Original paper

Analysis of dosimetric improvements using hydrogel spacer in high-dose-rate brachytherapy for prostate cancer

Moe Honda, MD[1,2], Tomoya Oshikane, MD, PhD[1], Motoki Kaidu, MD, PhD[3], Eisuke Abe, MD, PhD[2,3], Takahiro Komiya, MD[3], Shumpei Yamako, MD[3], Yukiyo Goto, MD[3], Hisashi Nakano, PhD[3], Toshimichi Nakano, MD, PhD[1], Satoshi Tanabe, PhD[3], Atsushi Ohta, MD, PhD[3], Satoru Utsunomiya, PhD, DABR[4], Nobuko Yamana, MD[5], Fumio Ishizaki, MD, PhD[6], Hiroyuki Ishikawa, MD, PhD[1]

[1]Department of Radiology and Radiation Oncology, Niigata University Graduate School of Medical and Dental Sciences, Chuo-ku, Niigata 951-8510, Japan, [2]Division of Radiation Oncology, Nagaoka Chuo General Hospital, Nagaoka 940-8653, Japan, [3]Division of Radiation Oncology, Niigata University Medical and Dental Hospital, Chuo-ku, Niigata 951-8510, Japan, [4]Department of Radiological Technology, Niigata University Graduate School of Health Sciences, Chuo-ku, Niigata 951-8518, Japan, [5]Department of Radiology, Niigata Prefectural Shibata Hospital, Shibata, Niigata 957-8588, Japan, [6]Department of Urology, Niigata University Graduate School of Medical and Dental Sciences, Chuo-ku, Niigata 951-8510, Japan

The research was conducted at the Department of Radiology and Radiation Oncology, Niigata University Graduate School of Medical and Dental Sciences, 1-757 Asahimachi-dori, Chuo-ku, Niigata 951-8510, Japan.

Abstract

Purpose: This study primarily aimed to evaluate the effects of a hydrogel spacer (HS) on dosimetric distribution in the planning target volume as well as on rectal and urethral doses in high-dose-rate brachytherapy (HDR-BT) for prostate cancer, and to identify prostate sub-regions with improved dosimetric parameters and patient conditions that particularly benefit from the use of HS.

Material and methods: This study included 28 patients, who underwent HDR-BT using HS. Treatment plans with HS and simulated plans without HS were compared. The prostate was divided into six regions: ventral and dorsal in the dorsoventral direction, and apex, mid-gland, and base in the craniocaudal direction. $V_{100\%}$ and $D_{90\%}$ were evaluated in each region, along with dose assessments for the rectum and urethra. Paired *t*-tests were performed to analyze significance, and effect sizes were calculated using Cohen's d.

Results: HS significantly improved $V_{100\%}$ in the dorsal regions ($p < 0.05$), particularly in the dorsal apex and dorsal mid regions (median $V_{100\%}$ with and without HS: apex, 100.00 vs. 97.10; mid, 100.00 vs. 97.22). $D_{90\%}$ showed improvement across all regions ($p < 0.05$), with greater effects observed in the dorsal apex and dorsal mid regions (median $D_{90\%}$ with and without HS: apex, 110.15 vs. 103.56; mid, 113.31 vs. 106.21; $d \geq 0.8$). Rectal dose parameters improved significantly ($p < 0.05$), whereas urethral dose changes were not significant ($p = 0.14$).

Conclusions: HS effectively reduced rectal doses and improved $V_{100\%}$ and $D_{90\%}$ in the dorsal apex and dorsal mid regions of the prostate. These regions are anatomically closer to the rectum and are often subject to dose constraints as well as critical areas for sufficient dose delivery because of the frequent localization of prostate cancer lesions. Therefore, HS is particularly beneficial for patients with dominant lesions in these regions.

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Key words: prostate cancer, hydrogel spacer, high-dose-rate, brachytherapy, dosimetry.

