EVALUATION OF SOURCE LOADING POSITION IN HDR BRACHYTHERAPY DOSE CALCULATION FOR PATIENTS WITH ORAL TONGUE CANCER.

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by

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Dissertation submitted in partial fulfilment
of the requirements of the degree of
Bachelor of Medical Radiation (Honours)

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CERTIFICATE

This is to certify that the dissertation entitled Evaluation of Source Loading Position in HDR Brachytherapy Dose Calculation for Patients with Oral Tongue Cancer is the bona fide record of research work done by Ms. Mathilda Roshini A/P Britonathan during the period from October 2024 to June 2025 under my supervision. I have read this dissertation and that in my opinion it confirms the acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation to be submitted in partial fulfilment for the Degree of Bachelor of Health Sciences (Honours) (Medical Radiation).

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DECLARATION

I hereby declare that this dissertation is the result of my own investigations, except where otherwise stated and duly acknowledged. I also declare that it has not been previously or concurrently submitted as a whole for any other degrees at Universiti Sains Malaysia or other institutions. I grant Universiti Sains Malaysia the right to use the dissertation for teaching, research and promotional purposes.

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MATHILDA BRITONATHAN

Date: …………………

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LIST OF ABBREVIATIONS

AAPM	American Association of Physicist in Medicine
ABS	American Brachytherapy Society
BD	Basal Dose Rate
BT	Brachytherapy
CT	Computed Tomography
CTV	Clinical Target Volume
DFS	Disease-free survival
DNA	Deoxyribonucleic Acid
DVH	Dose Volume Histogram
EBRT	External Beam Radiotherapy
EBT	Electronic Beam Radiotherapy
GTV	Gross Tumor Volume
HDR	High dose rate
HDR ISBT	High dose rate interstitial brachytherapy
HPV	Human papillomavirus
HRCTV	High-risk clinical target volume
ICRU	International Commission on Radiation Units and Measurements
IMRT	Intensity Modulated Radiation Therapy
ISBT	Interstitial Brachytherapy
LDR	Low dose rate
MDR	Medium dose rate
MRI	Magnetic Resonance Imaging
OAR	Organ at risk

ORN	Osteoradionecrosis
OTSCC	Oral Tongue Squamous Cell Carcinoma
PCM	Pharyngeal Constrictor Muscle
PDR	Pulsed dose rate
PGO	Point Graphical Optimization
PTV	Planning Target Volume
QOL	Quality of Life
ROI	Region of Interest
RT	Radiotherapy
SCC	Squamous Cell Carcinoma
SMG	Submandibular gland
UICC	Union for International Cancer Control
VMAT	Volumetric Modulated Therapy

LIST OF SYMBOLS

Gy	Gray
cm	Centimeter
mm	Millimeter
$V_{100\%}$	% volume of target receiving 100% of the prescribed dose
$V_{200\%}$	% volume of target receiving 200% of the prescribed dose
D_{90}	Dose received by 90% of the target volume
D_{2cc}	Minimum dose received by the most irradiated 2 cubic centimeters
$D_{0.5cc}$	Minimum dose received by the most irradiated 0.5 cubic centimeters
$D_{0.2cc}$	Minimum dose received by the most irradiated 0.2cubic centimeters
$cGy \cdot h^{-1} \cdot U^{-1}$	Dose rate constant – the dose rate in cGy per hour per unit air kerma strength (U). Commonly used in brachytherapy to specify the source strength of isotopes like Ir-192.

