The application of high-dose-rate brachytherapy in the treatment of postoperative floor of the mouth tumours and dosimetric comparison with modern external beam radiotherapy modalities in localization of floor of the mouth and tongue tumours

PhD thesis

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1. Introduction

Oral cavity (tongue, floor of mouth, buccal mucosa, gingiva, hard palate) squamous cell carcinomas rank as the sixth most common tumours globally. In 2020, there were 377,713 new cases reported worldwide, resulting in 177,755 deaths from this disease, placing it similarly at the 6th position among all malignancies. Men are affected 2-3 times more frequently than women. The 5-year overall survival rate is 60 %. In Hungary, in 2020, 3,015 new cases were diagnosed, with 1,628 fatalities, ranking it as the 4th most common in incidence and the 6th highest in mortality globally. Unfortunately, floor of mouth carcinomas represent approximately 28% of all oral cavity lesions, with the majority being diagnosed at advanced stages. In Hungary, 97 new cases with this diagnosis were confirmed in 2020.

The occurrence of oral tumours is generally more prevalent in developing countries, with factors such as alcohol and tobacco use, poor oral hygiene, excessive sunlight exposure in lip malignancies, and immunosuppression following kidney and liver transplants playing significant roles in their development. Surgical intervention primarily drives their management, while smaller lesions can be effectively treated with laser resection, cryotherapy, or radiotherapy with comparable outcomes to surgery. In advanced cases, due to the increasing incidence of neck metastases, postoperative irradiation +/- chemotherapy following surgery is recommended, while for unresectable tumours, the combination of radiotherapy (RT) and anticancer drugs proves most effective.

Currently, the most advanced and routinely utilized radiation technique for oral cancer treatment is intensity-modulated radiation therapy (IMRT), enabling precise tracking of the three-dimensional shape of the target volume by the reference isodose surface using a multileaf collimator (MLC), significantly reducing exposure to critical organs. An enhanced version of this approach is volumetric-modulated arc therapy (VMAT) or rotational IMRT, enhancing the precise irradiation of highly intricate target volumes like in head and neck tumour regions, further reducing exposure to critical organs.

For smaller target volumes in external irradiation, a recent innovation is stereotactic radiotherapy (SRT), characterized by techniques such as the Cyberknife (CK) approach. This method aims to deliver the highest dose feasible to the tumour using multiple non-coplanar beams, minimizing exposure to surrounding healthy tissues.

However, maximal external radiation dose delivery to the target volume (the tumour or its site post-surgery) generally leads to unnecessary radiation exposure of critical organs in the vicinity (salivary glands, jawbones, masticatory muscles, etc.), resulting in increased occurrence of side effects in normal tissues (xerostomia, osteoradionecrosis, fibrosis, trismus, etc.). Even though IMRT significantly reduces radiation-induced toxicity, brachytherapy (BT) remains an extremely advantageous method in managing malignant oral lesions due to its potential for dose escalation in this localization, minimizing radiation-related normal tissue damage during the short treatment period by placing radioactive sources directly in or near the tumour.

Until the end of the 20th century, low-dose-rate (LDR) BT served as the gold standard, backed by extensive literature based on years of experience. Presently, LDR BT is being replaced by high-dose-rate (HDR) and pulse-dose-rate (PDR) BT in numerous institutions globally, allowing for optimal dose distribution by varying the dwell time of the remote-controlled radiation source as opposed to LDR. HDR BT proved to be comparable to LDR BT in terms of local tumour control and complications. In the management of oral cancer, BT predominantly plays a vital role in the initial stages of lip, buccal mucosa, hard palate, floor of mouth, and tongue tumours. In advanced cases, it can also be used as an adjunct to external radiotherapy.

For this study, I utilized significant, statistically analyzed articles and studies from the past 30-40 years related to a larger cohort of patients in order to write the thesis. Employing the MEDLINE® database (via PubMed) and searching based on keywords such as "BT, HDR, VMAT, CK, and oral (floor of mouth) tumours," I conducted the literature search.

By focusing on the exclusive role of HDR BT in a retrospective study of postoperative radiotherapy for floor of mouth carcinomas, I aimed to investigate its effectiveness compared to surgery alone, exclusive radiotherapy, and LDR techniques. Additionally, the dosimetric comparison of this therapeutic approach with modern external radiotherapy techniques in localizations of the tongue and floor of the mouth was of interest.