Purpose

Localized prostate cancer is treated with surgery, radiotherapy (RT), and endocrine therapy. RT includes external beam RT (EBRT), high-dose-rate brachytherapy (HDR-BT), low-dose-rate brachytherapy, carbon ion therapy, and proton therapy. Since the 1990s, HDR-BT has been used to improve local control rates [1, 2]. However, long-term outcomes in high-risk patients remain suboptimal, highlighting the need for further improvements [3-6]. Hydrogel spacers (HS) increase the prostate-rectum distance, improve rectal dose-volume histograms (DVH),

Address for correspondence: Tomoya Oshikane, Department of Radiology and Radiation Oncology, Niigata University Graduate School of Medical and Dental Sciences, 1-757 Asahimachi-dori, Chuo-ku, Niigata 951-8510, Japan, phone: +81-25-227-2315, fax: +81-25-227-0788, ✉ e-mail: oshi@med.niigata-u.ac.jp

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and reduce radiation proctitis [7, 8]. However, its use involves challenges, such as invasiveness, cost, and potential complications. Therefore, careful patient selection for HS placement is essential, and research on optimizing patient selection criteria is ongoing [9, 10].

In HDR-BT, HS reduces rectal $V_{30\%}$-$V_{80\%}$ and alleviates acute and late grade 1 rectal toxicities. However, few studies have examined whether HS improves the dose distribution within planning target volume (PTV) or the prostate [11, 12]. This study evaluated the impact of HS on the PTV, rectal, and urethral doses in HDR-BT as well as explored conditions, in which HS is most beneficial.

Material and methods

Human subjects

This retrospective observational study included 28 consecutive patients with prostate cancer, who underwent HDR-BT with HS placement at a tertiary care hospital between November 2019 and March 2024. Patients with unfavorable intermediate- to high-risk localized prostate cancer without urinary obstruction were included. HS employed in this study was SpaceOAR® (Boston Scientific Inc., Waltham, MA, USA). For cases with seminal vesicle invasion, HS was used only when no extension in dorsal lesions was detected on magnetic resonance imaging (MRI). Disease staging was determined according to the TNM classification (UICC, 8th edition), and risk stratification was performed using the National Comprehensive Cancer Network risk classification (version 4.2019). This study was approved by the Ethics Committee of the authors' institution (approval No. 2021-0379).

Radiation therapy

Of the 28 patients included in this study, 27 received combined therapy with EBRT and HDR-BT, whereas one patient, who had undergone bilateral femoral head replacement and could not tolerate EBRT, received HDR-BT alone. In 25 patients, HDR-BT was administered following EBRT, with a mean interval of 9 days between the completion of EBRT and initiation of HDR-BT. EBRT (39 Gy/13 fractions) was delivered using intensity-modulated RT (IMRT) or three-dimensional conformal RT, with irradiation field determined according to the T classification. HDR-BT was performed using the Flexitron HDR system (Elekta, Stockholm, Sweden) with the following dose fractionation schedules:

1. EBRT + HDR-BT: 18 Gy/2 fractions/1 day (equivalent dose in 2 Gy fraction – EQD_2: 54 Gy; total EQD_2 for EBRT + HDR-BT: 104 Gy).
2. HDR-BT alone: 42 Gy/6 fractions/3 days (EQD_2: 102 Gy).

EQD_2 was calculated with an α/β ratio of 1.5 [13, 14]. A minimum interval of 6 hours was maintained between HDR-BT fractions.

Table 1. Optimization criteria by inverse planning simulated annealing

For PTV	cGy	Weight
PTV		
Surface	Min 900	200
Volume ($D_{100\%}$)	Min 900	100
For OARs	**cGy**	**Weight**
Rectum		
Surface	Max 700	1
Volume ($D_{100\%}$)	Max 600	180
Urethra		
Surface	Min 1,000	1
Volume ($D_{100\%}$)	Min 1,000	150

PTV – planning target volume, OARs – organs at risk

Treatment planning

Treatment planning images were acquired using computed tomography (CT, Aquilion Lightning, Canon Medical Systems Corporation, Tochigi, Japan), with a slice thickness of 2 mm and a field of view of 25 cm. CT data were imported into Eclipse version 15.5 (Varian Medical Systems, Palo Alto, CA, USA), while structures (the prostate, seminal vesicles, rectum, urethra, bladder, and HS) were contoured. Clinical target volume (CTV) included the prostate ± seminal vesicles according to the stage, with a margin applied as per institutional protocol. PTV was defined as equivalent to the CTV. All structures were contoured independently by a physician with over 5 years of experience in radiation therapy, and reviewed by two board-certified radiation oncologists with over 10 years of experience. The contoured CT data were transferred to treatment planning system Oncentra Brachy version 4.6.2 (Elekta, Veenendaal, Netherlands), and plans were generated using inverse-planning simulated annealing (IPSA) algorithm. To mitigate the influence of planner expertise, treatment plans were generated with only one optimization run without manual adjustments. The optimization parameters used are summarized in Table 1. For each patient, two treatment plans were created:

