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Original Research Article

Reirradiation for patients with recurrence head and neck squamous cell carcinoma: A single-institution comparative study

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ABSTRACT

Background and objective: In the last decade, the number of publications that report on the use of external beam radiotherapy and high-dose-rate brachytherapy (HDR-BRT) in the treatment of recurrent head and neck cancer has increased, but no studies compare external beam radiotherapy and HDR-BRT. The aim of this study was to evaluate and to compare the efficacy and toxicity of the three-dimensional conformal radiotherapy (3D-CRT) and HDR-BRT in the treatment of recurrent head and neck cancer.

Material and methods: A total of 64 patients with head and neck cancer recurrence were randomly assigned at a 1:1 ratio to receive either 3D-CRT (50 Gy/25 fractions) in the control group or HDR-BRT (30 Gy/12 fraction) in the experimental group.

Results: The overall survival rate of patients treated with HDR-BRT at 1 and 2-years was 74% and 67%, respectively, compare to 3D-CRT group – 51% and 32%, respectively ($P = 0.002$). Local control at 1- and 2-years in patients who received HDR-BRT was 77% and 63% compare with 47% and 25%, respectively, for the patients who received the 3D-CRT ($P < 0.001$). Most patients developed mild to moderate acute mucositis and dermatitis. In the 3D-CRT group, severe late toxicity was determined in 11 patients (35.5%), and in the HDR-BRT group, in 1 patient (3.1%) ($P = 0.001$). There was no grade 5 toxicity.

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Conclusions: Following our results, we concluded that HDR-BRT is a more effective and safer treatment approach for head and neck cancer recurrences than 3D-CRT.

1. Introduction

Despite advances in multidisciplinary treatment for head and neck cancer after radical treatment, approximately 20–50% of patients are diagnosed with locoregional recurrence during the first two years [1–4]. The main treatment for recurrent disease is surgery, but it is possible only for 15–30% patients, and the five-year overall survival rate is 16–36% [1–3,5–9]. The possibilities for reirradiation with external beam radiotherapy (EBRT) are limited by normal tissue complications [7,10–13]; in cases of high-dose-rate brachytherapy (HDR-BRT), a high total dose can be delivered directly to the tumour and rapid dose fall-off above planning target volume (PTV) allows for sparing of normal tissue [6,12–14]. The results of retrospective studies presented in the literature, using repeated three-dimensional radiotherapy (3D-CRT) for head and neck cancer recurrence, according to a 2-year overall survival (OS), local control (LC) and toxicity, are poor: OS was 15.2–42%, LC – 24–50%; the rate of grade 3 and 4 late toxicity was 1.4–47%, the rate of grade 5 (lethal) late toxicity was 2–16.5% [10,15–17]. The results of several phase II and retrospective studies related to the use of the HDR-BRT for treatment of head-neck cancer patients are published so far; fractionation regimes are being actively discussed. In these studies, 3–4 Gy fractions up to 30–40 Gy total dose are administered to treat the head and neck cancer recurrence most often, and 2-year OS rate was 19–63%, LC – 67–71%; rate of toxicity grade 3 and 4 was 8–22.2% [6,12,13,18]. There are discussions available regarding the possibility to reduce the rate and grade of late toxicity through the use of less than 3 Gy per fraction in HDR-BRT group while increasing the total number of fractions. Although the number of publications, presenting the results of repeated 3D-CRT and results of HDR-BR when treating the head and neck cancer recurrence, increased recently, the research comparing the effectiveness and safety of treatment using the three-dimensional radiotherapy and high-dose-rate brachytherapy have been not accomplished yet so far.

The aim of this study was to evaluate and to compare the efficacy and toxicity of the 3D-CRT and HDR-BRT in the treatment of recurrent head and neck cancer.

2. Material and methods

From October 1, 2008, to February 11, 2011, a prospective single-institution study was conducted in the Hospital of Lithuanian University of Health Sciences Kaunas Clinics. Sixty-four patients with head and neck relapse were randomly assigned in a 1:1 ratio to receive either 3D-CRT (50 Gy/25 fractions) in the control group or hypofractionated HDR-BRT (30 Gy/12 fractions) in the experimental group. Randomisation was performed using a computer program. One patient in the control group after randomisation was removed from analysis due to myocardial infarction. The permission to conduct this clinical study was obtained from the Kaunas Regional Biomedical Research Committee (No. BE-2-15).

