Vital role of volume and number of needles in HDR brachytherapy (HDR-BT) of prostate cancer

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Abstract

Purpose: The quality of HDR-BT of prostate cancer depends on operator skills, anatomy, prostate volume and relation to surrounding tissues as well as previous diseases and treatments of a patient. There is a rare data available concerning the minimum number of needles and its influence on dose distribution, side effects and long-term outcome. The study is to determine the minimal prostate volume and minimum number of needles suitable for HDR-BT in order to obtain an implant of good quality.

Material and methods: 181 patients with localized prostate cancer were treated with interstitial HDR-BT boost. 15 Gy from HDR-BT was administered after 50 Gy from EBRT. Clinical, volumetric and dosimetric data were collected. Treatment plans were divided into Group A, consisted of optimal treatment plans (P-D90 > 90%, P-V200 < 15%, U-D10 < 125%, U-Dmax < 160%, R-D10 < 85%) and Group B, with suboptimal plans.

Results: The difference between two groups was statistically significant (p = 0.013) with regard to number of needles. There was no statistically significant difference concerning prostatic volume. Median number of inserted needles in the first and the second group resulted in 15 (range 9-18) and 13 (range 8-18), respectively. Differences were the most eminent in patients with prostate glands of small volume (< 20 cc). In the study, either the minimum number of needles nor minimal prostate gland volume were not clearly defined in terms of high probability of achieving a good quality implant.

Conclusions: Larger volume and higher number of needles are related to an advanced probability of treatment plan with all DVC fulfilled. The minimum number of needles suggested is > 9, optimally ≥ 13. Furthermore, the minimal prostate volume recommended is > 12 cc, optimally ≥ 18 cc. The volume of insufficient size and/or small number of needles results in suboptimal treatment plans.

Key words: prostate cancer, HDR brachytherapy, volume, number of needles.

Purpose

One of the current approaches for the management of localized prostate cancer is a combination of external beam radiotherapy (EBRT) with interstitial high-dose-rate brachytherapy (HDR-BT) boost with or without additional hormonal therapy. Its safety and effectiveness has been proven elsewhere [1-3]. According to different authors, 5-year long biochemical control of the disease is achievable in 53 to 93% of cases [4-9].

As it is well known to the professionals accustomed to this method, the quality of prostate cancer interstitial brachytherapy depends on operator skills, anatomy of prostate, its volume and relation to surrounding tissues (pubic arc interference) as well as previous diseases and treatments of a patient (e.g. TURP, hormonal therapy). Clinical practice prove that the number of implanted needles is also very important. However till date, only an occasional data is available regarding the minimum number of needles and its influence on dose distribution, side effects and long-term outcome [1, 10-15].

In consecutive series of patients certain characteristic relation was noticed. The prostate glands of small volumes were obviously implanted with low number of needles, which, in turn, caused increased occurrence of suboptimal treatment plans. Suboptimal plans were described as a set of treatment plan parameters exceeding any of dose-volume constraints (DVC) established in the department (Table 1). Such situations were much less common during treatment of large prostate glands.

There is a few data available that indicate the dose values and homogeneity index (HI) in treated volume to be dependent on such prognostic factors as prostate gland volume, location of intraprostatic portion of urethra and the number of interstitially inserted applicators.
Material and methods

From April 2007 till December 2008 a number of 181 patients (median age 64, ranged 51-70) with localized prostate cancer (T1-3aN0M0) were treated with interstitial HDR-BT in the Brachytherapy Department in Greater Poland Cancer Centre (Table 2). In all cases, the treatment was a combination of external beam radiotherapy (EBRT) and HDR-BT. Boost of 15 Gy was administered as a single dose after 50 Gy delivered from EBRT.

Study inclusion criteria were such as: men aged 50 to 70 years with prostate cancer confined to the gland (T1-3aN0M0), no regional and/or distant metastases, optional neoadjuvant hormonal therapy (3 to 6 months) and a written consent. The exclusion criteria were as follow: ≤ 6 months after transurethral resection of prostate (TUR-P), concomitant diseases disqualifying the patient from general anesthesia, expected survival < 5 years, the presence of metastases, anatomical obstacles – pubic arch interference, adenomectomy in anamnesis and large defect after TUR-P. Detailed clinical, volumetric and dosimetric data were collected. All 181 treatment plans were analyzed, paying special attention to meeting the requirements of dose values for target coverage and dose limits for organs at risk (dose-volume constraints, DVC) (Table 1). Subsequently, all plans were split into two groups. Group A consisted of treatment plans which met every requirement of a good implant, whereas Group B consisted of suboptimal treatment plans, in which not all DVC met their recommended values. The aim of each good quality (optimal) implant was to deliver more than 90% of prescribed dose to at least 90% of the target volume (D90 > 90%). The most important dose volume limitations in urethra and rectal wall were D10 < 125% and < 85%, respectively. For delivery of radiation the operators used microSelectron® HDR remote afterloader (Nucletron B.V., SWIFT®) with blind inverse planning optimization.

