

# Curative Brachytherapy for Recurrent/Residual Tongue Cancer

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**Purpose:** The efficacy of curative low-dose-rate (LDR) brachytherapy for recurrent and/or residual cancer following radical operation or irradiation and posttreatment quality of life (QoL) were assessed.

**Patients and Methods:** Between January 1979 and April 2004, 88 patients who had received curative LDR brachytherapy (28 with postoperative close or positive margins, six with postoperative recurrence, six with recurrence after external-beam irradiation, and 48 with recurrent/residual cancer after curative brachytherapy) were analyzed retrospectively. Late complications were assessed based on the RTOG/EORTC late radiation morbidity score scheme.

**Results:** The 5-year relapse-free and cause-specific survival rates were 92% and 96%, respectively, in the close/positive margin group and 52% and 56%, respectively, in the postbrachytherapy recurrence or residual cancer group. The incidence of late side effects was 8% (2/26) in the close or positive margin group and 22% (4/18) in the postbrachytherapy group. The only grade 4 late complication (bone exposure) was observed in one patient in the postbrachytherapy group.

**Conclusion:** LDR brachytherapy as reirradiation for recurrent/residual tongue cancer was effective, and there was no increase in complications.

**Key Words:** Tongue cancer · Recurrent cancer · Residual cancer · Brachytherapy

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## Kurative Brachytherapie bei Rezidiv und/oder Resttumor eines Zungenkarzinoms

**Ziel:** Die Wirksamkeit einer kurativen Brachytherapie mit niedriger Dosisleistung (LDR) bei Rezidiv und/oder Resttumor nach radikaler Operation oder Bestrahlung wurde bezüglich der Lebensqualität nach Behandlung untersucht.

**Patienten und Methodik:** 88 Patienten, die zwischen Januar 1979 und April 2004 eine LDR-Brachytherapie erhalten hatten, wurden retrospektiv analysiert (28 mit knappen oder positiven Schnitträndern, sechs mit postoperativem Rezidiv, sechs mit Rezidiv nach Teletherapie sowie 48 mit Rezidiv bzw. Resttumor nach Brachytherapie). Späte Komplikationen wurden auf der Grundlage des „late radiation morbidity score scheme“ der RTOG/EORTC klassifiziert.

**Ergebnisse:** Die rezidivfreie und die tumorspezifische 5-Jahres-Überlebensrate betragen in der Gruppe mit knappen oder positiven Schnitträndern 92% und 96% sowie in der Gruppe mit Rezidiv oder Resttumor nach Brachytherapie 52% und 56%. Die Rate später Nebenwirkungen lag in der Gruppe mit Heilung/positivem Resultat bei 8% (2/26) und in der Gruppe nach Brachytherapie bei 22% (4/18). Die einzige Spätfolge des Grades 4 (Knochenfreilegung) war bei einem Patienten in der Gruppe nach Brachytherapie zu verzeichnen.

**Schlussfolgerung:** Die LDR-Brachytherapie als erneute Bestrahlung erwies sich bei Rezidiv oder Resttumor eines Zungenkarzinoms als wirksam. Es kam zu keinem Anstieg der Komplikationen.

**Schlüsselwörter:** Zungenkarzinom · Rezidiv · Resttumor · Brachytherapie

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## Introduction

Recurrence of tongue cancer is not uncommon, and patients with recurrent and/or residual tongue cancer are at risk of significant treatment-related morbidity, which can have a substantial impact on posttreatment quality of life (QoL) [2, 17]. Early research focused on psychosocial issues related to extensive surgical resection and its consequences [17]. Management options for recurrent and/or residual squamous cell carcinoma of the tongue have long been considered to be nonradiation means and external-beam irradiation (EBRT) and interstitial radiation therapy have long been considered noncurative [2, 4, 9, 20, 25].

Many advances have been made in both radiotherapy and surgical management of recurrent/residual head-and-neck cancer. Brachytherapy of primary tongue cancer has the advantage of preserving the function of the tongue and providing good posttreatment QoL [5, 12, 14, 21, 24], but there have been few reports concerning the effectiveness and complications of the curative radiotherapy for recurrent and/or residual tongue cancer [11, 17].