2. Objevtives

To conduct a detailed discussion of the following topic groups related to the study of interstitial HDR brachytherapy applied postoperatively for tongue base tumours, and to draw conclusions:

1. Examination of the effectiveness of postoperative HDR brachytherapy in pT1-2N0 stage tongue base tumours.

2. Comparison of results - based on the literature - with postoperative LDR and PDR techniques, sole surgical treatment, and sole percutan postoperative radiotherapy.
3. Analysis of the local and locoregional tumour control, as well as prognostic factors influencing tumour-specific and overall survival, in tongue base cancer patients treated with postoperative brachytherapy.
4. Comparative dosimetric analysis of modern external beam radiotherapy modalities: VMAT and CK, as well as HDR brachytherapy technique, in terms of organs at risk for tongue and tongue base tumours operated upon.

3. Material and methods

Since 1992, high-dose-rate (HDR) brachytherapy has been employed at the National Institute of Oncology's radiotherapy department in the radiation treatment of malignancies of the oral cavity, mouth, and nasal cavity. This study retrospectively analyzes the therapeutic and survival data of 44 patients with floor of mouth cancer who were treated with postoperative brachytherapy between January 1998 and December 2017, as well as compares the dosimetry of tongue (n=14) and floor of mouth (n=6) tumours treated with postoperative brachytherapy using EBRT techniques (VMAT, CK) between March 2013 and August 2022. The study was conducted in full compliance with the Helsinki Declaration and ethical norms related to human experimentation in Hungary. Both the retrospective and dosimetric analyses involved selecting participants based on the following criteria:

- tumours sized pT1-2(3) pN0-1 according to the UICC TNM system /7th edition/(Table 1.), absence of distant metastasis and other malignant processes,

- histologically confirmed and surgically treated floor of mouth/tongue tumours,

- exclusive postoperative HDR interstitial brachytherapy as the type of radiotherapy,

- no prior therapeutic irradiation in the region,

- patients with regular follow-up, including necessary clinical and laboratory tests (complete blood count, sedimentation rate, liver function, kidney function), chest X-ray, abdominal ultrasound, diagnostic computer tomography (CT) and/or magnetic resonance imaging (MRI) of the oral cavity-neck region, possibly Positron Emission Tomography, and if needed, scintigraphy for clarifying bone pain causes.

In line with the study objectives, two research topics were distinguished:

Group A: Postoperative HDR brachytherapy of floor of mouth cancer patients (n=44)

Group B: Dosimetric comparison of postoperative brachytherapy of tongue and floor of mouth cancers within a model study framework using modern external irradiation methods (n=20)

The type of postoperative radiotherapy (brachytherapy or EBRT) was determined by the oncoteam and the treating physician team, but ultimately, after detailed information, the patient could decide on the type of postoperative radiation therapy.

3.1. *Postoperative brachytherapy in patients with squamous cell carcinoma of the floor of the mouth (Group A)*

Between January 1998 and December 2017, 44 patients with pT1-3pN0-1M0 squamous cell carcinoma located in the floor of the mouth were treated postoperatively exclusively with interstitial high-dose rate brachytherapy.

During surgery, exclusive primary tumour excision was performed in 12 cases (27%). In these patients, elective neck dissection was not performed due to the low risk of cervical metastasis (tumour size < 3 cm; invasion depth < 5 mm; well-differentiated grade 1-2; absence of lymphatic and perineural invasion, clinically N0 status /n=11/), as well as due to frail physical condition, older age, and clinically negative neck status (n=1). Ipsilateral (n=30; 68%) or bilateral (n=2; 5%) neck dissection was performed in 32 cases. Levels I-IV dissection was carried out in T3 and/or N1 status, while levels I-III dissection was conducted in T1-2 N0 status. Among the patients with pT3 status (n=5), no regional metastasis was detected.

The average time between surgery and the first fraction of interstitial HDR brachytherapy was 42 days (range 35-71). Flexible plastic catheters were used in 30 cases (68%), while rigid metal needles were used in 14 cases (32%). The implantation was performed in the operating room under general anesthesia, through a submental approach. Trocars were used for inserting the plastic catheters, pulled through the lumen of these devices, and then the trocars were removed. The ends of the catheters were secured submentally with plastic buttons and on the surface of the tongue.

The determination of the target volume (tumour bed + 5 mm, planning target volume: PTV) was aided by the primary CT/MRI imaging, as well as palpation of the tumour bed. The Paris system rules were applied to the geometry of implant placement. The number of rigid metal needles/catheters and the distance between them (usually 1-2 cm) were determined considering the extent of the target volume.