Additionally, both implant quality groups were investigated in terms of differences in prostate gland volume, PTV and the number of implanted needles. Prostatic volume was assessed on the basis of the measurements derived from transrectal ultrasound (TRUS), which in every case was performed by a radiologist before the treatment. TRUS was also used to define the initial technical applicability of HDR-BT and was enabled to exclude patients with pubic arch interference. CT scans collected in purpose of EBRT, especially in patients with prostate volume ≥ 50 cc played the same role [18].

In analyzed series, out of 181 patients, 121 (66.8%) received a neoadjuvant hormonal therapy. The purpose of such management was to diminish the risk of a relapse in intermediate and high risk groups of patients, according to current recommendations. The investigated group was also divided into two subgroups of patients treated with hormonal therapy and no hormonal therapy administered. Both subgroups were compared on the subject of prostatic volume.

Statistical analysis of the above relations was prepared with the assistance of Mann-Whitney U test; assumed significance level p < 0.05.

Results

In radiological assessment of prostatic volume (P-Vol) the difference was not significant between two groups (Fig. 1;
In case of PTV one could notice only slight tendency towards suboptimal treatment plans in the group of small volumes (Fig. 2, \( p = 0.060 \)). The lower limit of prostate gland volume, below which any implant would certainly be suboptimal was not identified on the basis of investigated material. Such threshold could be a contraindication for using HDR-BT.

The lowest number of needles that is necessary to prepare an implant and achieve an optimal treatment plan was also not identified on the basis of investigated material. That demonstrate, that in both situations, there is no simple transformation to numbers, which could be clearly verified by statistics. However, under real clinical circumstances, there are many additional factors of possible great importance to have an influence on the final DVH, such as: anatomy of a patient (shape, mobility of prostate gland and its capsule flexibility, localization of the urethra, pubic arch interference, etc.). In the study, the median number of needles in Group A was 15, and in Group B – 13. Nevertheless, on the basis of collected data one can assume, that the minimum number of implanted needles should exceed 9, optimally \( \geq 13 \). The minimal volume of the prostate gland suitable for HDR-BT should exceed 12 ml, optimally \( \geq 18 \) ml (Figs. 1-3).

In subset of patients with intermediate and large prostate volumes obtaining satisfactory or excellent target coverage (high values of D90 and V100) along with proper dose distribution (less hot-spots with lowered V200), HDR-BT was possible thanks to implantation of a large number of needles (maximally 18) and ability to place the needles in a safe distance from the urethra (recommended > 5 mm). Under such conditions, DVC can easily meet their requirements. Nevertheless, in spite of a large volume, in some patients suboptimal treatment plans originated from sudden occurrence of pubic arch interference, excessively large defects after TUR-P, unusual anatomy, asymmetric benign hypertrophy or massive calcifications.

Amongst the investigated group, 7 out of 181 (3.8%) and 41 out of 181 (22.6%) patients were assessed to have prostate gland volume \( \leq 12 \) cc and \( < 18 \) cc, respectively. There were also 6/181 (3.3%) and 49/181 (27.1%) patients which were implanted with \( \leq 9 \) and \( < 13 \) needles, respectively.

It was proven, that subgroup of patients with additional hormonal therapy differed significantly from the subgroup without additional treatment (\( p < 0.001 \)) (Fig. 4). Hormonal therapy prescribed before HDR-BT decreased the prostate gland during the treatment. The mean prostate volume in hormonally treated patients was 23.3 cc and 33.5 cc in these without neoadjuvant treatment. Hormonally triggered shrinkage of prostate gland resulted in 30% reduction of volume.

Additional analysis of the hormonal therapy regimens (antiandrogens alone, LH-RH analogues alone or both) and
the duration of treatment did not reveal any statistically significant differences in regard to the degree of prostate gland shrinkage.