2.1. Patients

Before reirradiation, all patients were evaluated for eligibility and the following selection criteria were applied: (1) histologically confirmed head and neck squamous cell cancer relapse; (2) locoregional relapse identified in an area that had been irradiated during previous radiotherapy using a total dose of ≥50 Gy; (3) Karnofsky Performance Score ≥ 80; (4) no distant metastases; and (5) no late grade 3 and 4 toxicity after the primary radiotherapy. The patients' characteristics are presented in Table 1.

2.2. Three-dimensional conformal radiotherapy methodology used to treat the control group patients

For patients' immobilisation, thermoplastic masks with five fixation points were used. A computed tomography (CT) scan from the base of the skull, including the neck, with 3-mm slices was used for three-dimensional (3D) treatment planning. The gross tumour volume (GTV – the volume of tumour, identified by clinical and radiological tests) was defined in the 3D planning system ''Eclipse''. The clinical tumour volume (CTV) was obtained by adding 5-mm margins along all directions around the GTV. To generate the PTV, a 3–5 mm isotropic margin was added to the CTV. Organs at risk (OAR) (e.g., spinal cord, mandible, carotid artery) were delineated. The total dose was calculated at the isocenter, so that the PTV would be covered by ≥95% of the prescribed dose, and the maximum dose level would not exceed 107% of the prescribed dose. This also ensured that the cumulative dose for the spinal cord would not exceed 50 Gy. During this study, the total dose of 50 Gy per 25 fractions was prescribed to all of the patients by administering 2-Gy single fractions (Fig. 1).

2.3. High-dose-rate brachytherapy methodology used to treat the patients from the experimental group

When treating patients with recurrent locoregional head and neck cancer, the principles of the Paris system are applied [19]. The loop technique was used to treat the local recurrences of the oral cavity and oropharyngeal tumours. The closed-end tube technique was used most often after the disease relapse had been diagnosed at the regional lymph nodes of the neck, at the sites of localised salivary gland cancer recurrence, or at the

Table 1 – Patients' characteristics in the control (3D-CRT) and experimental (HDR-BRT) groups.

Characteristic	3D-CRT	HDR-BRT	P
Sex			0.414
Male	25 (80.6)	23 (71.9)	
Female	6 (19.4)	9 (28.1)	
Age, median (range), years	59 (46–78)	59 (39–75)	0.904
<60 years	16 (51.6)	17 (53.1)	
≥60 years	15 (48.4)	15 (46.9)	
Tumour localisation			0.926
Oropharynx	7 (22.6)	6 (18.8)	
Hypopharynx	3 (9.7)	2 (6.2)	
Oral cavity	9 (29)	12 (37.5)	
Cancer unknown primary	1 (3.2)	1 (3.1)	
Larynx	2 (6.5)	2 (6.2)	
Parotid salivary gland	1 (3.2)	1 (3.1)	
Paranasal sinuses	6 (19.3)	6 (18.8)	
Lip	2 (6.5)	2 (3.1)	
Tumour degree of differentiation			0.78
G1–2	22 (71)	24 (75)	
G3–4	9 (29)	8 (25)	
T			0.898
T1–2	15 (48.4)	16 (50)	
T3–4	16 (51.6)	16 (50)	
N			0.85
N0	7 (22.6)	9 (28.1)	
N1–2	18 (58.1)	18 (56.2)	
N3	6 (19.3)	5 (15.7)	
Primary treatment			0.428
RT only	4 (12.9)	3 (9.4)	
Surgery and RT	6 (19.3)	9 (28.1)	
Surgery and chemoradiation	8 (25.9)	13 (40.6)	
Chemoradiation	13 (41.9)	7 (21.9)	
Primary RT dose, median (range), Gy	66 (50–70)	66 (50–70)	0.535
<60 Gy	12 (38.7)	10 (31.2)	
≥60 Gy	19 (61.3)	22 (68.8)	
Time to reirradiation, median (range), months	15.2 (6.8–22.1)	14.9 (3–26.1)	0.707
<15 months	15 (48.4)	17 (53.1)	
≥15 months	16 (51.6)	15 (46.9)	
Localisation of recurrence			0.938
Oropharynx	5 (16.1)	5 (15.6)	
Oral cavity	5 (16.1)	8 (25)	
Parotid salivary gland	1 (3.2)	1 (3.1)	
Paranasal sinuses	6 (19.4)	5 (15.6)	
Neck lymph nodes	14 (45.2)	13 (40.6)	
Treatment			0.898
Surgery and RT	15 (48.4)	16 (50)	
RT	16 (51.6)	16 (50)	
PTV, median (range), cm^3	177.3 (94.6–277.4)	34.8 (8–107)	0.001

