V100-V150)/V100*
CI	Coverage Index, *CI= V100/100*
COIN	Conformal Index [14]

$$COIN = \frac{PTV_{ref}}{V_{PTV}} \cdot \frac{PTV_{ref}}{V_{ref}},$$

where V_{ref} is the volume irradiated by the RD ($V_{ref}=V_{100}$), PTV_{ref} is the absolute volume of the PTV irradiated by the RD.

Dose parameters of OARs:

All dose values were given in percentage of to the RD (D_{ref}=10 Gy, 100%).

D_r	maximal dose in the rectum reference points
D_u	maximal dose in the urethra reference points
D_2	dose to volume of the most exposed 2 cm^3 of the rectum
$D_{0.1}$	dose to volume of the most exposed 0.1 cm^3 of the urethra
*D*1	dose to volume of the most exposed 1% of the urethra.

Evaluation of needle number:

The plans were divided into three groups according to the number of implanted needles, and dose volume parameters and indices were calculated and compared for the groups separately. The first group contained 62 plans with low number of needles: <15 (LNG: low number group), the second one (56 plans) with needles between 15 and 17 (MNG: medium number group), and the third one (56 plans) with needles >17 (HNG: high number group).

Statistical Analysis

For statistical evaluation the StatSoft Statistica 7.0 software was used. Kruskal-Wallis analysis of variance and non-parametric post hoc tests were used to describe the dosimetrical differences between the groups created by the number of needles. Nonparametric rank order correlation was applied between the needle number and the volume and the central cross-section of the prostate. A p value of ≤ 0.05 was considered as a statistically significant difference.

Results

The median number of implanted needles was 16 (range: 12–23) (Fig. 2), and the mean prostate volume was 27.1 cm^3 (range: 6–65.4 cm^3). Regarding the effect of needle number on the dose parameters we found differences only in the prostate volumes, high dose volumes in the prostate and volumetric doses to rectum and urethra. V_p was larger when more needles were used with the values of 22.8 cm^3, 28.0 cm^3 and 30.9 cm^3 for the LNG (<15), MNG (15–17) and HNG (>17) ($p_{LNG\text{-}MNG}$=0.0133, $p_{LNG\text{-}HNG}$= 0.0001), and more needles were used, when the central

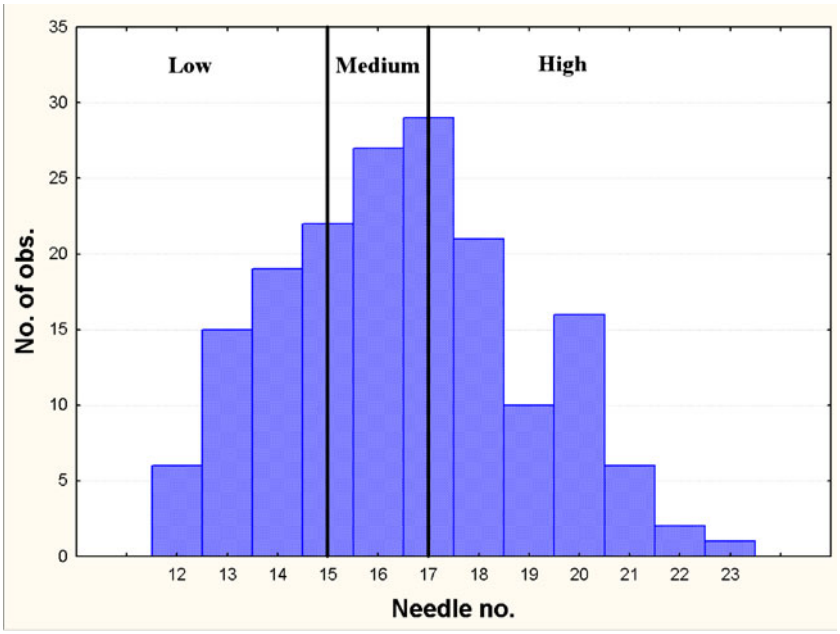

Fig. 2 Histogram for the number of implanted needles. The black lines separate the three groups with low-, medium- and high number of needles (LNG, MNG and HNG). The patient numbers were 62, 56 and 56 in the groups, respectively

