Is Brachytherapy Feasible After Head and Neck Cancer Reconstructive Surgery? Preliminary Report

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Abstract

The purpose of the study was to evaluate the influence of interstitial postoperative brachytherapy for the vitality and quality of flaps used for reconstruction of tissue defects after head and neck cancer salvage resection. We aimed at presenting six consecutive patients with recurrent squamous cell carcinoma in head and neck region who underwent salvage surgery and tissue reconstruction with a regional or free flap followed by brachytherapy. Reconstruction was performed with a free radial forearm flap in 2 cases, with a free thigh flap in 2 cases, and with a myocutaneous lateral upper arm flap in the next 2 cases. In all patients, pulsed-dose-rate brachytherapy was used with a median value of 0.7 Gy (range 0.6–0.8 Gy) per pulse and a median total dose of 20 Gy (range 20–40 Gy). In the analyzed group, there were no serious wound and flap complications after brachytherapy. In one case, peripheral skin necrosis was noticed. No revision surgery was needed but only surgical debridement of the necrotic margins. All wounds healed within 14 days after surgery as well as donor sites which healed within 4 weeks. Based upon our data, pulsed-dose-rate brachytherapy seems to be a safe option that can be performed at the site of reconstruction in immediate postoperative period with minimal wound complications and with no impact on flap survival. Further clinical study based on larger patient series is needed to present statistically proven results.

Keywords PDR brachytherapy · Recurrent head and neck cancers · Free flap · Pedicle flap

Introduction

The management of recurrent head and neck cancers is a challenge and always requires individualized therapy planned by a team of surgeons, oncologists, and radiotherapists. Unfortunately, curative options for this group of patients are very often limited. In most cases, salvage approach includes large resections followed by sophisticated microsurgical reconstructions [1–4]. The difficulty to assess sufficient clear margins together with the inability to re-treat the tumor bed

with external beam radiotherapy (EBRT) due to the excessive morbidity and complications rates brings the need to use other options. Brachytherapy (BT) provides specific, intensive local irradiation of the oncologically unsafe regions in the immediate postoperative period, allowing protection of surrounding structures and preserving organ functions [5, 6]. The question arises whether it can be associated with delayed wound healing and its breakdown. Flap necrosis due to vascular coagulation and fibrosis creates an additional strongly documented risk for the patient, and all factors that can increase it should be considered [7–9].

The aim of the study was to evaluate the influence of interstitial postoperative brachytherapy for the vitality and quality of flaps used for reconstruction of tissue defects after head and neck cancer salvage resection.

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Patients and Methods

Six consecutive patients with recurrent squamous cell carcinoma in head and neck region who underwent salvage surgery and tissue reconstruction with a regional or free flap followed by BT were included into the study. In all cases, recurrence

appeared in previously irradiated region. Historical patients' records were analyzed (Table 1).

Four patients were men, while two were women, and mean age was 56 years (range 38–65). Two patients underwent total

laryngectomy with partial resection of the hypopharynx and/or esophagus, two patients had a salvage surgery of the stomal recurrence, one patient had recurrent cancer of the oral cavity and pharynx resected, while one patient was operated due to

Table 1 Patients characteristics, methods of treatment, and wound/flap complications

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Sex	Man	Man	Woman	Man	Man	Woman
Age	58	59	38	62	53	65
Comorbidities	Ischemic heart disease, hypertension	–	Diabetes	Hypertension	–	Chronic myeloid leukemia
Previous oncological treatment	Primary RChT (full dose of EBRT) due to laryngeal cancer (SCC)	Primary RChT (full dose of EBRT) due to laryngeal cancer (SCC)	Total laryngectomy, cervical lymphadenectomy + RChT (full dose of EBRT) (SCC)	Total laryngectomy, cervical lymphadenectomy + RChT (full dose of EBRT) (SCC)	Primary RChT (full dose of EBRT) due to the cancer of the base of the tongue (SCC)	Primary RT (full dose of EBRT) due to the neck tumor (CUP syndrome; SCC)
Disease-free duration	16 months	18 months	24 months	13 months	11 months	4 months
Recurrence characteristics	rT4N1M0 Advanced recurrence in the larynx with the infiltration of the hypopharynx and esophagus, neck metastases	rT4N1M0 Advanced recurrence in the larynx with the infiltration of the esophagus, neck metastases	rT4N1M0 Recurrence in the stomal region, neck metastases	rT4N0M0 Recurrence in the stomal region	tT4N2M0 Recurrence localized in the tongue, infiltrating palatine tonsil, neck metastases	rTxN3M0 Advanced neck nodal recurrence in regions IIa, IIb, and V
Salvage surgery	-Total laryngectomy with partial resection of the hypopharynx and esophagus, lymphadenectomy	-Total laryngectomy with partial resection of the esophagus, lymphadenectomy	-Salvage surgery of the stomal recurrence, lymphadenectomy	-Salvage surgery of the stomal recurrence	-Resection of the recurrent cancer of the oral cavity and pharynx, lymphadenectomy	-Advanced neck nodal recurrence resection
-Type	-Free thigh flap	-Free thigh flap	-Free radial forearm flap	-Myocutaneous lateral upper arm flap	-Free radial forearm flap	-Myocutaneous lateral upper arm flap
-Flap						
BT-Method	-PDR	-PDR	-PDR	-PDR	-PDR	-PDR
-Localization of applicators	-Neck	-Stoma	-Stoma	-Stoma	-Neck	-Neck
-Number of catheters	-5	-3	-4	-4	-5	-3
Flap perfusion (tissue color, turgor, temperature, capillary refill, bleeding)	12 h after surgery abnormal flap perfusion (bluish color, high turgor, rapid refill, dark bleeding) No abnormalities after revision surgery, after BT and in the follow-up period	No abnormalities	7 days after surgery and 2 days after BT abnormal perfusion in peripheral parts of the flap (dark color, no refill, no bleeding)	No abnormalities	No abnormalities	No abnormalities
Complications	Venous thrombosis (before BT)	–	Peripheral skin necrosis	–	–	–
Management of the complications	New venous anastomosis creation	–	Surgical debridement of the necrotic margins	–	–	–