Values are number (percentage) unless otherwise indicated.
RT, radiotherapy; PTV, planning target volume.

presence of localised recurrences in nasal cavity or paranasal sinuses. In both techniques, the catheters were placed as near as possible at 10- to 15-mm intervals with a security margin of 10 mm in all directions around the target.

After the catheter implantation, all of the patients underwent a CT scan, with a slice thickness of 2.5 mm. The CT study was transferred to the 3D planning system Oncentra (Nucletron, The Netherlands). The GTV was delineated as identified by clinical and radiological tests. The CTV encompassed the GTV and possible surrounding microscopic tumour margins, and in most cases fell into the range of 5 mm; PTV did not differ from the CTV; the OAR was delineated. Prescribed and reported doses were specified by D90 as determined by dose-volume histogram (DVH) (Fig. 2). Dose heterogeneity was specified by V100 (the percentage of PTV receiving 100% of the prescribed dose), V150 (the percentage of PTV receiving 150% of the prescribed dose), and V200 (the percentage of PTV receiving 200% of the prescribed dose) [20]. In our study, the mean values were as follows: D90 = 2.25 Gy (range, 1.9–2.5 Gy), equivalent to 90.2% of the reference dose of 2.5 Gy, V100 = 70.01% (range, 44.1–95.2%), V150 = 25.13% (range, 14–40.7%), V200 = 12.1% (range, 8.74–21.2%). The mean values of the homogeneity index and dose non-uniformity ratio were estimated to be 0.62 (range, 0.54–0.76) and 0.3 (range, 0.23–0.4), respectively. During this study, all patients received two daily fractions of 2.5 Gy to a total dose of 30 Gy, with an interfractional interval of at least 6 h.

2.4. *Statistical analysis*

Statistical analysis was performed using the SPSS software package (Statistical Package for Social Sciences 20 for Windows). To assess the association of qualitative indications, the chi-square χ^2 criterion was used. When testing the statistical hypotheses, a significance level of 95% ($P < 0.05$) was selected. To determine and compare the effectiveness of radiotherapy, the median survival, 1- and 2-year overall survival (OS) and local control (LC) was assessed in both groups of patients using the Kaplan–Meier method. Statistical comparison between two groups was accomplished using the log rank criterion. The acute and late toxicities were assessed using RTOG/EORTC toxicity criteria [21,22].

3. Results

3.1. *Overall survival*

The median survival of patients treated with hypofractionated HDR-BRT was 33.4 months, and the 1- and 2-year OS reached 74% and 67% (Table 3), respectively, compare to patients treated with 3D-CRT the median survival was 11.9 months, and the 1- and 2-year OS was 51% and 32% (Table 2), respectively (hazard ratio [HR] = 0.4, 95% CI = 0.2–0.71; $P = 0.002$) (Fig. 3).

First, we performed a univariate Cox analysis on the relevant factors that may be prognostic: N stage, the dose of first radiation, the reirradiation volume, surgery before reirradiation and the interval between primary irradiation and reirradiation. Second, we performed a multivariable analysis including those factors in which the significance level in the univariate analysis did not exceed 0.2. After performing the multivariate Cox analysis, it was determined that the factors associated with better OS in the control group