The purpose of this study was to assess the efficacy of curative low-dose-rate (LDR) brachytherapy for recurrent and/or residual cancer following radical operation or irradiation and posttreatment QoL. The reported series is a single-institution brachytherapy for residual and/or recurrent tongue cancer.

## Patients and Methods

Between January 1979 and April 2004, 88 patients with squamous cell carcinomas of the tongue, including 28 with close or positive margins, six with postoperative recurrence, six with recurrence after EBRT, and 48 with recurrent/residual cancer after curative brachytherapy for primary tongue cancer, were included in the analysis. The primary treatment of all patients consisted of full-course radiation therapy or curative surgery. Recurrence and residual cancer were diagnosed pathologically and/or by physical examination. Mean patient age at the start of the second course of treatment was 60 years (range 23–92 years), and there were 57 men and 31 women. At the start of curative brachytherapy for recurrent/residual tumor, 28 patients with close or positive margin had rT0 N0 cancer according to the UICC (2002) classification, 28 had rT1 N0 cancer, and the other 32 had rT2 N0 cancer. Patient records were reviewed retrospectively to assess toxicity, response, and survival since the start of curative brachytherapy for recurrent/residual tumor.

All recurrent/residual tumors were managed by LDR brachytherapy alone. In 65 patients they were treated with  $^{198}\text{Au}$  seeds, and in the other patients with  $^{226}\text{Ra}/^{137}\text{Cs}$  needles (16 patients) and/or  $^{198}\text{Ir}$  hairpins (seven patients).

The median cumulative radiation dose was 70 Gy (57–81 Gy) in 7 days. The Manchester system which is based on Paterson-Parker distribution rules was used for dose calculation. The appropriate radiation source was selected according to the clinical target volume and, as a result, the clinical target volume in the  $^{198}\text{Au}$  seed group was small, around 5 cm<sup>2</sup>, and it was 11.5 cm<sup>2</sup> in the  $^{226}\text{Ra}/^{137}\text{Cs}/^{192}\text{Ir}$  group.

As for the salvage brachytherapy, 17 close/positive margin patients were treated by  $^{198}\text{Au}$  seeds and eleven by  $^{226}\text{Ra}/^{137}\text{Cs}/^{192}\text{Ir}$  sources and received 70 Gy in 7 days (60–70 Gy in an average of 7 days). Of the patients with postoperative recurrence, four were treated by  $^{226}\text{Ra}/^{137}\text{Cs}$  and another two by  $^{198}\text{Au}$  seeds and received 70 Gy in 7 days on average. In the post-EBRT group, two patients were treated by  $^{226}\text{Ra}$  or  $^{192}\text{Ir}$  and the other four patients by  $^{198}\text{Au}$  seeds and also received 70 Gy in 7 days on average. Of the 48 patients with postbrachytherapy recurrence/residual cancer, 42 were treated with  $^{198}\text{Au}$  seeds and the other six with  $^{226}\text{Ra}/^{192}\text{Ir}$  sources and received a total dose of 65 Gy in 7 days on average (Table 1). Among these 48 patients, the intervals between the first and the second treatment ranged from 1 month to 70 months, and the median interval was 4 months. Spacers were introduced for use in brachytherapy in 1987, and they have been used in all patients undergoing postbrachytherapy for recurrent/residual tongue cancer ever since then. Spacers were also used in the groups treated with  $^{226}\text{Ra}/^{137}\text{Cs}/^{192}\text{Ir}$ .

Late complications found in and around the treated area after the disappearance of radiation mucositis and also at the last visit were defined following the RTOG/EORTC late radiation morbidity score scheme. Patients who had recurrent tumor or died within 24 months following curative brachytherapy for recurrent/residual cancer were excluded from the analysis of late complications.

The Kaplan-Meier method was used to analyze the cause-specific survival and overall survival. The final examination or date of death was used as the endpoint.

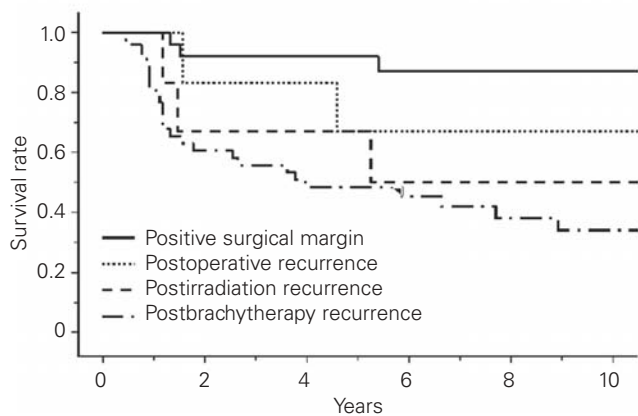
## Results

40 patients were alive, 29 patients had died of tongue cancer, and the other 19 patients had died of other diseases; the overall median follow-up period was 6 years (4 months to 26 years).