RChT radiochemotherapy, EBRT external beam radiotherapy, SCC squamous cell carcinoma, CUP carcinoma of unknown primary, BT brachytherapy, PDR pulsed-dose-rate

the advanced neck nodal recurrence. Reconstruction was performed with a free radial forearm flap in 2 cases, with a free thigh flap in 2 cases and with a myocutaneous lateral upper arm flap in the next 2 cases (Table 1). BT catheters were implanted parallelly with a constant distance of 1–1.5 cm to achieve homogenous dose distribution in the regions of unsafe margins: around the stoma in 3 cases, in the II–IV regions of the neck in the following 3 cases, and then all were sealed with the flaps. An average of 4 (3–5) catheters was inserted. All patients were given antibiotics preventively. The target volume was defined postoperatively, just before BT, with the use of CT and MRI scans. Standard geometric optimization was used to plan the treatment, while prescription dose was based on the modified Paris dosimetry scheme. All parameters were determined by the tumor location and the proximity to adjacent critical organs. BT started 3–7 days after surgery. In all patients, pulsed-dose-rate BT (PDR-BT) was used with a median value of 0.7 Gy (range 0.6–0.8 Gy) per pulse and a median total dose of 20 Gy (range: 20–40 Gy) delivered in 20–24 h with a time interval of 1 h between the pulses. In the treatment, the following equipment (Nucletron BV®, Veenendaal, Netherlands) was used: IBU (integrated brachytherapy unit), PLATO or Oncentra planning system, and microselectron PDR with Iridium-192 sources used for treatment delivery. PDR-BT was chosen as a method that combines physical advantages of high-dose-rate (HDR) BT (isodose optimization, planning flexibility, and radiation safety) with radiobiological advantages of low-dose-rate (LDR) BT (repair advantages).

All flaps were monitored every 2 h for the first 3 days after surgery, every 6 h for 14–28 days directly after BT, and then every month during follow-up visits. Tissue color, turgor, temperature, capillary refill, and bleeding were estimated and noted (Table 1).

Results

In the study group, there were no hematomas, flap infections, or wound breakdowns resulting in fistulas. Four flaps had a favorable outcome—no monitor abnormalities were noted. In one case, peripheral skin necrosis was noticed. It appeared 7 days after surgery and 2 days after BT. It was free radial forearm flap used for the reconstruction of the stomal region. No revision surgery was needed but only surgical debridement of the necrotic margins. The wound healed by granulation. In one case, the signs of venous thrombosis appeared 12 h after surgery. Revision surgery revealed thrombus in the anastomosis. It was removed, and new venous anastomosis was created. The free thigh flap survived. There were no abnormalities noted after BT and in the follow-up time after referral (Table 1).

In the analyzed group, there were no serious wound and flap complications after BT. All wounds healed within 14 days after surgery as well as donor sites which healed within 4 weeks.

In the supplementary material, figures presenting following stages of one patient's treatment are presented.

Discussion

Surgical salvage is advocated as the best treatment option in terms of survival and locoregional control in patients with resectable recurrence in irradiated head and neck field [10]. As recurrent disease is typically multifocal and infiltrative, which can be undetectable in imaging or intraoperative view, it is worth to consider adjuvant tools to improve the oncological outcomes, especially in cases of uncertain margins. BT, as the method that allows the delivery of irradiation to the area where EBRT could be related to the high risk of complications and morbidity, should be placed into the treatment schemes in such cases [11–13].

The question posted in the paper concerned the feasibility of BT in tissues reconstructed with pedicle or free flaps and its potential to increase the risk of flap necrosis.