1. With HS: based on actual patient data with a HS in place.
2. Without HS: simulating the absence of a HS.

For the plans without HS, the rectal contour was adjusted anteriorly to approximate pre-HS anatomy (Figure 1). The plans were generated using IPSA using standardized institutional parameters (Table 1). The prostate was divided into the following six regions, and $V_{100\%}$ and $D_{90\%}$ for each region were evaluated: ventral apex, ventral mid, ventral base, dorsal apex, dorsal mid, and dorsal base. The method of region division is illustrated in Figure 2, and a 3D visualization of the segmented regions is shown in Figure 3.

In addition to the primary evaluation, the following parameters were analyzed as secondary endpoints:

1. V_{100} (%), V_{150} (%), and D_{95} (%) for both the PTV and entire prostate.
2. $D_{0.1}$ (cc), D_2 (cc), D_5 (cc), and V_{100} (%) for the rectum.
3. $D_{0.1}$ (cc) for the urethra.

The shortest distance from the dorsal surface of the prostate to the anterior wall of the rectum (prostate-rectum distance) was measured, and the correlation between the site-specific prostate-rectum distance and dosimet-

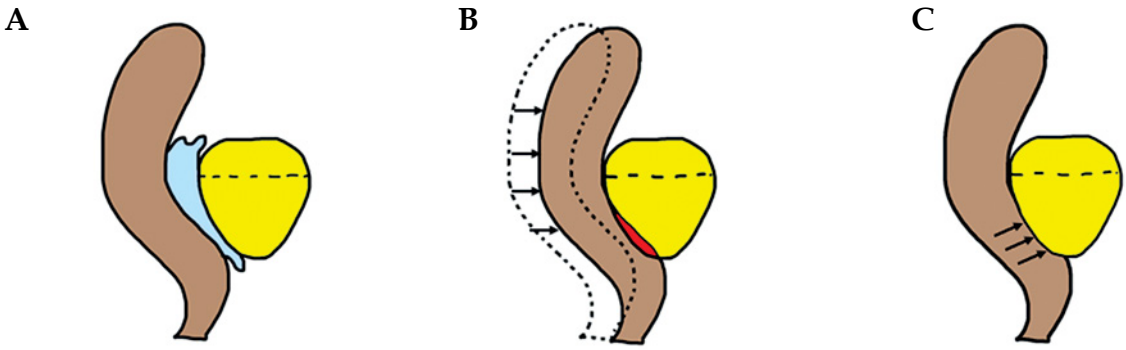

Fig. 1. Creating plans without hydrogel spacer that corrects the backward movement of the rectum. **A**) Structures of the rectum, hydrogel spacer, and prostate (from left to right). **B**) Move the rectum to touch the prostate. **C**) Then, cut the lapping part

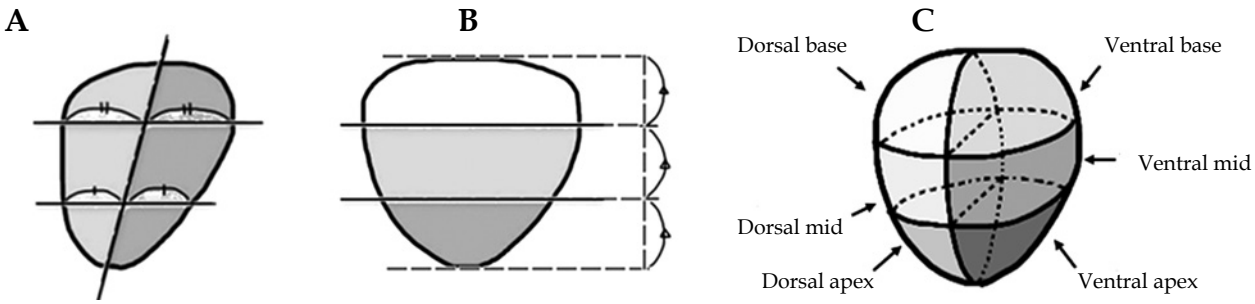

Fig. 2. The prostate was divided into two equal parts using **A**) the sagittal views and into thirds using **B**) the coronal view, and **C**) the overlapping part of each was divided into six areas