LIST OF APPENDICES

ABSTRAK

Kesan dosimetrik daripada enam strategi pengaktifan dwell yang berbeza dalam brakiterapi interstisial kadar dos tinggi (HDR-ISBT) bagi karsinoma skuamos lidah (OTSCC) telah dianalisis secara retrospektif melibatkan dua puluh pesakit. Pelan rawatan dijana menggunakan Sistem Perancangan Rawatan Oncentra (TPS) dengan konfigurasi pemuatan sumber berbeza: pengaktifan awal (dwell pada setiap 0.25 cm secara seragam), Autoaktivasi yang dijana secara automatik oleh sistem, penjarakan tetap 0.50 cm, 0.75 cm dan 1.00 cm, serta corak Zig-zag yang menggunakan pola selang-seli antara kateter. Parameter dosimetrik yang dinilai merangkumi D90, V100% dan V200% bagi liputan tumor, serta D0.2cc dan D2cc bagi organ berisiko (OAR) seperti mandibula, otot konstriktor faring (PCM), dan kelenjar submandibular kanan dan kiri (SMG). Dos permukaan juga dianalisis sebagai indikator potensi ketoksikan mukosa. Analisis statistik dijalankan menggunakan SPSS versi 29. Ujian kenormalan diikuti dengan ujian Friedman dan Wilcoxon Signed-Rank, serta ANOVA ukuran berulang mengikut kesesuaian. Strategi pengaktifan dwell 0.50 cm menunjukkan profil dosimetrik paling optimum, dengan purata dos permukaan terendah (0.59 Gy) dan dos D0.2cc kepada mandibula (1.56 Gy), sambil mengekalkan liputan tumor yang mencukupi (purata D90: 5.17 Gy; V100%: 99.64%). Walaupun pelan awal memberikan D90 tertinggi (5.82 Gy), ia turut menghasilkan peningkatan dos kepada permukaan dan OAR. Corak Zig-zag memberikan perlindungan OAR yang setara dengan pola 0.50 cm tetapi dengan variabiliti antara pesakit yang lebih tinggi. Penjarakan dwell yang lebih luas (0.75 cm dan 1.00 cm) tidak meningkatkan liputan tumor dan dikaitkan dengan peningkatan dos kepada tisu normal sekitar. Pengurangan dos yang signifikan secara statistik diperhatikan bagi mandibula dan PCM apabila menggunakan konfigurasi dwell yang lebih rapat ($p < 0.05$). Pemilihan

posisi dwell memberi kesan ketara terhadap taburan dos dalam brakiterapi HDR untuk kanser lidah. Dalam kalangan strategi yang dinilai, jarak 0.50 cm menunjukkan keseimbangan terbaik antara keberkesanan rawatan tumor dan perlindungan tisu normal, sekali gus menyokong penggunaannya sebagai pola pemuatan sumber yang optimum dalam perancangan klinikal.

ABSTRACT

The dosimetric impact of six different dwell activation strategies in high-dose-rate (HDR) interstitial brachytherapy for oral tongue squamous cell carcinoma (OTSCC) was retrospectively investigated in twenty patients. Treatment plans were generated using Oncentra Treatment Planning System (TPS) with varying source loading configurations: Initial activation (uniform 0.25 cm spacing), system-optimized Autoactivation, fixed spacings of 0.50 cm, 0.75 cm, and 1.00 cm, and an alternating Zig-zag pattern. Dosimetric parameters assessed included D90, V100%, and V200% for target volume coverage, and D0.2cc and D2cc for organs at risk (OARs), specifically the mandible, pharyngeal constrictor muscles (PCM), and right and left submandibular glands (SMGs). Surface dose was also evaluated to estimate mucosal toxicity risk. All data were analyzed using SPSS version 29. Normality tests were followed by Friedman and Wilcoxon signed-rank tests, as well as repeated measures ANOVA where appropriate. The 0.50 cm dwell activation strategy demonstrated the most favorable dosimetric profile, yielding the lowest mean surface dose (0.59 Gy) and mandible D0.2cc (1.56 Gy), while maintaining adequate tumor coverage (mean D90: 5.17 Gy; V100%: 99.64%). Although the Initial plan resulted in the highest D90 (5.82 Gy), it was associated with elevated surface and OAR doses. The Zig-zag pattern achieved comparable OAR sparing to the 0.50 cm configuration but exhibited higher inter-patient variability. Wider activation intervals (0.75 cm and 1.00 cm) did not improve tumor coverage and were linked to increased dose exposure to adjacent healthy structures. Statistically significant dose reductions were observed for the mandible and PCM using tighter dwell configurations ($p < 0.05$). Dwell position selection significantly influenced dose distribution in HDR tongue brachytherapy. Among the strategies evaluated, the 0.50 cm dwell spacing provided the

most favorable balance between target coverage and OAR sparing, supporting its consideration as an optimal source loading pattern in clinical planning.

CHAPTER 1

INTRODUCTION

1.1 Background of Study

Oral cancer comprises malignancies originating in different anatomical regions of the oral cavity, with squamous cell carcinoma (SCC) being the predominant histological subtype. The most frequently involved sites include the tongue, buccal mucosa, floor of the mouth, gingiva, palate, and lips (Wang, G. R., et al., 2024). Oral cancers, particularly those of the tongue and floor of the mouth, are associated with higher morbidity and mortality rates due to their aggressive nature and tendency for early metastasis ((Kijowska, J., et al., 2024).