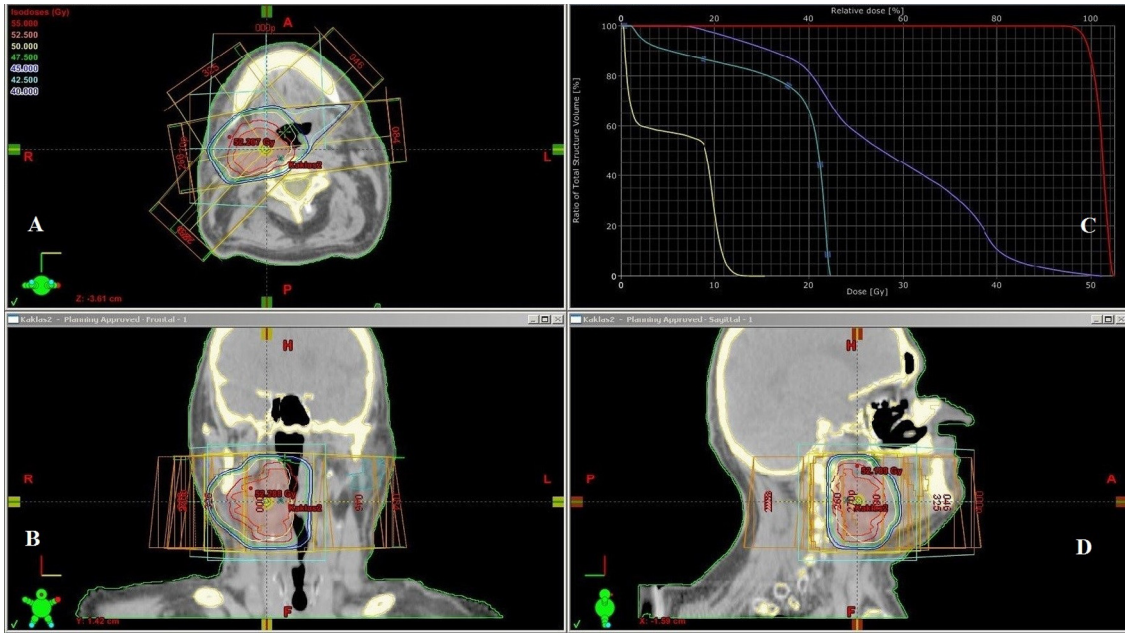

Fig. 1 – Conformal dose patterns for a patient with oropharyngeal recurrence cancer in axial (A), coronal (B) and sagittal (D) views. Dose-volume histogram (C): yellow curve – spinal cord (mean dose 6.06 Gy, min dose – 0.18 Gy, max dose – 15.3 Gy); red – PTV (mean dose 50.98 Gy, min dose – 44.5 Gy, max dose – 52.4 Gy); green – right parotid (mean dose 18 Gy, min dose – 1.03 Gy, max dose – 22.34 Gy); violet – left parotid (mean dose 28.51 Gy, min dose – 5.83 Gy, max dose – 51.24 Gy).