The average dose of brachytherapy was 26 Gy (range 10-48 Gy), the average EQD2(10) was 36 Gy (16.7-56.3 Gy), and the average EQD2(3) was 46 Gy (range 26-72 Gy). Fourteen patients received a single fraction of 10-14 Gy with rigid needles (average number 2, range 2-4). After 2000, with one exception (1x14 Gy), we transitioned to fractionated delivery of HDR brachytherapy using non-looped plastic catheters (average number 4, range 2-9). With this technique, an average dose of 36 Gy (range 14-48 Gy) was delivered in 1-15 fractions (average 10), 3-6 Gy per fraction (average 4 Gy), twice daily, with at least 6 hours apart . Mouthguards were not used during treatment.

Our institutional protocol mandated the initial surveillance evaluation at 8-10 weeks following brachytherapy application in the form of CT or MRI, supplemented by a physical examination. Subsequently, we conducted physical examinations every 3 months and repeated the CT or MRI every 6 months during the first two years. Chest X-rays and laboratory tests were performed annually. The survival time was calculated from the last fraction of HDR brachytherapy. Acute and late side effects were classified according to the recommendations of the Radiation Therapy Oncology Group (RTOG) / European Organisation for Research and Treatment of Cancer (EORTC).

3.2 *Dosimetric comparison of postoperative brachytherapy for tongue and floor of mouth cancer with modern external radiation methods (group B)*

At our institution, a model study included 20 patients treated between January 2016 and December 2021 with T1-3N0 stage disease who underwent postoperative brachytherapy and received the same total dose and fractionation, either for tongue or floor of mouth cancer. All of them underwent tumour resection and either unilateral (85%, 17/20) or bilateral (15%, 3/20) selective neck dissection following negative neck staging. No metastatic lymph nodes were confirmed on pathology. To justify local postoperative brachytherapy, one of the following criteria had to be met: pT3 tumour, surgical margin ≤2 mm, lymphatic vessel infiltration, or perineural invasion. Based on histopathological analysis, 20% of the lesions were pT3 in size (TNM 8), 85% had surgical margins of ≤2 mm, and 40% exhibited perineural spread. Treatments were delivered using HDR afterloader with Iridium-192 isotope (Flexitron, Elekta Brachytherapy, Veenendaal, The Netherlands) after placement of flexible catheters (median 6, range 6-8) into the tumour bed. Insertion was performed submentally using trocars in the operating room under general anesthesia. The average time between interstitial brachytherapy implantation and surgery was 54 days (range: 42-81 days). The total dose of brachytherapy was 45 Gy, delivered in 3 Gy fractions twice daily with a 6-hour interval (15x3 Gy).

3.3. *Comparison of plans*

The same dose and fractionation (15 x 3 Gy) were applied in all three techniques. Parameters calculated from the dose-volume histogram were used for plan comparison. The volume irradiated with the prescribed dose for the PTV (V100) was used to describe the target volume. Objective comparison was based on the same target volume coverage (V100=90%) for all three techniques. Thus, differences found among the plans were due solely to the characteristics of the irradiation techniques. A small volume of high-dose radiation was applied to characterize unintentional irradiation of OARs. The Dxcm3 represents the dose to the most exposed x cm3 portion of an organ (mandible, parotid gland). D2cm3 and D0.1cm3 values were calculated and compared for all OARs. The conformity of dose distributions was quantified using the conformal index (COIN), which takes into account both the target coverage and the unnecessary irradiation of normal tissues. Its maximum value is 1, and the higher the value, the more conformal the dose distribution. Dose homogeneity was characterized with the dose nonuniformity ratio (DNR) in BT plans, and homogeneity index (HI) in the VMAT and CK plans. DNR is the ratio of volume irradiated by 1.5 times the PD to volume irradiated by the PD. The HI was calculated according to recommendation of ICRU (International Commission on Radiation Units and Measurements) Report 83.21 By definition, HI = (D2%-D98%)/D50%.

4. RESULTS

4.1. *The Group A*

The median follow-up time for surviving patients was 122 months (range: 14-236 months). No patient was lost during this period. Local recurrence occurred in 4 patients (9%), regional metastasis in 12 patients (27%), and distant (lung) metastasis in 1 patient (2%). The salvage treatments were as follows: surgery in six cases (14%), external beam radiation therapy in eight cases (18%), surgery and external beam radiation therapy (EBRT) in two cases (5%), and palliative chemotherapy in four cases (9%). Among patients who experienced regional recurrence (n=12), as part of salvage care, surgery was performed in four cases, EBRT in four cases, surgery and external RT in two cases, and chemotherapy in two cases as well. Unfortunately, all 16 patients who received salvage treatment later died due to locoregional recurrence. Among other causes of death, second primary tumours (larynx, thyroid, esophagus, and rectum) were found in 4 patients (9%), while concomitant illness was listed in 10 patients (23%). The 5-year and 10-year probabilities of LC, RC, OS, and DSS were 89% and 89% (T1 95%, T2 82%, T3 80%), 73% and 67% (T1 68%, T2 63%, T3 80%), 52% and 32% (T1 40%, T2 27%, T3 0%), and 66% and 54% (T1 59%, T2 53%, T3 0%) (Figure 5).