**Table 1.** Patient distribution in the salvage brachytherapy groups. EBRT: external-beam radiation therapy.

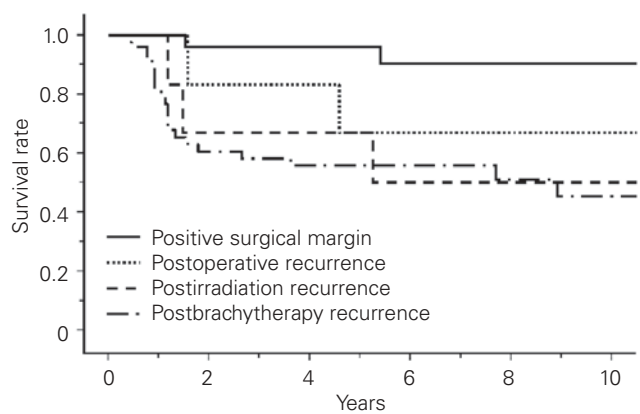
**Tabelle 1.** Patientenverteilung in den Brachytherapiegruppen. EBRT: externe Strahlentherapie.

Small sources used for salvage brachytherapy	Post operation Close/positive margin group	Recurrent tumor group	Post irradiation Post-EBRT group	Postbrachytherapy group
$^{137}\text{Cs}$ needles	1	2	–	–
$^{226}\text{Ra}$ needles	5	2	1	5
$^{192}\text{Ir}$ hairpins	5	–	1	1
$^{198}\text{Au}$ seeds	17	2	4	42



**Figure 1.** Overall survival.

**Abbildung 1.** Gesamtüberleben.



**Figure 2.** Cause-specific survival.

**Abbildung 2.** Tumorspezifisches Überleben.

The 5-year relapse-free and cause-specific survival rates were 92% and 96%, respectively, in the close/positive margin group, and 52% and 56%, respectively, in the postbrachytherapy recurrence and/or residual cancer group (Figures 1 and 2).

Local control was achieved by the second course of treatment in 86 patients, and there was residual cancer after the first brachytherapy in two of the 48 patients in the postbrachytherapy group. There were no cases of primary recurrence after the second course of treatment in 26 patients in the close/positive margin group, four in the postoperative recurrence group, two in the post-EBRT group, and 23 in the postbrachytherapy group (Table 2). A trend toward a better survival was observed in the subsets of patients in whom the interval between the end of the first and the start of the second course of treatment was > 12 months (4/7) as compared to the group with an interval of ≤ 12 months (21/41), but the difference was not statistically significant. One patient in the close/positive margin group and 18 in the postbrachytherapy group had a recurrence in a regional lymph node. There was regional lymph node metastasis in 18 of the 48 patients in the postbrachytherapy group (38%).

Side effects, such as local ulcer and bone exposure, were diagnosed in six of 48 patients who survived without local recurrence for > 2 years after reirradiation, but responded to conservative treatment and did not require surgery. The incidence of late side effects was low in the close/positive margin group (2/26 = 8%) and high in the postbrachytherapy group (4/18 = 22%). Three of the four late side effects in the postbrachytherapy cases were observed in patients treated without a spacer. Only

one patient in the postbrachytherapy group developed a grade 4 late complication (bone exposure), which, however, healed and became covered with healthy mucous membrane in response to conservative treatment without surgery (Table 3). This grade 4 late complication occurred in a patient treated without a spacer.