cross-section of the prostate was larger, A=8.13 cm^2, 9.59 cm^2, 11.32 cm^2 ($p_{LNG\text{-}MNG}$=0.0246, $p_{LNG\text{-}HNG}$=0.0014). Only p values at statistically significant difference are given. The V200 in MNG was lower than in LNG, but it was the same as in HNG (14%, 12%, 12%, $p_{LNG\text{-}MNG}$=0.0106). The dose to rectum was higher in MNG than in LNG, but it did not differ between MNG and HNG either (D_2: 47%, 51%, 51%, $p_{LNG\text{-}MNG}$=0.0440). The doses to the urethra were higher in HNG than in MNG, but no difference was found between LNG and MNG. The dose values were as follows: D1: 139%, 137%, 142%, $p_{MNG\text{-}HNG}$=0.0333 and $D_{0.1}$: 124%, 125%, 128%, $p_{LNG\text{-}HNG}$=0.0019 for groups with low-, medium- and high-number of needles. There was no significant difference in the dose-volume parameters of V90 (99%, 99%, 99%), V100 (96%, 96%, 96%), V150 (40%, 37%, 38%), D90 (109%, 109%, 109%), D_{min} (87%, 88%, 86%), in the quality indices of DNR (0.38, 0.36, 0.36), CI (0.96, 0.97, 0.97), DHI (0.59, 0.61, 0.60), COIN (0.66, 0.67, 0.66) and in the dose to OARs of D_u (119%, 119%, 120%), D_r (75%, 74%, 74%) between the three groups created by the number of needles (Tables 1, 2 and 3). However, it has to be noted that the increase of needles from low to medium number resulted in more homogeneous dose distribution (lower DNR and higher DHI), although this was not statistically significant.

Significant correlation was found between the needle number and both volume and central cross-section of the prostate, which was stronger with the cross-section. The Spearman rank order correlation coefficients were R(Needle number,V_p)=0.3847 (p=0.0001) and R(Needle number,A)=0.6187 (p<0.0001).

Discussion

HDR BT boost has been accepted as a standard technique for dose escalation in the curative treatment of localized prostate cancer [4, 6, 7, 9, 15–18], and recently several

Table 1 Volumetric and dose parameters for the groups of treatment plans created by needle number

	Mean ± SD			*p*-values between groups		
	<15	15–17	>17	<15 vs. 15–17	<15 vs. >17	15–17 vs. >17
V_p (cm^3)	22.8±8.5	28.0±10.2	30.9±12	0.0133	0.0001	0.6790
A (cm^2)	8.13±2.03	9.59±2.18	11.32±2.88	0.0133	0.0014	0.0687
V90 (%)	99±2	99±1	99±1	1	1	1
V100 (%)	96±2	96±4	96±1	1	1	1
V150 (%)	40±10	37±9	38±11	1	1	1
V200 (%)	14±5	12±3	12±4	0.0106	0.0655	1
D90 (%)	109±4	109±3	109±3	1	1	1
D_{min} (%)	87±5	88±5	86±5	1	0.5	0.2585

SD standard deviation, V_p volume of the prostate, *A* the largest cross-section of the prostate in the needle's-eye view, *V90, V100, V150, V200* volume of the PTV receiving 90, 100, 150 and 200% of the reference dose, *D90* relative dose delivered to 90% of the volume of PTV, D_{min} minimal dose in the PTV

Table 2 Quality indices of the dose distributions for the groups of treatment plans created by needle number

	Mean ± SD			*p*-values between groups		
	<15	15–17	>17	<15 vs. 15–17	<15 vs. >17	15–17 vs. >17
DNR	0.38±0.07	0.36±0.07	0.36±0.0.8	0.4062	0.4619	1
DHI	0.59±0.1	0.61±0.09	0.60±0.12	0.8623	1	1
CI	0.96±0.02	0.97±0.02	0.97±0.01	1	1	1
COIN	0.66±0.08	0.67±0.06	0.66±0.06	1	1	1

SD standard deviation, *DNR* Dose Nonuniformity Ratio, *DHI* Dose Homogeneity Index, *CI* Coverage Index, *COIN* Conformal Index

phase I/II studies have been initiated to test the feasibility of HDR BT as a monotherapy [19, 20]. In contrast to permanent seed implants with uniform source activity, the advantage of the stepping source HDR afterloading technique is that the shape of the dose distribution can be modified according to the shape of the target volume with selecting individual source dwell times in the needles which results in more conformal dose distribution. Dwell times are calculated with the use of dose optimization algorithms [21–25]. In addition to the evaluation of the quality of dose distributions by visual inspection slice by slice, the plans can be evaluated quantitatively using dose-volume parameters. The parameters used for the evaluation of dose distribution in permanent prostate brachytherapy—e.g. D90, D100, V100, V150, V200 [26, 27]—are applicable in HDR treatments, too. For the dose parameters in OARs, the Groupe Européen de Curiethérapie/European Society for Therapeutic Radiology and Oncology-European Association of Urologists (GEC/ESTRO-EAU) guidelines recommends the use of dose which irradiates 2 cm^3 of the rectum, and 0.1 cm^3 and 1% of the contoured volume of the urethra [28]. These parameters were used in our study, too.