The univariate analysis of prognostic factors confirmed the significant effect of lymphovascular invasion on 10-year RC (80% vs. 40%, p =0.0062) (Figure 6), DSS (66% vs. 31%, p = 0.0056), and OS (41% vs. 14%, p = 0.0325). In cases of neck recurrence (n = 12), the primary tumour histopathology revealed lymphatic invasion in 8 patients. Among the 12 patients treated without elective neck dissection, regional recurrence occurred in three cases (25%). Only one patient showed lymphovascular invasion in histopathology, but due to initial negative neck staging, advanced age (82 years), and poor general condition, elective neck surgery or neck EBRT was not carried out on them.

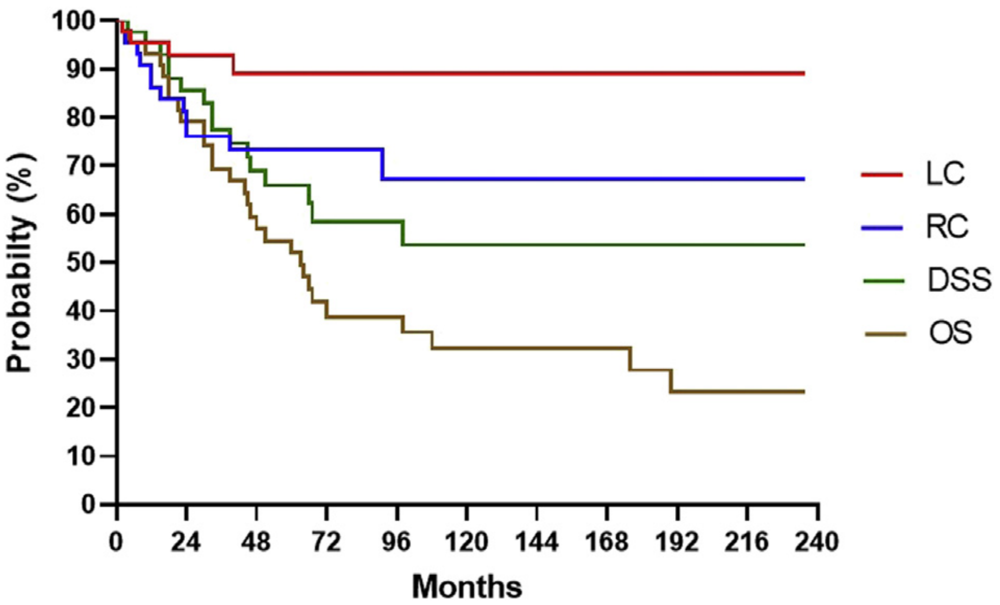

Figure 5. Local tumour control (LC), regional tumour control (RC), disease specific survival (DSS), and overall survival (OS). *(Ferenczi Ö., 2021)*