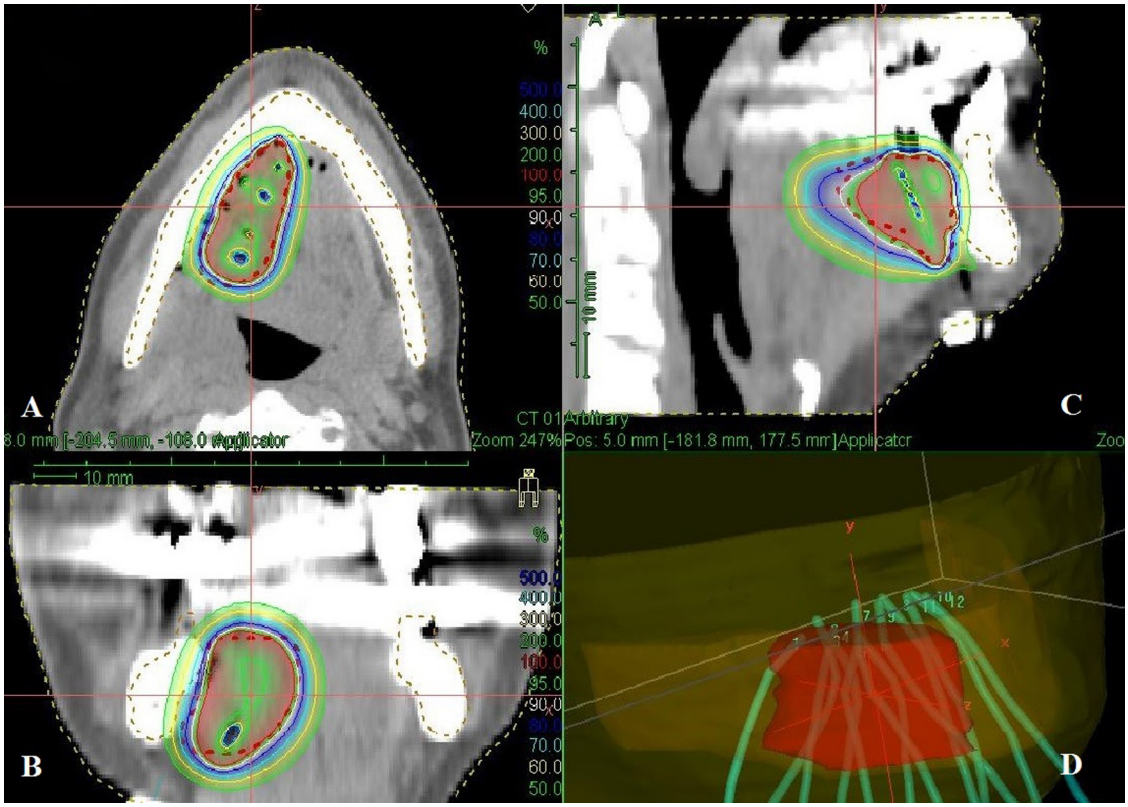

Fig. 2 – Treatment plan using loop technique of HDR-BRT for patient with tongue recurrent cancer (PTV – dotted red line). Isodose distributions on an axial (A), coronal (B) and sagittal (C) image are shown. 3D reconstruction of brachytherapy catheters and PTV (D).

Table 2 – Published data on EBRT for recurrent head and neck cancer.

Study	N	Dose of reirradiation	Chemotherapy	Late toxicity Grade 3–4	Outcomes/comments
Langendijk et al. [24]	34	60–66 Gy	–	24% – pharynx/oesophagus; 9% – mucous membrane	2-year OS – 28% 2-year LC – 27%
Popovtzer et al. [25]	66	15–79.6 Gy (median 68 Gy)	47 (71%) platinum-based	29%	2-year OS – 40% 2-year LC – 27%
Janssen et al. [27]	75	20–75 Gy (median 46 Gy)	10 pts.-CP 10 pts.-CB + TX 4 pts.-CP + 5-FU 1 pts.-5-FU 1 pts.-GMT 7 pts.-CTX	1.4%	1-year OS – 41% 2-year OS – 23% 1-year LC – 35% 2-year LC – 24%
Present study	31	50 Gy	–	35.5%	1-year OS – 51% 2-year OS – 32% 1-year LC – 47% 2-year LC – 25%

5-FU, 5-fluorouracil; HX, Hydroxyurea; CP, cisplatin; CB, carboplatin; TX, taxan; CTX, cetuximab; GMT, gemcitabine; OS, overall survival; LC, local control.

(3D-RT) were: N0-1 stage (vs. N2-3 stage, $P = 0.032$), a longer interval between the first course and reirradiation (≥15 months vs. < 15 months, $P = 0.016$) and lesser PTV volume (<177.3 cm^3 vs. ≥177.3 cm^3, $P = 0.025$); in the experimental group (HDR-BRT), those factors were: N0-1 stage (vs. N2-3 stage, $P = 0.006$) a longer interval between the first course and reirradiation (≥15 months vs. < 15 months, $P = 0.013$), a lesser PTV volume (<34.8 cm^3 vs. ≥34.8 cm^3, $P = 0.025$), and postoperative reirradiation (surgery and reirradiation vs. reirradiation, $P = 0.046$).

3.2. *Local control*

The median local control in experimental group was 28.1 months, and the one- and two-year LC was 77 and 63% (Table 3), respectively, compare to control group the median local control was 10.3 months, and the 1- and 2-year LC was 47% and 25% (Table 2), respectively (HR = 0.34, 95% CI = 0.14–0.7; $P < 0.001$) (Fig. 4).

After multivariate Cox analysis, it was determined that the factors associated with better LC in the control group (3D-RT) were: N0-1 stage (vs. N2-3 stage, $P = 0.012$), a longer interval between first course and reirradiation (≥15 months vs. < 15 months, $P = 0.044$), and lesser PTV volume (<177.3 cm^3 vs. ≥177.3 cm^3, $P = 0.044$); in the experimental group (HDR-BRT): a larger dose of the primary radiotherapy (≥60 Gy vs. < 60 Gy, $P = 0.007$), a longer interval between the first course and reirradiation (≥15 months vs. < 15 months, $P = 0.033$), a lesser PTV volume (<34.8 cm^3 vs. ≥34.8 cm^3, $P = 0.016$), and postoperative reirradiation (surgery plus reirradiation vs. reirradiation, $P = 0.001$).