ric parameters was analyzed in both groups with and without HS. The prostate-rectum distance was assessed using axial images from the treatment planning CT at the central slice in the cranio-caudal direction for each of the apex, mid, and base regions of the prostate.

Statistical analysis

A total of 60 treatment plans were generated from data of 28 patients (27 patients × 2 plans + 1 patient × 6 plans = 60 plans). Although multiple treatment plans were available for the same patient, each plan was treated as independent data because of anatomical variations caused by applicator position shifts, prostate edema, rectal stool accumulation, and bladder volume changes during an interval of at least 6 hours between the first and second irradiations. Paired *t*-tests were performed to analyze the evaluation parameters between the groups with HS and without HS. Significance was determined using a two-sided test with a *p*-value threshold of ≤ 0.05. Statistical analyses were done using EZR software version 1.68 [15]. In addition to significance, effect sizes were calculated using Cohen's d [16], interpreted according to Sawilowsky [17]. Cohen's d was calculated using the following formula:

$$d = \frac{M_b - M_a}{\sqrt{\frac{SD_a^2 + SD_b^2}{2}}}$$

where M_a and M_b are the means of the two groups, and SD_a and SD_b are their standard deviations.

d ≥ 1.2 indicated very large difference, 0.8 ≤ d < 1.2 – large difference, 0.2 < d < 0.8 – moderate difference, and d ≤ 0.2 – small difference.

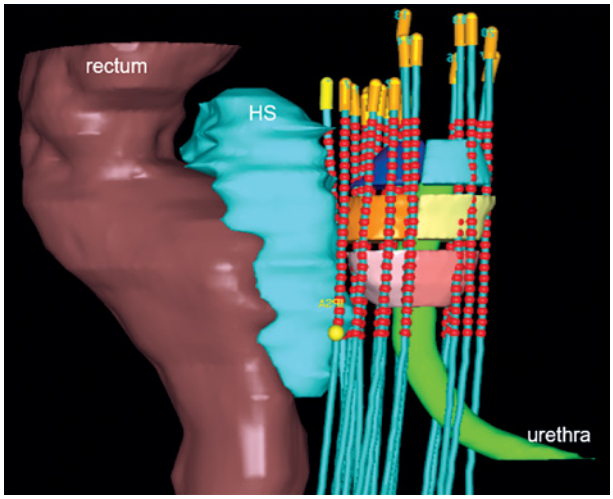

Fig. 3. Six regions of the prostate, hydrogel spacer, and organs at risk. Pink – ventral apex, Yellow – ventral mid, Light blue – ventral base, Light pink – dorsal apex, Orange – dorsal mid, Blue – dorsal base. The following parameters were also evaluated: (**1**) PTV and the entire prostate: $V_{100\%}$, $V_{150\%}$, and $D_{95\%}$; (**2**) Rectum: $D_{0.1cc}$, D_{2cc}, D_{5cc}, and $V_{100\%}$; (**3**) Urethra: $D_{0.1cc}$

For other endpoints, paired *t*-tests were similarly performed, with a *p*-value of ≤ 0.05 considered significant. Cohen's d was also calculated for each parameter. Furthermore, compliance with the following dose constraints proposed in the 2020 Radiotherapy Planning Guidelines by the Japan Society for Radiation Oncology (JASTRO) was evaluated for PTV and organs at risk (OARs) [18].

PTV: $D_{95\%}$ > 100%, $V_{100\%}$ > 95%, $V_{150\%}$ < 50%
Rectum: $D_{0.1cc}$ < 100%
Urethra: $D_{0.1cc}$ < 125%

Results

Patient background

The patient characteristics are summarized in Table 2. The majority were high-risk patients (96%), and all received neoadjuvant androgen deprivation therapy. No serious complications associated with HS placement were observed.