Discussion

Even though the difference in the prostate gland volume between Group A and B was found to be statistically insignificant, the volume seem to be strongly associated with the number of needles [13-15, 19]. The prostate volume and urethra are the major factors to influence the location and number of needles. Relatively large prostate gland volume enables the usage of higher number of needles in order to obtain a good quality implant. On the other hand, a large volume may result in pubic arch interference at the site and increased late toxicity [1]. As it was presented in a related study, the number of needles was found to be directly proportional to PTV, prostatic D90 and V100 and inversely proportional to V200 [19]. Similar conclusions are shown in paper of Charra-Brunaud et al. who stated, that the smaller the prostate volume, the stronger the influence of number of needles on higher values of treatment plan parameters, particularly V150 in CTV and urethra [12].

Most prostate cancer tumors are found in a peripheral zone. Clinicians intentionally follow this phenomenon by implanting the needles to the periphery in order to acquire an excellent target coverage and to minimize the urethral dose. Such approach is recommended by most of the authors [4, 8, 12-14]. However, in case of a very small prostate volume it is quite difficult to place the needles far from the urethra and the reference dose prescribed to CTV1 (prostate capsule) may cause difficulties. In such case certain compromise on particular DVC in target and/or organs at risk is necessary. One of the method to overcome this problem is to prescribe 100% isodose to CTV2 (peripheral zone) or even CTV3 (tumor volume) [1, 20, 21].

The study suggest to treat the organ which can be implanted with more than 13 needles. Mate et al. [22] recommended to use 18 to 22 needles in order to achieve an excellent target coverage with 100% isodose (\( V_{100} > 90\% \)). Similar conclusions were published by Dinges et al. [23], who suggested implanting at least 20 needles to limit the dose delivered to 10 cc of target below 135% of reference dose. Furthermore, Borghede et al. [21] proved, that lesser dose heterogeneity inside the target can be easily achieved by placing higher number of needles. Focused rather on morbidity, Akimoto et al. [10, 11] suggested to implant more than 12 needles in order to minimize genitourinary (GU) toxicity. Furthermore, Duchesne et al., in order to decrease the risk of late GU morbidity, recommends to limit the level of \( V_{200} < 15\% \) of PTV with higher number of needles in a large prostate glands [24]. Other published data share this presented view [12, 13, 15, 19]. On the contrary, Kovács et al. [1] intentionally uses small number of needles and prescribes reference dose to CTV2 (peripheral zone of the prostate) to cover the critical structures by relatively low dose areas.

According to the current recommendations, patients with intermediate and high risk of prostate cancer should be treated with neoadjuvant and/or adjuvant hormonal treatment [25, 26]. In the study they constituted a group of 141 out of 181 (78.4%) patients. The number of 121 (66.8%) patients were treated with hormonal drugs for up to 6 months before the actual HDR-BT. Statistical analysis revealed a significant influence of hormonal therapy on prostate volume in patients treated with HDR-BT.
Up till now, the minimal prostate volume suitable for HDR-BT and minimum number of needles sufficient for interstitial treatment were not clearly determined. We suggest to remain the minimal number of needles used for each implant > 9, optimally ≥ 13. Prostates of volume less than 12 cc should not be qualified for HDR-BT, optimal threshold ≥ 18 cc. Patients with prostates of 12 to 18 cc constitute a specific “grey zone”. Within this group of patients, HDR-BT treatment is still feasible, however under certain conditions such as small volume not accompanied by e.g. oblique urethra, asymmetric central lobe hypertrophy, post TUR-P defects and/or pubic arch interference.

Defining more strict indications for HDR-BT of prostate cancer could be advantageous. In our opinion, more precise selection of patients permits to avoid some cases which in the end are unintentionally treated with suboptimal treatment plans. Unsatisfactory target coverage, even in a small portion, may result in significant reduction in probability of cure [27]. On the other hand, properly administered HDR-BT has a double advantage: it increases the probability of local cure concomitantly with minimizing the incidence and severity of side effects.

Conclusions

In HDR-BT treatment of prostate cancer it is important, that relatively larger prostate volume and higher number of needles is related to a higher probability of achieving a treatment plan which meets the requirements of DVC. Suggested minimum number of needles that should be used for each implant is > 9, optimally ≥ 13. Recommended minimal prostate volume qualified for HDR brachytherapy should not be less than 12 cc, optimally ≥ 18 cc. Not sufficient volume of prostate and/or low number of implanted needles results in suboptimal treatment plans with disturbed target coverage, exceeded DVC and/or increased inhomoogeneity.

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