3.3. *Toxicity*

Most patients developed mild-to-moderate acute mucositis and dermatitis. There was no grade 5 toxicity. In the experimental group, severe (grade 3 and 4) acute toxicity was shown in 11 patients (34.4%). Similarly to the data of the experimental group, the severe acute toxicity in control group was observed in 17 patients (54.8%) ($P = 0.102$).

Severe late toxicity occurred significantly less frequently in the experimental group patients, in comparison to control group patients: 3.1% ($n = 1$) and 35.5% ($n = 11$), respectively ($P = 0.001$).

Osteoradionecrosis occurred in 1 patient (3.1%) in the HDR-BRT group over 3.5 months after the brachytherapy and was treated by surgery. In the 3D-CRT group, 1 patient (3.2%) developed skin ulceration, 2 patients (6.4%) developed fibrosis

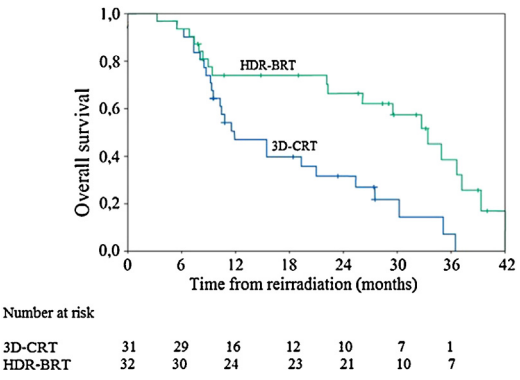

Fig. 3 – Overall survival of the experimental (HDR-BRT) and control (3D-CRT) groups from reirradiation.

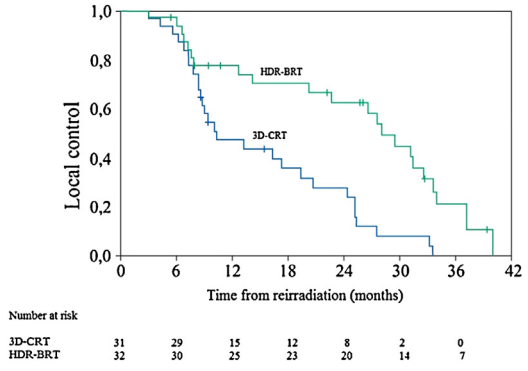

Fig. 4 – Local control of the experimental (HDR-BRT) and control (3D-CRT) groups from reirradiation.

Table 3 – Published data on HDR-BRT for recurrent head and neck cancer.

Study	N	EQD_2[a] (Gy) ($\alpha/\beta = 10$)	EQD_2[a] (Gy) ($\alpha/\beta = 3$)	Treatment	Late toxicity Grade 3–4	Outcomes/comments
Hepel et al. [12]	30	35.8	39.6	192Ir-HDR-BRT mean 34 Gy (range 18–48 Gy)	16%	1-year OS – 56% 2-year OS – 37% 1-year LC – 54% 2-year LC – 45%
Wiegand et al. [30]	12	32.5	36	192Ir-HDR-BRT 20–30 Gy	NA	1-year OS – 41% 2-year OS – 18%
Narayana et al. [13]	30	(a) 38 (b) 46.7 (c) 69.3	(a) 39.2 (b) 56 (c) 74	(a) OP + 192Ir-HDR-BRT 34 Gy/(n = 18) (b) 192Ir-HDR-BRT 40 Gy/(n = 9); (c) EBRT 40–50 Gy + 192Ir-HDR-BRT 20 Gy/(n = 3)	13% No grade 4 reactions	2-year OS – 63% 2-year LC – 71%
Schiefke et al. [18]	18	(a) 32.5 (b) 78.5	(a) 36 (b) 82	(a) OP + 192Ir-HDR-BRT, median dose 30 Gy (15–44.8 Gy)/(n = 10) (b) OP + 192Ir-HDR-BRT, median dose 30 Gy (15–44.8 Gy) + EBRT, median dose 45 Gy (6–49.6 Gy)/(n = 8)	22.2%	2-year OS – 59.8% 2-year LC – 64.8%
Present study	32	31.3	33	(a) OP + 192Ir-HDR-BRT 30 Gy/(n = 16) (b) 192Ir-HDR-BRT 30 Gy/(n = 16)	3.1%	1-year OS – 74% 2-year OS – 67% 1-year LC – 77% 2-year LC – 63%