Effect of HS on dose distribution

Tables 3 and 4 show each parameter and the analysis of the results. Figures 4 and 5 represent the results graphically.

In the dorsal regions, HS significantly improved $V_{100\%}$ and $D_{90\%}$, particularly at the apex and mid ($p < 0.05$, large effect sizes). At the base, minimal improvements were observed, and the ventral regions showed little change. HS significantly increased the prostate-rectum distance, especially at the apex and mid (very large effect sizes).

The PTV and prostate coverage ($V_{100\%}$, $D_{95\%}$) improved significantly with HS, with higher compliance with JASTRO constraints (compliance rates improved from 68.3% to 88.3% with HS placement). Although $V_{150\%}$ increased slightly, it remained acceptable. Rectal doses ($D_{0.1cc}$, D_{2cc}, D_{5cc}, V_{100cc}) were significantly reduced with HS, and all cases met the JASTRO $D_{0.1cc}$ constraint compared with 23.3% without HS. No significant differences were noted for the urethra dose.

Table 2. Patient characteristics

Variable	Median (IQR)
Age at RT (years)	71 (71-73.3)
Pre-Tx PSA (ng/ml)	19.2 (19.2-27.8)
Gleason score	8.0 (8-9)
T stage (N0M0)	*n* (%)
T1a-c	0 (0)
T2a	4 (14)
T2b	5 (18)
T2c	7 (25)
T3a	10 (36)
T3b	2 (7)
NCCN risk group	*n* (%)
Very low	0 (0)
Low	0 (0)
Intermediate	1 (4)
High	18 (64)
Very high	9 (32)
	Median (IQR)
Prostate volume (cm^3)	21.15 (21.2-28.2)
Number of needles	18.5 (18.5-20)

RT – radiation therapy, Pre-Tx PSA – pre-treatment prostate-specific antigen, NCCN – National Comprehensive Cancer Network

Discussion

Prostate cancer has a low α/β ratio of approximately 1.5, making HDR-BT an effective boost when combined with EBRT, resulting in an improved biochemical recurrence-free survival (bRFS) [4, 19]. This study demonstrated that HS further optimized dose distribution, particularly in anatomically relevant regions. The most pronounced benefit was observed in the dorsal apex and dorsal mid regions of the prostate, the area close to the rectum where rectal sparing is critical. Importantly, the peripheral zone, a common site of cancer occurrence [20], demonstrated improved coverage with HS. In addition, the FLAME trial reported that dose escalation to intra-prostatic lesions improved the 5-year bRFS [21], supporting the clinical advantage of HS usage in focal dose-escalation strategies to these regions. Moreover, HS improved PTV coverage and JASTRO compliance rates, although $V_{150\%}$ increased slightly. Clinically, this suggests a better balance between coverage and conformity, despite a modest rise in hot spots.

For OARs, the rectal doses were significantly reduced, in agreement with prior reports [11, 12], supporting the clinical benefit of HS in reducing rectal toxicity. In contrast, the urethral doses showed no significant change, likely reflecting the IPSA weighting that prioritizes urethral sparing regardless of HS use.

Several limitations must be noted. First, rectal delineation was based on a virtual model, which may not reflect the actual rectal anatomy. Second, CT-based contouring was employed, whereas MRI could provide higher accuracy. Third, the same optimization parameters were applied to both groups, despite anatomical differences with and without HS. This approach could underestimate the true benefit of HS for the PTV dose coverage. Future studies should incorporate additional plans, in which OAR DVHs are standardized, and evaluate whether the resulting dose distributions are clinically acceptable.

Conclusions

In HDR-BT for prostate cancer, HS reduced rectal dose while improving $V_{100\%}$ and $D_{90\%}$ in the dorsal apex and dorsal mid prostate regions. Because these regions are both close to the rectum and frequent sites of tumor involvement, HS may provide particular clinical benefit in such cases.

Funding

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Disclosures

This study was approved by the Ethics Committee of Niigata University Medical and Dental Hospital (approval No. 2021-0379).