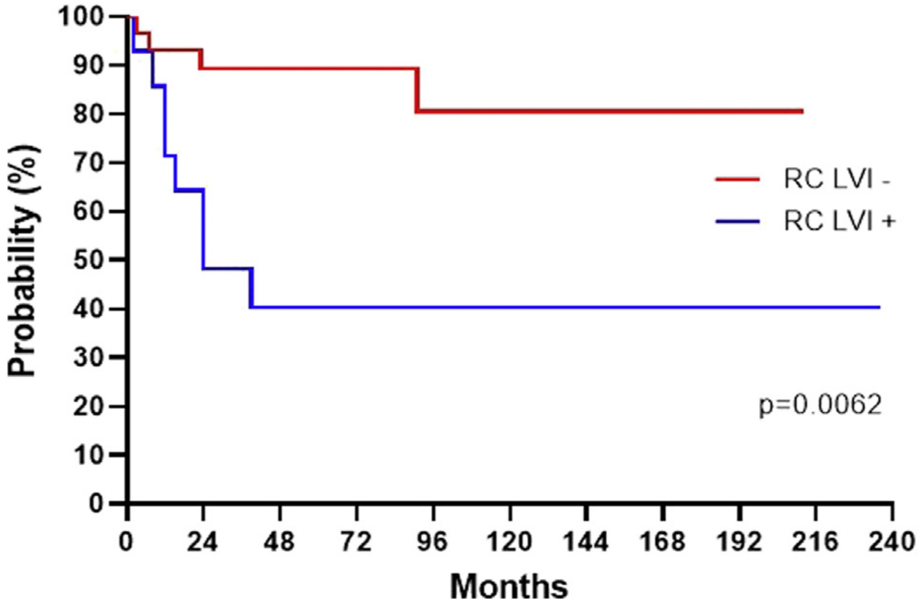

Figure 6. Regional tumour control (RC) in accordance with lymphovascular invasion (LVI -/+). *(Ferenczi Ö., 2021)*

The recurrence in the neck had a significantly negative impact on the 10-year DSS (81% vs. 0%, p<0.0001) and OS (46% vs. 0%, p<0.0001). In the multivariable analysis, the neck recurrence remained an independent prognostic factor for both DSS (p<0.0001) and OS (p=0.0001). Factors such as age (threshold 50 years), gender, perineural invasion, grade, total EQD2 biologically effective dose (with cutoffs at 35 Gy and 45 Gy), number of fractions (single vs. multiple), surgical margin (positive, ≤2 mm, >2 mm), tumour thickness (<, ≥5 mm), time between surgery and HDR brachytherapy did not influence the survival parameters.

Brachytherapy induced local mucositis of grade 1, 2, and 3 in 11 (25%), 28 (64%), and 5 (11%) cases, respectively. Bacterial infection occurred in 8 patients (18%), while fungal infection was seen in 9 patients (20%), all of whom responded to antibiotic and/or antifungal treatment. Severe (grade 4) side effects, such as soft tissue necrosis, occurred in four cases (9%) at 4 to 8 months (average 6 months) post-brachytherapy, but conservative management led to patient recovery. In these cases, the EQD2(3) was 59.7 Gy (7x5.2 Gy/n = 1, 7x5.4 Gy/n = 2, 9x5 Gy/n = 1) (Table 5). The average time to healing of the necrosis was 4 months (range 3-5 months). Only one patient required percutaneous endoscopic gastrostomy for nutrition. Osteoradionecrosis (ORN) did not occur in any case. The average D2cm3(%) for the mandible was 57.7% (range 39.9-73.1%), and the D2cm3(Gy) was 2 Gy (range 1.6-2.2 Gy). Long-term toxicities such as xerostomia, swallowing difficulties, and neck fibrosis did not occur (except in the surgically treated neck).

4.2 *The Group B*

The dose coverage of the target volume was 90.0% in all modalities due to the identical dose prescription (V100=90%). Figure 7. illustrates the representative dose distributions of the three examined techniques. It is evident that the target volume was adequately irradiated in all cases, but significant differences can be observed in the volumes irradiated with doses corresponding to the middle and lower isodose values (<70%). In the brachytherapy plan, these volumes were the smallest, particularly in regions close to the target volume. Table 5. presents the dosimetric data related to the planning target volume (PTV). Due to the safety margins employed in the volumetric modulated arc therapy (VMAT) and CyberKnife (CK) plans, the largest volume was observed in VMAT, whereas the smallest was in the brachytherapy plan.

The plans of EBRT were more conformal compared to brachytherapy. The most conformal plans were found in the CK cases, likely due to the presence of many non-coplanar beams. However, the VMAT plans were more homogeneous than the CK plans (homogeneity index: 0.09 vs. 0.20). It is evident that the homogeneity is much poorer with brachytherapy, and comparison with EBRT is not relevant. Table 6. displays the quantitative dosimetric parameters of the organs at risk (OARs). The dose to the jaw was the lowest with brachytherapy application (average D2cm3: 47.4%, $p<0.001$) compared to the other modalities: VMAT (92.2%) and CK (68.4%).

Regarding the salivary glands, the CK technique resulted in the lowest dose on both ipsilateral and contralateral sides (i.e., parotid gland, contralateral parotid gland, and contralateral submandibular gland - CK average D2cm3: 2.3% ($p<0.001$), 1.5% ($p<0.001$), 3.6% ($p<0.001$) vs. BT: 4.8%, 3.5%, 7.3% vs. VMAT: 7.3%, 6.8%, 9.0%) (Table 5). Similar results were obtained when comparing the D0.1cm3 values. The data in Table 5 unequivocally show that among the three techniques, VMAT resulted in the highest dose to the protected organs. Figures 8. and 9. graphically compare the D2cm3 values for the jaw and parotid gland.