OP, surgical treatment; 192Ir, iridium 192; HDR-BRT, high-dose-rate brachytherapy; EBRT, external beam radiotherapy; OS, overall survival; LC, local control; NA, not available.
[a] EQD calculated according to mean or median of total HDR-BRT dose.

of deep connective tissue, 1 patient (3.2%) developed complete dryness of mouth, 3 patients (9.6%) developed stricture of pharynx, 1 (3.2%) developed severe oedema of the larynx, and 2 patients (6.4%) developed osteoradionecrosis.

4. Discussion

Surgical treatment and radiotherapy of head and neck tumours increases the probability of chronic pain and the disruption of main vital functions: speech, mastication, swallowing, respiration, and social interaction. 3D-CRT prolongs the survival of patients with diagnosed head and neck cancer; however, the development of xerostomia, dysphagia, dysgeusia, and post-radiation tooth decay reduces quality of life [23]. The comparison of results obtained during our investigation with results from other studies is problematic due to several reasons:

- There are no completed clinical studies in which 3D-CRT would be compared against HDR-BRT;
- Different criteria for patient inclusion into the study;
- In most cases, acute toxicity was not evaluated according to RTOG/EORTC toxicity criteria, and late reactions were evaluated according to modified RTOG/EORTC toxicity criteria or using some other criteria.

In the literature, the results of retrospective studies have been presented most often; in these studies, heterogeneous patient groups have been analysed and different treatment regimens have been applied (Table 2).

Langendijk et al. accomplished a prospective phase II study, during which 34 patients were reirradiated using 3D-CRT [24]. The mean interval between primary radiation and reirradiation was 90 months (range 12–233 months). The results of this study indicated that among patients who were treated for locoregional recurrence and second primary cancer, there was no statistically significant difference determined when assessing 2-year LC (14% and 35%, $P = 0.75$) and OS (medians 14.9 and 11.8 months, $P = 0.49$). We compared these parameters with results from the control group (3D-RT) of our study. Despite the shorter interval between primary radiotherapy and reirradiation, the results achieved by a lower total dose were equivalent. Similar to our research, in this study, mucositis (mostly grade 2) was observed in all patients, although the rate of grade 3 or greater late toxicity in the pharynx and oesophagus was considerably higher compared with our research results (24% vs. 9.7%) and the rate of toxicity in other organs was similar.

Popovtzer et al. published results of a study that involved 66 patients treated for the nonresectable recurrent or second primary squamous cell head and neck cancer [25]. Reirradiation was implemented using 3D-R or IMRT techniques, and 47 (71%) patients also received platinum-based chemotherapy. Popovtzer et al. included patients in their study who were diagnosed with nasopharynx cancer relapse. According to the literature data, the results of nasopharynx cancer recurrence treatment are significantly better compared to the cancer recurrence treatment results in other head and neck localisations (5-year LC reached 47–85%, OS 47–65%) [26]. In this study, a total dose higher than 68 Gy and concurrent chemotherapy did not improve LC, this

explains why the results of 2-year LC and OS were similar to our research. A higher rate of acute and late toxicities in our study could have been caused by the fact that Popovtzer et al. used IMRT equipment and the time between primary radiotherapy and reirradiation was longer.

A retrospective analysis was performed by Janssen et al. [27]. A total of 75 patients were treated for head and neck cancer recurrence. The median total dose of reirradiation was 46 Gy (range 20–75 Gy). The 2-year OS was 23%, and LC was 24%. Similar results of 2-year OS (32%) and LC (25%) were obtained; however, the rates of acute and late toxicities differed. The lower rate of complications could have been because some patients were administered a lower total dose of reirradiation, and the time between primary radiotherapy and reirradiation was slightly longer.

After comparing the results of the control group from our study (3D-RT) with the findings of other scientists, it is possible to draw the following conclusions: the control group patients were administered a sufficient total dose of reirradiation (50 Gy), and administering chemotherapy in combination with reirradiation does not improve the overall survival or the results of LC. Treatment toxicity was acceptable.