In prostate BT, it is usually accepted that the target volume is the whole prostate, but with respect to the homogeneity of the dose distribution there are significant differences in the literature [28]. Several implantation techniques exist according to the number and placement of needles [3, 7, 11, 12, 21, 29–31]. By placing a few needles peripherally, the dose is larger in the peripheral zone, while distributing more needles uniformly the whole prostate can be irradiated more homogeneously. Martin et al. [9] treated 35 patients with prostate BT with 4 needles, and according to their results the maximal urethral dose was two-three times higher than the RD, while the maximal rectum dose was 110–150%. Charra-Brunaud et al. [12] performed a model study with treatment plans of 24 patients made by geometrical optimization to determine the ideal number of needles. They changed the needle number between 9 and 21 for each patient, and investigated the effect on the V150, DHI and COIN. Using low number of needles the V150 increased significantly, but over 15 needles there was no significant difference between the corresponding volumes. The increased number of needles resulted in more homogeneous and conformal dose distribution, but the DHI and COIN values with 18 and 21 needles differed only slightly. They conclude that a needle number between 15 and 18 results in an appropriate dose distribution in most cases, though the ideal number of needles depends on the size and shape of the PTV, and the position of the urethra, too. Pinkawa et al. [10] found that the low number of the needles resulted in less homogeneous dose distributions.

In our study the number of needles was between 12 and 23. Our calculations were based on the real positions of the needles while Charra-Brunaud et al. [12] used ideal needle placements. Moreover, we applied graphical optimalization, too in order to get at least 95% dose coverage. We found differences in the prostate volume (V_p) between the three

Table 3 Dose parameters of the rectum and urethra for the groups of treatment plans created by needle number

	Mean ± SD			*p*-values between groups		
	<15	15–17	>17	<15 vs. 15–17	<15 vs. >17	15–17 vs. >17
D_r (%)	75±9	74±8	74±8	1	1	1
D_2 (%)	47±8	51±9	51±9	0.0440	0.1328	1
D_u (%)	119±4	119±3	120±4	0.4866	1	0.4061
$D_{0.1}$ (%)	124±7	125±6	128±7	0.6867	0.0019	0.0932
D1 (%)	139±13	137±14	142±12	0.8783	0.4956	0.0333

SD standard deviation, D_r maximal dose in the rectum reference points, D_2 dose to volume of the most exposed 2 cm^3 of the rectum, D_u maximal dose in the urethra reference points, $D_{0.1}$ dose to volume of the most exposed 0.1 cm^3 of the urethra, $D1$, dose to volume of the most exposed 1% of the urethra

groups created by number of needles, more needles were used for larger prostates. However, there was no significant difference between the volumes of prostates in MNG and HNG. This can be explained by the fact that the optimal needle number is not explicitly defined by the volume, but rather by the largest cross-section of the prostate in the needle's-eye view, which is shown by the higher Spearman correlation coefficient between the cross-section and needle number in our data. Similar phenomenon was observed with the high dose volume (V200) which was smaller in MNG than in LNG, but it did not change between the MNG and HNG. According to our results the use of larger needle number increased the dose to OARs. The reason can be that at large number of needles some of them are in close proximity to the OARs. Based on our results, except for extreme small and large volumes, medium number of needles (15–17) is recommended to use in HDR prostate BT.

Others investigated the relations between the number of needles and clinical side effects. Pinkawa et al. [10] found increased urinary toxicity with increased needle number. Vargas et al. [11] came to similar conclusion, when they found increased genitourinal toxicity with higher number of needles.

Conclusions

Different number of needles results significant differences in treatment plans for HDR prostate BT. However, the optimal needle number depends on not only the size of the prostate, but also the individual anatomy of the patient. Furthermore, the possible side effects have to be also taken into account, and a compromise has to be found between a dosimetrically optimal implant and an acceptable toxicity to OARs. Based on our results, in most cases needle number of 15–17 is sufficient to get a good quality implant in HDR prostate brachytherapy.

Conflict of Interest Statement Authors state that there is no actual or potential conflict of interest. None of the authors has had relationship with an entity that has a financial interest in the subject matter discussed in this manuscript.

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