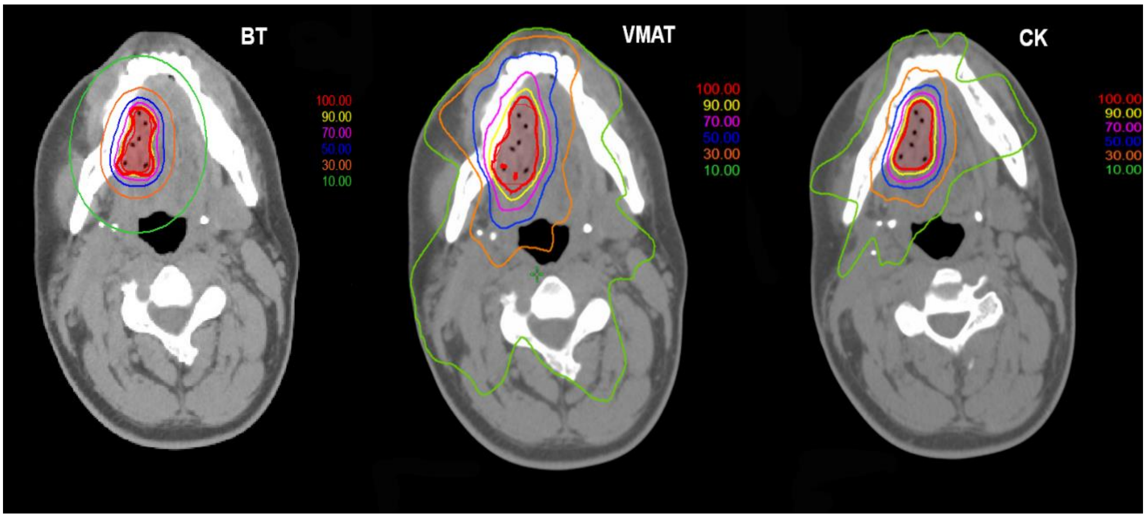

Figure 7. Representative dose distributions in a brachytherapy (BT), a volumetric modulated arc therapy (VMAT) and a Cyberknife (CK) plan. *(Ferenczi Ö., 2023)*

Table 5. Mean dosimetic parameters of PTV with ranges *(Ferenczi Ö., 2023)*

	BT	VMAT	CK	p-value*	BT vs. VMAT**	BT vs. CK**	VMAT vs. CK**
V_{PTV} (cm^3)	12.5 (2.6-21.5)	26.5 (7.7-42.6)	17.5 (5.6-33.6)	<0.001	<0.001	0.5553	0.0043
COIN	0.62 (0.48-0.80)	0.84 (0.78-0.87)	0.86 (0.79-0.93)	<0.001	<0.001	<0.001	0.5480
HI	DNR=0.38 (0.30-0.50)	0.09 (0.05 - 0.10)	0.20 (0.17-0.20)	na.	na.	na.	<0.001

Abbreviations: PTV, planning target volume; BT, brachytherapy; VMAT, volumetric modulated arc therapy; CK, Cyberknife; DNR, dose non-uniformity ratio, COIN, conformal index; HI, homogenity index, V_{PTV} = volume of the PTV

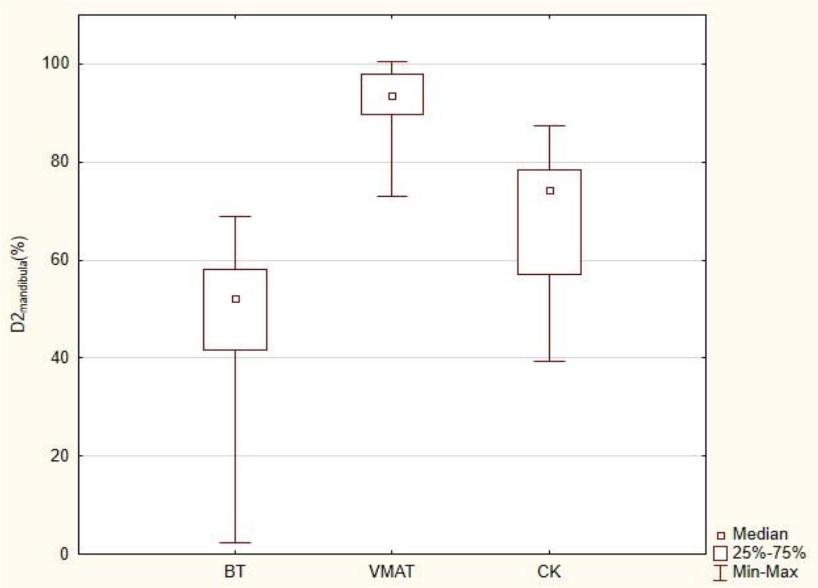

Figure 8. Mean dose in % to the most exposed 2 cm^3 volume of the mandible

Abbreviations: BT = brachytherapy; VMAT = volumetric modulated arc therapy; CK = Cyberknife; *(Ferenczi Ö., 2023)*