Tongue cancer stands out as a major subtype, accounting for an estimated 389,846 new cases globally in 2022 (World Cancer Research Fund, 2022). Due to the tongue's essential role in articulation and deglutition, this disease poses serious risks to speech, swallowing, and ultimately the patient's overall quality of life (Curtis, 2023). It accounts for approximately 1% of all cancer diagnoses worldwide (Curtis, 2023). While its occurrence varies geographically, higher incidence rates of tongue cancer are reported in countries like India, several European regions, and Malaysia, where it accounted for 12.6% of all deaths in 2022, largely due to varying risk factors (Gupta, Ariyawardana, & Johnson, 2020; Ghanem, Memon, & Nagy, 2024; Bernama, 2024). The contributing factors include tobacco use, excessive alcohol consumption, and human papillomavirus (HPV) infection (Curtis, 2023).

Surgery remains the cornerstone for tongue cancer treatment, particularly in early and resectable stages, due to its ability in achieving clear oncological margins and allowing oncologists to do pathological staging (de Carvalho et al., 2023). It is frequently regarded as the principal curative strategy because it directly removes the tumor and facilitates precise histopathological evaluation of margins and nodal involvement. In more advanced stages, surgery is typically followed by adjuvant radiotherapy (RT) or chemoradiotherapy to improve tumor control and survival (Arboleda et al., 2023). In addition to these standard methods, other therapeutic options include RT, like external beam radiotherapy (EBRT) and brachytherapy (BT), chemotherapy, targeted therapy, and immunotherapy, either alone or in combination, depending on the tumor's stage, location, and biological behavior (Sattar et al., 2025).

BT, also known as internal RT, has been employed for more than two decades, delivering concentrated radiation directly to the tumor while sparing the surrounding healthy tissues. Recent studies underscore the effectiveness of BT in treating tongue cancer. For instance, a study reported that oral tongue cancer patients with T1-2 and N0 stages treated with BT alone achieved both 5-year overall survival (OS) and disease free survival (DFS) rates of 86%, surpassing outcomes from EBRT alone with OS and DFS rates of 65% and 59%, respectively (Shojaei, et al., 2024). These findings highlighted the BT's potential in providing local disease control and survival benefits.

In terms of treatment delivery to tongue tumors, BT offers distinct advantages compared to surgery and EBRT (Tucek, Vošmik, & Petera, 2022). Its capacity to administer high radiation doses with pinpoint accuracy significantly limits damage to nearby structures, preserving the tongue’s essential functions such as speech and swallowing (Tucek, Vošmik, & Petera, 2022). Moreover, BT's shorter treatment time and reduced hospital stays benefits both elderly patients and those with comorbidities (Samson, et al., 2021). Although clinically beneficial, BT technique is still not widely adopted due to technical demands, high costs, and lack of infrastructure in many centers worldwide (Tucek, Vošmik, & Petera, 2022; de Carvalho et al., 2023). Consequently, while BT is a viable option particularly for early-staged tongue lesions, of the tongue it is not yet widely accessible as a standard treatment modality. Technological innovations, including advanced treatment planning systems (TPS) like Oncentra TPS, require ongoing evaluation to maximize precision and therapeutic outcomes.

Given the high degree of anatomical and functional complexity in the oral tongue, dwell position configuration where the radioactive source is temporarily stationed within the the implanted BT applicators plays a vital role in shaping radiation dose distribution. Variations in source loading or dwell position activation strategies can significantly impact both tumoricidal dose coverage and the radiation dose received by surrounding organs at risk (OAR) (Shimamoto, Ooura, & Ono, 2024). The only suggestions on source loading were made by AAPM Task Group (TG) 56, who recommended that the dwell position accuracy should be within ±1 mm (Richardson, et al, 2023).

High-dose-rate interstitial brachytherapy (HDR ISBT) introduces an advanced therapeutic alternative uniquely tailored for the anatomical intricacies of the oral tongue. Unlike conventional approaches, HDR ISBT enables anatomy-adaptive radiation delivery through catheter-based implantation, which can be dynamically customized during treatment planning. Notably, this technique facilitates volumetric optimization via computer-controlled dwell time adjustments, allowing clinicians to modulate dose deposition at submillimeter accuracy (Yoshida et al., 2019). Such spatial flexibility is particularly significant when managing tumors situated in close proximity to functioncritical structures, as it minimizes radiation spillover into the mucosa and neurovascular interfaces (Murakami et al., 2018).