Flap survival depends on sufficient tissue perfusion. Postoperative circulatory failure requiring revision surgery and restoration of anastomosis patency still occurs in up to 28% of patients even in the most experienced hands [14, 15]. Soft tissue necrosis concerns 2 to 45% of patients treated with BT. It is noted more often in HDR (5–45%) than in PDR (2–13%) method [16–18]. In our material in one patient, peripheral necrosis of the flap was noticed. However, that distal ischemia was probably caused by incorrect reconstruction planning: too large flap in relation to feeding vessels.

In the literature, contrary data is presented concerning wound healing complication rates experienced by patients with head and neck tumors undergoing surgery with flap reconstruction followed by intraoperative or postoperative BT.

Ross et al. [19] documented the higher risk of wound complications in head and neck cancer patients treated with salvage surgery, microsurgical free flap reconstruction, and intraoperative BT (IOBT) compared with the non-IOBT group ($p < 0.01$). An overall complication rate of 38.33% was noticed in cases with an implanted bed as compared with 15.87% when IOBT was not used. The most common complication in the IOBT patients was wound dehiscence (11/60 patients; 18.33%) followed by delayed complications like carotid exposure/rupture and osteoradionecrosis (which were seen in 11.67% of patients each).

A very high complication rate for IOBT was also presented by Geiger et al. [20]. In the group of 93 patients with head and neck cancers treated with IOBT, 94% with a prior history of RT, 51.6% experienced flap complications, the most common

of which was flap dehiscence (32% of patients). The risk of developing any type of flap complication was significantly higher when mandibular plates were used (odds ratio, 3.7; $p = 0.009$). In another publication, Geiger et al. [21] compared complication rates between 55 pedicle flaps and 50 free flaps used for covering IOBT implants placed after head and neck tumor resection. An overall complication rate of 68% was noted in free flap reconstructions while 36.4% in pedicle flaps (OR = 2.9, $p = 0.037$). Moreover, in free flap reconstruction with IOBT, the need for operative revision was significantly higher than in pedicle flap group (OR = 3.5, $p = 0.048$). The authors conclude that the improved outcomes associated with pedicle flap reconstruction are related to the comparatively increased muscle bulk of pedicle flaps compared with most free flaps.

Conversely, Moscoso et al. [22] noticed no significant complications in the group of 15 patients with advanced recurrent head and neck cancers who underwent surgical resection followed by implantation of the tumor bed with Iridium-192 after-loading catheters (13 patients) or Iodine-125 seeds (two patients) and coverage of the implanted area with regional myocutaneous flaps (10 patients) and microvascular free flaps (5 patients). An overall complication rate of 33% was reported. The authors did not notice flap necrosis. In one patient, after reconstruction of posterior pharyngeal wall defect with a radial forearm, a fistula appeared.

Panchal et al. [23] also concluded that interstitial BT can be delivered in the early postoperative period following free flap reconstruction without an increase in the frequency of wound breakdown. In 9 out of 10 patients treated with wide excision of soft tissue sarcomas and head and neck carcinomas followed by microvascular free flap reconstruction and BT with Iridium-192 wires, the wounds healed uneventfully. According to some authors, such good results were determined by delayed BT (it was administered 1 to 4 weeks postoperatively) which could have increased wound strength [20].

Schiefke et al. [24] also did not observe important problems neither in the microvascular free flaps nor in the pedicle flap used to reconstruct tissue defect and cover BT applicators in the group of 13 patients with recurrent, previously irradiated head and neck cancers treated with curative approach by tumor resection and HDR-BT. All flaps healed successfully, and there was no flap loss. Only minor surgical procedures were needed in 2 patients. The authors conclude that short-term irradiation of the flap prior to the establishment of collateral blood flow does not adversely affect wound healing and flap survival. On the other hand, microvascular defect reconstruction is necessary because it provides sufficient soft tissue cover for BT. The same experience emphasizing the role of covering BT catheters with flaps which decreases the risk of complications was presented by Stafford and Dearnaley [25] and Cornes et al. [26].

In the literature, the wide variability of data concerning the influence of BT for wound healing and flaps vitality in patients with recurrent head and neck cancers can be found. Such visible discrepancy in presented results may partly be due to the variety of cases included into the studies, the diversity of treatment schemes used, the potential impact of other risk factors affecting proper healing, as well as the heterogeneity of BT application. The incidence of pedicle and free flap complications associated with IOBT reported in the literature is higher than in postoperative BT. Further investigations should be undertaken to explore this field. We are aware of the limitations of our study (small and heterogeneous group), so we state conclusions very carefully. Therefore, our preliminary results are promising, and we intend to include BT in treatment schemes in a larger group of our patients.

Conclusions

Based upon our data, pulsed-dose-rate brachytherapy seems to be a safe option that can be performed at the site of reconstruction in immediate postoperative period with minimal wound complications and with no impact on flap survival. Certainly, further clinical study based on larger patient series is needed to present statistically proven results.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethics Approval The protocol of the investigation has been approved by the Institutional Review Board of the Poznan University of Medical Sciences.

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