The authors report no conflict of interest.

Table 3. Median radiation dose to the target and organs at risk in patients with and without a hydrogel spacer

Variable		With HS	Without HS	*p*-value	d-value
		Median (IQR)	Median (IQR)		
$V_{100\%}$ (%)					
Ventral	Apex	100.00 (99.98-100.00)	100.00 (99.87-100.00)	0.06	0.27
	Mid	99.97 (98.61-100.00)	99.93 (98.25-100.00)	0.07	0.04
	Base	100.00 (99.58-100.00)	100.00 (99.54-100.00)	< 0.05	0.04
Dorsal	Apex	100.00 (99.56-100.00)	97.10 (89.34-98.92)	< 0.05	0.98
	Mid	100.00 (99.72-100.00)	97.22 (94.43-98.87)	< 0.05	1.22
	Base	100.00 (100.00-100.00)	100.00 (99.75-100.00)	< 0.05	0.09
$D_{90\%}$ (%)					
Ventral	Apex	111.18 (107.40-114.73)	110.34 (106.66-113.36)	< 0.05	0.17
	Mid	109.50 (106.44-114.49)	108.81 (105.72-113.26)	< 0.05	0.13
	Base	112.16 (108.29-116.94)	110.90 (107.74-115.98)	< 0.05	0.04
Dorsal	Apex	110.15 (105.29-112.13)	103.56 (99.76-106.48)	< 0.05	1.31
	Mid	113.31 (109.71-115.75)	106.21 (102.68-110.01)	< 0.05	1.22
	Base	118.86 (113.77-123.57)	115.37 (110.74-120.94)	< 0.05	0.23
PTV	$V_{100\%}$ (%)	98.75 (97.61-99.80)	96.29 (94.42-98.07)	< 0.05	0.66
	$V_{150\%}$ (%)	30.47 (26.89-36.25)	28.81 (24.76-34.49)	< 0.05	0.35
	$D_{95\%}$ (%)	105.96 (102.81-109.79)	101.99 (99.36-104.54)	< 0.05	0.64
Prostate	$V_{100\%}$ (%)	99.74 (99.07-100.02)	98.36 (95.97-99.38)	< 0.05	0.66
	$V_{150\%}$ (%)	26.04 (19.50-32.19)	24.71 (18.69-32.29)	< 0.05	0.08
	$D_{95\%}$ (%)	108.14 (104.36-111.83)	103.74 (100.47-107.37)	< 0.05	0.77
Rectum	$D_{0.1cc}$ (cGy)	692.38 (652.98-742.37)	1,135.73 (911.46-1,532.06)	< 0.05	1.73
	D_{2cc} (cGy)	542.86 (488.07-575.51)	734.56 (679.62-796.39)	< 0.05	2.06
	D_{5cc} (cGy)	444.34 (406.70-492.25)	610.23 (553.39-667.95)	< 0.05	2.51
	$V_{100\%}$ (cc)	0	0.45 (0.12-1.20)	< 0.05	1.34
Urethra	$D_{0.1cc}$ (%)	120.47 (117.32-125.43)	119.82 (116.04-124.24)	0.14	0.03

HS – hydrogel spacer, PTV – planning target volume

Table 4. Median prostate-rectum distance at the apex, mid-gland, and base in patients with and without a hydrogel spacer

Variable	Prostate-rectum distance		*p*-value	d-value
	With HS group	Without HS group		
	Median (IQR)	Median (IQR)		
Apex (mm)	5.2 (1.3-10.9)	0.0 (0.0-0.7)	< 0.001	1.45
Mid (mm)	8.4 (1.7-10.8)	0.1 (0.0-0.6)	< 0.001	1.86
Base (mm)	14.1 (2.4-19.3)	4.3 (0.9-9.7)	< 0.001	0.93