**Discussion**

Radiotherapy has long been considered a curative treatment modality for primary cancer of the tongue. The 5-year actuarial rate of tongue cancer tolerating a normal diet by interstitial brachytherapy is 86%, and all long-term survivors have had normal speech function [1]. Although radiotherapy has not long been considered the main treatment for recurrent and/or residual cancer of the head and neck, there are several reports

**Table 2.** Results of salvage therapy. EBRT: external-beam radiation therapy.

**Tabelle 2.** Behandlungsergebnisse. EBRT: externe Strahlentherapie.

	Close/positive margin	Recurrent tumor	Post EBRT	Post brachytherapy
Recurrence after salvage	2	2	4	23
Residual after salvage	–	0	0	2
No primary recurrence after salvage	26	4	2	23

**Table 3.** Late side effects after salvage brachytherapy. EBRT: external-beam radiation therapy.

**Tabelle 3.** Spätfolgen nach der Brachytherapie. EBRT: externe Strahlentherapie.

	Close/positive margin	Recurrent tumor	Post EBRT	Post brachytherapy
Grade 1	1		1	3
Grade 2	1			
Grade 3		1		
Grade 4				1

on the results of radiation therapy for recurrent or residual cancer of the head and neck [3, 6, 10, 11, 15, 19, 23–25]. Pomp et al. and de Crevoisier et al. reported the 5-year survival of patients with recurrent head-and-neck cancers treated by external reirradiation to be poor (< 20%) [3, 19]. The best local control rate, 48%, has been obtained in patients with recurrent tumors reirradiated with high dose, i.e.,  $\geq 50$  Gy [19]. Krull et al. reported a poor 2-year local control rate by interstitial high-dose-rate (HDR) brachytherapy for recurrent cancer (34%) [10]. Although median survival was better than generally obtained with palliative chemotherapy, the incidence and severity of late toxicity following external reirradiation are much higher than after the first course of radiation therapy [3]. Mazon et al. recommend reirradiation by brachytherapy for recurrent or new malignancies arising in a previously irradiated oropharynx, and salvage brachytherapy for oropharynx cancers that recur following external irradiation, and they obtained a 5-year local control of 60% [15].

Wang et al. observed no severe local complications after external reirradiation with  $\geq 130$  Gy for recurrent laryngeal carcinoma by using the reduced radiation portal limited to the recurrent lesion [31]. The incidence of late postbrachytherapy complications is closely related to the dose of external irradiation, the brachytherapy source used, dose rate, total dose, and use of a spacer [5, 13, 16]. The severest late complication of our curative brachytherapy for recurrent/residual cancer was bone exposure, and it healed without requiring surgery. The tongue mostly consists of muscle, and because it is more radio-resistant than the mandible, after the introduction of spacers second-look salvage brachytherapy became more widely indicated and there was no increase in late complications. HDR brachytherapy has become prevalent in the treatment of oral cancer and it is as safe as LDR brachytherapy [18, 26], but there are few studies especially on reirradiation cases like a postbrachytherapy group in this study. LDR brachytherapy may be more appropriate, because there is a greater difference in radiation tolerance between normal mucous membrane and tumor than with HDR brachytherapy [27, 28]. As for the better dose rate used for reirradiation, further studies are necessary.

Tumor should be evaluated with computed tomography (CT) and/or magnetic resonance imaging (MRI) as well as biopsy and/or by physical examination because tumor size and thickness are risk factors of local control and neck lymph node metastases [7, 22, 29, 32]. Physical examination, especially manipulation, in scheduled clinical follow-up is more useful to detect recurrent/residual cancers before they grow up. Most of recurrent/residual tumors are treated within 1 cm thick.

In the treatment of local recurrence or secondary tumors in previously irradiated area, brachytherapy is of special value [30]. Brachytherapy can be processed with minor target volume rather than external irradiation, and when a recurrent/residual lesion is located in the tongue. A minimum target volume can be selected with  $^{198}\text{Au}$  seeds, and they seem to be a

reasonable option. Median survival after brachytherapy was better than generally obtained by palliative chemotherapy alone and/or external irradiation. Interstitial radiation therapy alone can only eradicate recurrent/residual tumor of the tongue, and brachytherapy combined with external irradiation is associated with a high rate of soft-tissue and mandibular complications [8]. Many patients with recurrent head-and-neck cancer are aged and at risk of heart and lung morbidity, which are contraindications to general anesthesia for extensive operations, and the additional operation would have substantially compromised posttreatment QoL. Reirradiation for tongue cancer by brachytherapy was associated with acceptable acute toxicity and minimal late adverse effect. Full-dose curative LDR brachytherapy is feasible for patients with residual and/or recurrent tongue cancer.

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