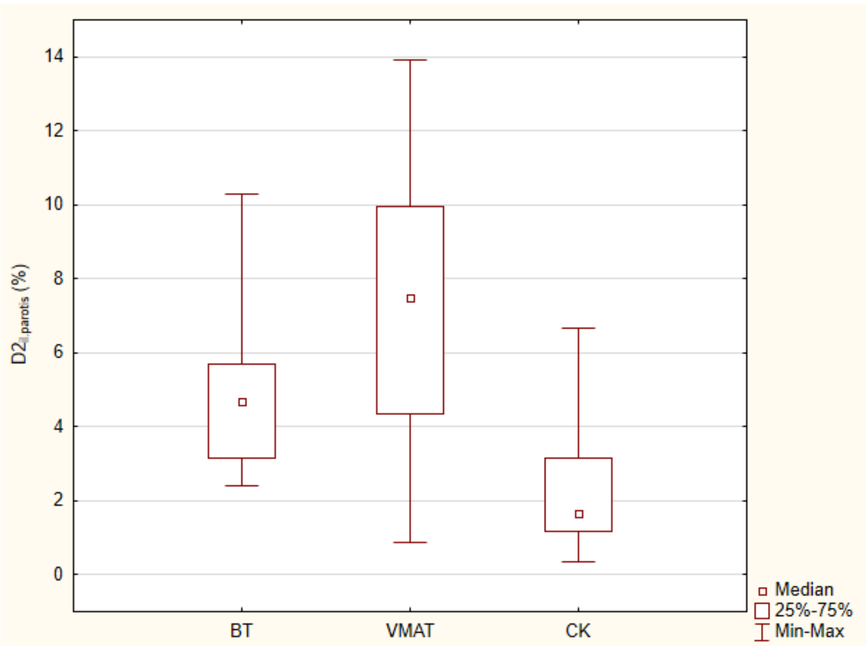

Figure 9. Mean dose to the most exposed 2 cm^3 volume of the ipsilateral parotid

Abbreviations: BT = brachytherapy; VMAT = volumetric modulated arc therapy; CK = Cyberknife; *(Ferenczi Ö., 2023)*

Table 6. Mean dosimetric parameters of OARs with ranges (*Friedman ANOVA **LSD post hoc test NS: non-significant) *(Ferenczi Ö., 2023)*

		BT	VMAT	CK	p-value*	**BT vs. VMAT****	**BT vs. CK****	**VMAT vs. CK****
mandible	D2 (%)	47.4 (29.2-73.4)	92.2 (73.1-100.4)	68.4 (39.3-87.3)	<0.001	<0.001	<0.001	<0.001
	D0.1 (%)	73.9 (1.7-93.9)	101.8 (97.1-103.9)	92.3 (72.7-100.7)	<0.001	<0.001	<0.001	NS
Il. parotid	D2 (%)	4.8 (2.5-11.9)	7.3 (0.9-13.9)	2.3 (0.3-6.7)	<0.001	0.0011	NS	<0.001
	D0.1 (%)	6.7 (3.5-19.0)	13.8 (3.7-25.0)	5.1 (0.3-12.3)	<0.001	<0.001	NS	<0.001
Cl. parotid	D2 (%)	3.5 (0.0-7.6)	6.8 (0.6-15.8)	1.5 (0.0-4.7)	<0.001	0.0018	NS	<0.001
	D0.1 (%)	4.9 (0.0-11.9)	10.9 (0.9-20.2)	3.3 (0.3-14.0)	<0.001	0.0105	NS	0.0020
Cl. submand	D2 (%)	7.3 (3.9-16.3)	9.0 (0.8-17.7)	3.6 (2.0-6.0)	0.0098	NS	0.0198	0.0016
	D0.1 (%)	9.4 (6.2-21.4)	14.3 (2.1-23.1)	5.6 (3.0-11.3)	0.0098	NS	0.0146	<0.001