HS – hydrogel spacer

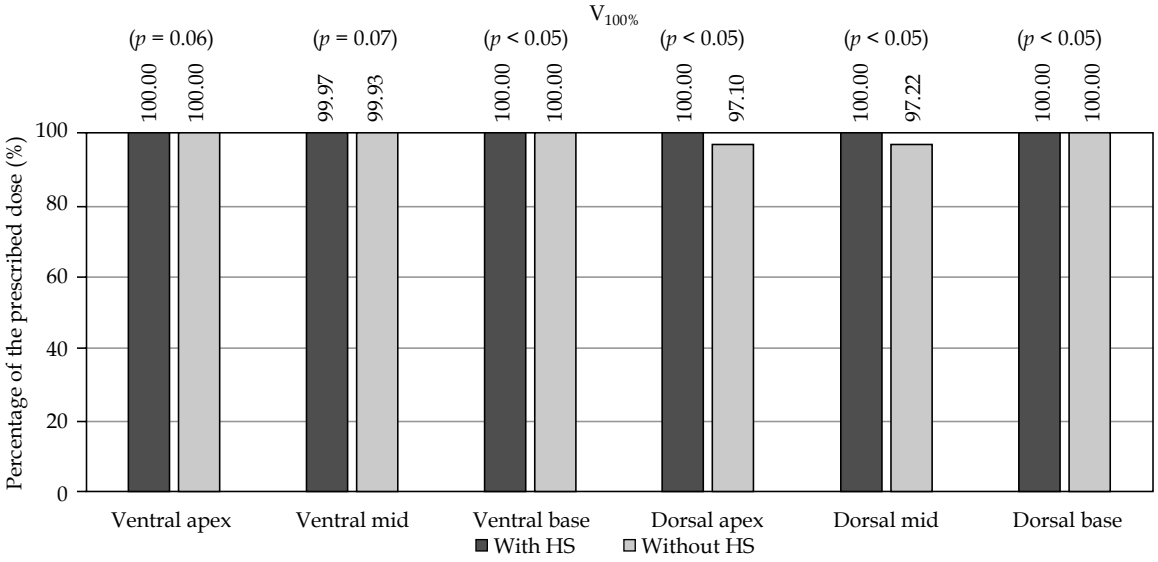

Fig. 4. Percentage of the prescribed dose of $V_{100\%}$ in six regions

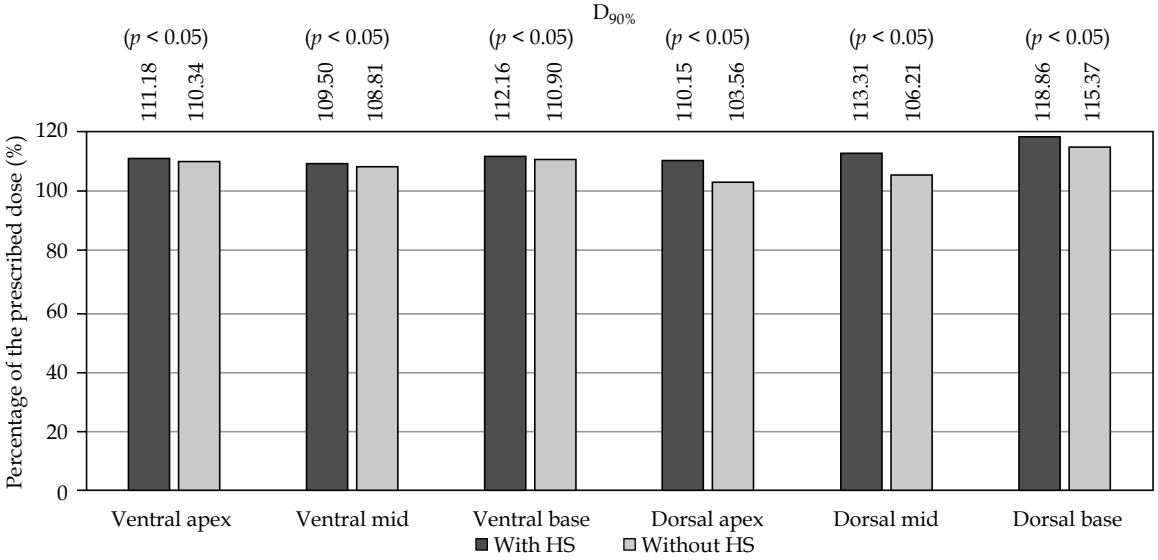

Fig. 5. Percentage of the prescribed dose of $D_{90\%}$ in six regions

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