Additionally, recent studies have highlighted the efficacy of HDR ISBT in managing irregular tumor geometries, where edema during treatment risks underdosage in static plans. Novel implant devices, like tongue spacers or edema-mitigating systems, have been developed to maintain dose homogeneity throughout fractionated sessions (Yoshida et al., 2019; Nakamura et al., 2025). These adaptations ensure a consistent therapeutic ratio while preserving the mobility and functionality of the oral tongue.

Furthermore, comparative dosimetric analyses have demonstrated that HDR ISBT achieves superior target conformity indices compared to hybrid intracavitary-interstitial techniques or external beam modalities, particularly in early-stage and lateralized lesions (Thariyan & Khanna, 2021; Alva et al., 2020). As HDR ISBT continues to evolve, its integration with advanced TPS and real-time image guidance could redefine standards for functional organ-preserving therapy in oral tongue cancer.

Despite technological advances in TPS such as Oncentra TPS, limited research has been conducted to systematically evaluate how different source loading patterns influence the dosimetric outcomes in tongue cancer treatment. Therefore, this study aims to investigate the effects of varying dwell position activation strategies on dose distribution. By analysing and comparing different activation techniques, the study seeks to identify planning approaches that could enhance treatment efficacy while minimizing exposure to critical surrounding structures.

1.2 Problem Statement

In HDR ISBT, there is a procedure called treatment planning which relies heavily on advanced TPS to ensure precise and optimal radiation delivery to tumor, while sparing the surrounding healthy tissues. TPS facilitates the entire treatment planning process, which begins with catheters' reconstruction to source activation, followed by dose calculation and finally, dose optimisation, thereby enabling tailored approaches for individual patients.

The current HDR ISBT treatment planning approach mostly involves activating all dwell positions within the tumor region during the activation phase, leading to dose inhomogeneity, hence resulting in "hot spots" formation (almost 200% of the prescribed dose) within tumor (Soror, T., ,2021). In addition to that, significantly increasing the risk of tongue tissue toxicity and potential necrosis. If all dwell positions are activated, the dose distribution is primarily concentrated at the center of the tongue, with insufficient coverage at the edges and scattering effect can cause unintended dose to teeth.

This planning method also increases the surface dose to the tongue, necessitating prolonged dwell times to achieve adequate dose coverage, which in turn raises the risk of adverse effects. In the field of BT for head and neck cancers, particularly for sites with complex anatomy such as the tongue and base of the mouth, the accurate positioning of dwell radioactive source positions within the applicator is crucial for effective treatment. Small deviations in source positioning can lead to significant inaccuracies in dose distribution, increasing the risk of complications such as osteoradionecrosis (ORN) and soft tissue necrosis (STN), and compromising tumor control outcomes (Damek-Poprawa, M., 2013).

This study, therefore, aims to address the problem of dose variability and hotspot formation by investigating the dosimetric and differences in clinical outcomes between the selective activation and the current practice of full dwell position activation, particularly focusing on dose distribution uniformity, surface dose, and dose impact on organs at risk.

1.3 Objective

1.3.1 General Objective

To study the effectiveness and safety of oral tongue HDR ISBT by comparing two treatment planning methods in the activating phase, which are the activation of all dwell positions and the selective activation.

1.3.2 Specific Objective

a. To compare the differences in surface dose levels outputs between activating all dwell positions and selective activation.

b. To compare the differences in tumor dose coverage between activating all dwell positions and selective activation during treatment planning in the activating phase.

c. To compare the differences in dose impact to the specific OARs, including the mandible, pharyngeal constrictor muscle, and both right and left submandibular glands between activating all dwell positions and selective activation.

1.4 Significance of the Study

Despite the advancements in HDR ISBT for oral tongue cancer, there is a notable lack in literature on evaluation of the source loading variations and strategies, particularly in Oncentra TPS. While existing studies have explored various aspects of Oncentra TPS, such as optimization techniques and dosimetric accuracy, they have not delved into how dwell position selection impacts both dose distribution to the tongue lesions and nearby OARs (Thomas et al., 2024; Peppa, et al., 2016; Tagliaferri, et al, 2022).

For instance, Huang et al. (2021) introduced a meta-optimization framework aimed at automating treatment planning processes. Their study focused on optimizing hyperparameters to enhance plan quality but did not study into dwell activation schemes specific to Oncentra TPS or tongue cancer cases (Huang, Nomura, Yang, & Xing, 2022). Similarly, Liu et al. (2021) developed an interactive treatment planning module for HDR ISBT, emphasizing real time plan modifications. While their work contributes to the field of BT planning, it does not address about the dwell position management within Oncentra TPS for tongue cancer treatment (Liu, et al., 2021).