Abbreviations: BT = brachytherapy; VMAT = volumetric modulated arc therapy; CK = Cyberknife; PTV = planning target volume; il. parotid = ipsilateral parotid gland; cl. parotid = contralateral parotid gland; cl. submand = contralateral submandibular gland; DX = dose to the most exposed X cm^3 volume

5. Conclusion

This study presents data on high dose rate (HDR) brachytherapy about solitary postoperative BT for floor of mouth cancers for the first time. Based on the analysis, solitary HDR BT is a suitable method for postoperative radiation treatment of malignant T1-2N0-1 stage floor of mouth tumours, in conjunction with appropriate surgical treatment of the neck. The results are comparable and similar to those of solitary surgical and radiation treatments reported in the literature. However, it is important to highlight that in cases of close (<5 mm) or positive surgical margins, the advantages of postoperative radiation therapy are always observed, demonstrating the superiority of BT over external beam radiation therapy (EBRT). Data from limited and small-scale postoperative low dose rate (LDR) studies are comparable and draw attention to the enhancing effect of postoperative BT on local tumour control, which can counterbalance the negative impact of positive or close resection margins, as opposed to exclusive surgical treatment. The risk of severe complications is low with the HDR method.

Univariate analysis of prognostic factors confirmed the significant negative prognostic impact of lymphovascular invasion on recurrence-free survival, disease-specific survival, and overall survival, as well as on neck recurrence and distant metastases. Therefore, neck radiation following elective neck dissection should still be considered in cases of lymphovascular invasion, alongside solitary postoperative BT, to reduce neck recurrences.

This is the first study in the literature to perform dosimetric comparisons of volumetric modulated arc therapy (VMAT), CyberKnife (CK), and HDR BT techniques with respect to critical organs in head and neck cancers, specifically in operated tongue and floor of mouth tumours. It was observed that the dose received by the jaw was most favorable with BT, while CK resulted in the lowest dose to the salivary glands (parotid and submandibular glands). The highest dose to critical organs was observed with VMAT. These findings reinforce that despite being an invasive technique, BT has clear dosimetric benefits in the treatment of oral cavity tumours and is worth considering in radiation therapy, not only as definitive treatment but also postoperatively. The application of CK in the head and neck region requires further investigation.

6. Bibliography of the candidate's publications

List of publications on the topic of the dissertation:

English-language peer-reviewed publications:

Ferenczi Ö, Major T, Akiyama H. (2020) Results of postoperative interstitial brachytherapy of resectable floor of mouth tumors. Brachytherapy Journal, 20(2):376-382

IF: 1.9

Ferenczi Ö, Major T, Fröhlich G. (2023) Dosimetric comparison of postoperative interstitial high-dose-rate brachytherapy and modern external beam radiotherapy modalities in tongue and floor of the mouth tumours in terms of doses to critical organs, Radiol Oncol. 57(4):516-523

IF: 2.4

Hungarian-language peer-reviewed publications:

Ferenczi Ö, Major, T, Takácsi-Nagy Z. (2021) A brachytherapia szerepe az ajak-szájüregi daganatok kuratív ellátásában = The role of brachytherapy in the curative treatment of oral cavity tumors, Orv Hetil. 12:162(37):1471-1479

IF: 0.7

The cumulative impact factor of publications on the topic of the dissertation: 5.0

Peer-reviewed publications closely related to the topic of the dissertation:

Takácsi-Nagy Z, Ferenczi Ö, Major T. (2022) Results of sole postoperative interstitial, high-dose-rate brachytherapy of T1-2 tongue tumours. Strahlenther Onkol, 198: 812-819

IF: 3.1

Akiyama H, Pesznyák C, Béla D, Ferenczi Ö. (2018) Image guided high-dose-rate brachytherapy versus volumetric modulated arc therapy for head and neck cancer: A comparative analysis of dosimetry for target volume and organs at risk. Radiol Oncol, 52: 461-467

IF: 2.4

Other publications on the treatment of head and neck cancer:

Mónika Révész, Ferenc Oberna, András Slezák, Erika Tóth, Örs Ferenczi (2024). EZH2 Expression in Head-and-Neck Squamous Cell Cancer in Young Patients. Int. J. Mol. Sci. 25(10), 5250

IF: 4.9

Mónika Révész, Ferenc Oberna, András Slezák, Örs Ferenczi (2023). The characteristics of head and neck squamous cell cancer in young adults: A retrospective single-center study. Pathol Oncol Res. 24:29:1611123.

IF: 2.3

Total cumulative impact factor of the author of the dissertation: 17.7