Up till now, there are insufficient data in the literature regarding applications of HDR-BRT during treatment of head and neck cancer recurrences. In 2012, Yamazaki et al. surveyed the significance of HDR-BRT when treating head and neck cancer; only five studies analysing the application of this method in disease relapse treatment were included in this survey [28]. A comparison of HDR-BRT results when treating recurrent head and neck cancer is given in Table 3. To compare the effectiveness and toxicity of treatments from these studies, an equivalent to conventionally fractionated radiotherapy dose formula (EQD_2) was used, when $\alpha/\beta = 10$ for tumour and acute reactions and $\alpha/\beta = 3$ for late reactions [29].

Hepel et al. published results of treatment involving 30 patients diagnosed with head and neck cancer recurrence who were treated using 192I-HDR-BRT [12]. The mean total dose was 34 Gy (range 18–48 Gy), the mean implant volume was 85 cm3 (range 34–265 cm^3). The 2-year OS was 37%, and LC was 67%; moderate grade mucositis was observed in most of patients, late grade 3 and 4 reactions were diagnosed in 5 patients (16%), and grade 5 complications were not observed. Better OS and LC outcomes in our study could be associated with smaller PTV volume, although the EQD2 for tumours in our study was lower. A lower rate of severe late complications was conditioned by smaller PTV and lower EQD2 for late reactions.

Wiegand et al. treated 12 patients who were diagnosed with recurrent squamous head and neck carcinoma [30]. Recurrent cancer had been identified at the base of the tongue in eight patients, in the floor of the mouth in three patients and in the tonsillar region in 1 patient. During high-dose-rate brachytherapy, a total dose of 20–30 Gy had been delivered by administering daily fractions of 2–3 Gy per fraction. The median OS was 8.5 months, while 2-year OS was 18%. The different OS rates in these studies could be due to the fact that our study included patients who were diagnosed with recurrent cancer in other locations, including the larynx, paranasal sinuses, salivary glands, and lips, and a portion of patients received a combined surgical and HDR-BRT treatment. The rates of toxicity were not evaluated by Wiegand et al.

Narayana et al. published results of treatment involving 30 patients diagnosed with recurrent head and neck cancer [13]. Eighteen patients had undergone surgery before HDR-BRT; they then received a total dose of 34 Gy, with two daily fractions of 3.4 Gy. Nine patients had received a stand-alone HDR-BRT, with total doses of 40 Gy and two daily fractions of 4 Gy. The 2-year OS and LC in all study subjects were 63% and 71%, respectively. Acute grade 3 and 4 complications were diagnosed in 4 patients, the rate of grade 3 late toxicity was 13%, and no grade 4 and 5 toxicities were noted. Our study had a higher rate of acute toxicity: acute reactions were diagnosed in 11 patients, but there were less late grade 3 and 4 complications – 1 patient (3.1%) was diagnosed with osteoradionecrosis, possibly due to a lower single dose of 2.5 Gy. Considering the EQD2 for tumour and late radiotherapy reactions, it can be stated that the fractionation regimen using 2.5 Gy had the same effectiveness and caused less severe late reactions.

Schiefke et al. used high-dose rate brachytherapy to treat 18 head and neck cancer patients: 5 patients were treated for primary head and neck cancer, and 13 patients were treated for disease recurrence [18]. All patients from this study received surgical treatment, 8 patients received a concurrent 3D-CRT, and seven patients received chemotherapy. The 2-year OS and LC in patients treated for recurrent disease were 59.8% and 64.8%. The rate of grade 3 or greater late toxicity was 22.2%. The longer 2-year overall survival and lower rate of severe toxicity in our study may be associated with a lower EQD2 for tumours and late reactions.

Comparing the results of the HDR-BRT test group analysed in our study with the findings of other authors, it can be concluded that the fractionation regimen based on lower doses delivered to patients included in our study (2.5 Gy per fraction, two daily fractions to a total dose of 30 Gy) is an effective treatment method; administering concurrent chemotherapy does not improve the overall survival or local control results.

5. Conclusions

Following our results, we concluded that hypofractionated high-dose-rate brachytherapy is a more effective and safer treatment approach for head and neck cancer recurrences than external beam radiotherapy. Concurrent chemoreirradiation is not better than reirradiation alone.

Conflict of interest

The authors state no conflict of interest.

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