Regarding OAR dose tolerances, recent studies continue to extrapolate data from EBRT contexts. Yamic et al. (2024) compared doses to the parotid gland, temporomandibular joint, and PCM using different radiotherapy techniques for oropharyngeal cancer. Their findings underscore the importance of dose constraints for these structures but do not provide specific guidelines for HDR ISBT in tongue cancer (Yamic, Koca, Tuncel, Aksoy, & Korcum, 2024).

These gaps in knowledge poses a challenge for radiation oncologists and medical physicists in aiming to protect these OARs while maximizing radiation dose coverage to tumor, hence resulting in good local control. Therefore, by evaluating the variations in source loading positions that can influence the dose distribution to both tumor and OARs, this study contributes to a better understanding of treatment planning decisions and potentially supports the development of radiation tolerance dose guidelines for OAR specifically in HDR ISBT for tongue cancer.

Ultimately, this research aims to improve patient safety and clinical outcomes by providing evidence-based recommendations for source activation strategies and encouraging further studies on dose tolerance thresholds for non-target tissues in head and neck BT. It aims to provide practical data on how varying dwell position selections affect critical structures such as the mandible, submandibular glands, and pharyngeal constrictor muscles. By identifying safer activation strategies, this work can support better treatment planning decisions, reduce long-term complications (like osteoradionecrosis or xerostomia), and ultimately improve patient outcomes. It may also lead to more consistent clinical practice in institutions that utilize Oncentra TPS.

This study also highlights the need for the establishment of standardized planning protocols or dose tolerance guidelines specifically tailored to HDR ISBT in oral cancers. With current clinical recommendations largely based on EBRT data, this study may serve as an evidence base for developing more brachytherapy-specific dose limits. While advancements in radiotherapy planning and optimization continue, there remains a significant gap in the literature concerning dwell activation strategies within Oncentra TPS for tongue cancer HDR ISBT. Additionally, the lack of established dose tolerance protocols for critical structures like the mandible, pharyngeal constrictor muscles, and salivary glands in the context of HDR ISBT highlights the need for dedicated research in this area.

CHAPTER 2

LITERATURE REVIEW

2.1 Tongue cancer

The oral cavity serves as the entry point of the digestive and respiratory systems, comprising several distinct anatomical subregions including the lips, buccal mucosa, hard and soft palate, floor of mouth, alveolar ridges, retromolar trigone, and tongue. Tongue is enclosed anteriorly by the lips, superiorly by the hard palate, and inferiorly by the floor of the mouth, with its posterior boundary leading into the oropharynx (Beddok et al., 2023; Wang et al., 2024). Each component plays a critical role in essential functions such as mastication, speech, taste, and swallowing, and is lined by specialised mucosa that varies in thickness and keratinisation depending on the region.

The tongue, as shown in Figure 2.1, is anatomically defined as part of the oral cavity, composed of the mobile anterior two-thirds (oral tongue) and the base of the tongue, which contributes to the oropharynx (Sharma, J., & Bisht, S.,2024). The most prevalent type is oral tongue squamous cell carcinoma (OTSCC), originating from the flat cells lining the tongue's surface (Chen, K. J., et al, 2025).

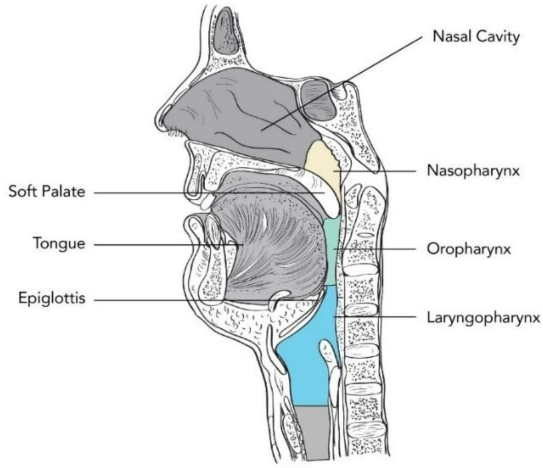

Figure 2.1: Anatomy of the upper airway, including the nasal cavity, pharyngeal regions, tongue, and epiglottis.

According to Wang et al. (2024), the most frequently involved anatomical regions in oral cancer include the tongue, buccal mucosa, floor of the mouth, gingiva, both the hard and soft palate, and the lips. Most SCC cases often exhibit aggressive local behaviour with a high tendency for lymphatic spread, especially because of the tongue's rich lymphatic drainage. The prognosis is generally poorer in cases with advanced local invasion or nodal metastasis (Ionna, F.,et al, 2024).

2.1.1 Statistic

OTSCC ranks among the top 20 most common cancers in Malaysia, with a five-year prevalence of 2,199 cases, and its incidence is estimated to double by 2040 due to age-specific incidence trends and population growth (Raman, et al., 2022). Notably, among Malaysian Indians, OTSCC is the 8th most common malignancy in males and the 4th in females (Chiesa-Estomba, C. M., et al. 2024; Chan, et al., 2023). Local cultural practices, such as betel quid chewing, along with tobacco and alcohol use, are significant contributors to the oral tongue cancer burden in the country (Chan, et al., 2023). These risk factors are particularly prevalent in rural communities, exacerbating the disease's impact. Despite the high prevalence, there is a need for improved public awareness, early detection strategies, and access to specialised treatments to address oral cancer effectively (Chan, et al., 2023).

2.1.2 Symptoms and Diagnosis

OTSCC patients typically present with non-healing ulcers, pain, or discomfort in the tongue. Other symptoms include painful or difficulty in swallowing, which are commonly known in medical term as odynophagia or dysphagia respectively, altered speech, or presence of mass that may restrict tongue movement (Bradley, P. T., et al, 2024). On examination, lesions may appear ulcerative, exophytic, or infiltrative. Diagnostic evaluation begins with a thorough clinical examination and biopsy for histopathological confirmation. Imaging is essential to assess tumor extent and detect lymph node involvement. Magnetic resonance imaging (MRI) is preferred for evaluating soft tissue infiltration, while computed tomography (CT) is useful for detecting bone invasion. Positron emission tomography-computed tomography (PET-CT) is employed particularly for staging advanced cases and identifying distant metastases (Lapeyre et al., 2022; NCI, 2023).

2.1.3 Staging

OTSCC staging is based on the TNM (Tumour, Node, Metastasis) classification by the Union for International Cancer Control (UICC), as shown in Table 2.1.

Table 2.1: Classification according to stage of cancers of the oral cavity and of the lip.

Stage	T	N	M
I	T1	N0	M0
II	T2	N0	M0
III	T3	N0	M0
	T1-3	N1	
IVa	T4a	N0-1	M0
	T1-4a	N2a-2c	
IVb	T1-4	N3a-3b	M0
	T4b	N1-3b	
IVc	T1-4	N0-3b	M1

`

In the 8th edition, emphasis was added to tumor depth of invasion, which significantly influences the prognosis. T1 tumours are ≤ 2 cm in size with ≤ 5 mm depth of invasion; T2 includes tumours either ≤ 2 cm but with > 5 mm depth or up to 4 cm with ≤ 10 mm depth; T3 includes tumours > 4 cm or > 10 mm depth. T4a indicates invasion into nearby anatomical structures such as the mandible or skin, while T4b represents advanced involvement of the masticatory space or skull base as summarised in Table 2.2.

Table 1.2: The classification of clinical (c) and postoperative pathological (p) of primary tumor (T) in oral cavity and lip cancers, according to the UICC 2017 guidelines based on the tumor's largest dimension.

Stage	**Criteria**
Tis	Carcinoma in situ
T1	Tumor $\leq$ 2 cm and infiltration in depth $\leq$ 5 mm
T2	Tumor $\leq$ 2 cm and infiltration in depth > 5 and $\leq$ 10 mm or tumor > 2 cm and $\leq$ 4 cm and infiltration $\leq$ 10 mm
T3	Tumor > 4 cm or infiltration in depth > 10 mm
T4a Oral Cavity	Tumor invading the cortical bone of the mandible or the maxillary sinus or the skin
T4a Lips	Tumor invading the cortical bone, the lower alveolar nerve, the floor of the mouth or skin (chin or nose)
T4b	Tumor invading the masticatory space, the pterygoid processes, the base of the skull or the area surrounding the internal carotid artery

The N category is based on the size and number of lymph nodes involved, as well as whether there is extracapsular spread, which significantly upgrades staging (Lapeyre et al., 2022).

Table 2.2: The classification of clinical (c) and pathological (p) lymph node (N) involvement in oral cavity and lip cancers based on UICC 2017.

Stage	Criteria
N0 (c/p)	No regional lymph node involvement
N1 (c/p)	Single ipsilateral metastasis ≤ 3 cm without extracapsular spread
cN2a	Single ipsilateral metastasis > 3 cm or ≤ 6 cm, without extracapsular spread
pN2a	Single ipsilateral metastasis > 3 cm or ≤ 6 cm, without extracapsular spread or Single ipsilateral metastasis ≤ 3 cm with extracapsular spread
N2b (c/p)	Multiple ipsilateral metastases ≤ 6 cm without extracapsular spread
N2c (c/p)	Contralateral or bilateral metastases, ≤ 6 cm, without extracapsular spread
N3a (c/p)	Tumour invading the cortical bone, the lower alveolar nerve, the floor of the mouth or skin (chin or nose)
cN3b	Single or multiple metastases, with extracapsular spread (indifferent size)
pN3b	Single or multiple metastases, ipsi or contralateral(s), > 3 cm, with extracapsular spread

2.1.4 OTSCC treatment options

Treatment strategies for OTSCC commonly include surgery, RT, and chemotherapy, often used alone or in combination depending on the tumor stage and location. Surgery remains the primary approach for early and resectable tongue cancers due to its ability to achieve oncological clearance and enable pathological staging. However, microscopic residual disease can lead to recurrence, especially in more advanced stages (de Carvalho et al., 2023). RT, including advanced techniques such as high dose rate interstitial brachytherapy (HDR ISBT), is frequently used as an adjunct to surgery or as a definitive modality in patients unfit for surgery. While RT offers the advantage of organ preservation and targeted tissue destruction, it can also damage surrounding healthy structures, particularly in a complex area like the oral cavity (Guinot et al., 2024; Merring-Mikkelsen et al., 2024).

Chemotherapy is typically reserved for locally advanced or metastatic cases and is known to target the rapidly dividing cancerous cells. However, its non-specificity often results in toxicity to normal tissues, hence affecting patients' quality of life (Anand et al., 2023). Moreover, chemotherapeutic and radiotherapeutic interventions may induce selective pressure on the tumor cells, leading to the survival and expansion of more resistant clones, thereby promoting tumor progression and recurrence (van den Boogaard, Komninos, & Vermeiji, 2022; Brown et al., 2023). These limitations underscore the need for personalised, multimodal approaches that not only eradicate the primary tumor but also address mechanisms of resistance and tumor plasticity to improve long-term outcomes in tongue cancer patients.

2.2 RT in treating OTSCC

RT is a cornerstone in the multimodal treatment of OTSCC, functioning by delivering high-energy radiation that induces irreparable damage to the DNA of malignant cells, ultimately causing cell death (Chen et al., 2024). RT is broadly categorised into external beam radiation therapy (EBRT) and internal radiation therapy, commonly referred to as brachytherapy (BT). These modalities differ significantly in their delivery approach, anatomical precision, and impact on surrounding tissues.

EBRT involves delivering radiation from an external machine and is commonly used in the definitive or adjuvant treatment of tongue cancer, particularly in cases where surgical margins are positive or lymph node involvement is suspected. Advanced EBRT techniques such as intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT) allow clinicians to sculpt radiation doses to conform to the complex anatomy of the oral cavity, thus sparing adjacent healthy tissues like the salivary glands and mandible (Guinot et al., 2024; Merring-Mikkelsen et al., 2024). Despite its precision, EBRT still poses a risk of radiation-induced complications, such as xerostomia and osteoradionecrosis, particularly in high-dose regions (Merring-Mikkelsen et al., 2024).

For OTSCC, HDR ISBT is the most widely employed BT technique. HDR ISBT is especially beneficial in early-stage tumors or recurrent cases where EBRT has already been administered and reirradiation via external means poses excessive risk (Nakamura et al., 2025). However, brachytherapy requires technical expertise, specialised infrastructure, and meticulous catheter placement, which limits its widespread availability (Tucek et al., 2022).

In summary, both EBRT and BT have crucial roles in the treatment of tongue cancer. EBRT remains the standard for a wide range of stages, especially with nodal involvement, while HDR ISBT provides a targeted, function-preserving alternative for localised disease, offering high tumor control with reduced collateral damage when performed in expert settings.

2.3 Fundamentals of Brachytherapy

HDR ISBT uses implanted catheters to deliver radiation from within the tongue tissue (Figure 2.2), allowing for extremely localised dosing with steep dose gradients, thereby minimising exposure to adjacent normal structures. (Guinot et al., 2024; Brovchuk et al., 2025). Unlike chemotherapy, which applies systemic pressure on cancer cells and may unintentionally drive resistance by affecting both malignant and healthy cells (van den Boogaard, Komninos, & Vermeiji, 2022), HDR ISBT reduces the effect on the healthy tissues by targeting only the tumor. This localised focus limits the emergence of resistant cell populations elsewhere in the body (Brown, et al., 2023).

Moreover, BT often involves fewer treatment sessions and fewer systemic side effects than chemotherapy, which is known to cause long-term damage to healthy tissues and contribute to premature ageing in cancer survivors (van den Boogaard, Komninos, & Vermeiji, 2022). The treatment duration also makes it advantageous for elderly patients or those with significant comorbidities (Alva et al., 2020). These benefits make brachytherapy a favourable option for patients requiring targeted therapy without the burden of various toxicities (Chen, Qiu, Wang, Momin, & Yang, 2024). While it is most effective for localised tumors and not typically suitable for metastatic cancers, brachytherapy offers a biologically rational and clinically effective approach. (Niu, et al., 2025).

Figure 1.2: Catheter insertions for tongue HDR ISBT (abcpenang, 2023).

2.3.1 High dose rate interstitial brachytherapy (HDR ISBT)

BT can be classified into temporary and permanent forms. Permanent BT, also known as seed implantation, involves placing radioactive seeds within the tumor that decay over time. This method's precision and localisation significantly reduce the risk of secondary malignancies, making it a compelling choice in specific clinical scenarios (Gibbons, 2020).

Temporary BT is where a radioactive source is temporarily placed within or adjacent to the tumor using applicators or catheters. Once the prescribed dose is delivered over a planned duration, the source is removed. This method offers high precision and control, making it especially effective for tumors located in anatomically complex areas, such as the oral cavity. A key advantage of temporary BT is the ability to tailor dwell times and positions to match the tumor's shape and location, thus optimising the therapeutic ratio while sparing nearby healthy tissues.

Moreover, temporary BT is further classified based on the rate of radiation dose delivery into low-dose-rate (LDR), medium-dose-rate (MDR), and HDR categories. LDR BT delivers radiation at 0.4 to 2 Gy per hour, typically administered over several hours or days. MDR, with dose rates ranging from 2 to 12 Gy per hour, is less frequently used in current practice due to logistical challenges and less favourable radiobiological profiles. In contrast, HDR brachytherapy, defined by a dose rate exceeding 12 Gy per hour, is delivered in brief treatment sessions lasting only a few minutes. HDR has become the preferred modality in many clinical settings owing to its efficiency, reduced treatment times, and compatibility with advanced planning systems (Guinot et al., 2024; Gibbons, 2020). An additional variant, pulsed-dose-rate (PDR) brachytherapy, attempts to mimic the biological effects of LDR by delivering radiation in periodic pulses (usually once per hour), combining the radiobiological advantages of LDR with the logistical benefits of HDR delivery systems (Guinot et al., 2024).

HDR ISBT is a preferred approach for OTSCC due to its capacity for precise and conformal dose delivery. Utilising a source after-loading system, HDR ISBT allows clinicians to dynamically control dwell times and positions within implanted catheters, thereby maximising tumour coverage while sparing adjacent critical structures such as the mucosa, mandible, and neurovascular tissues (Guinot et al., 2024). This level of control is particularly advantageous in the anatomically compact and functionally critical region of the oral cavity, where traditional EBRT may pose a higher risk of collateral damage (Tucek et al., 2022).

Figure 2.2: (A) and (B) Types of HDR remote after-loader available (Oncology Medical Physics, 2017). retrieved from https://oncologymedicalphysics.com/high-dose-rate-brachytherapy/

The Paris System is often used as a foundational dosimetric approach in HDR ISBT. It emphasises consistent geometry such as parallel source lines, equidistant spacing, and uniform source loading to achieve symmetric and homogeneous dose distributions within the target volume. Although originally developed for LDR systems, the Paris System principles are still applicable when using HDR after loading techniques, provided dwell steps and times remain uniform. For example, in HDR, a typical configuration involves dwell steps of 5 mm for a 3.5 mm long ^{192}Ir source. The fixed reference isodose in this system corresponds to 85% of the basal dose rate (BD), which itself is calculated as the average of the minimal dose rates in the central plane of the implant. The planner can subsequently calculate the required treatment time based on the prescribed dose and the kerma rate on the day of the implant. These strategies allow modern TPS systems to distribute the dose around complex anatomical structures, improving conformality while respecting dose constraints to organs at risk such as mucosa or bone structures (Marinello, G.,2009).

2.3.2 Brachytherapy Treatment Delivery

The primary and widely practised BT delivery methods include interstitial, intracavitary, and surface mould techniques. Each approach offers specific advantages depending on tumor location, size, and accessibility.

HDR ISBT involves the surgical implantation of flexible plastic catheters through or around the tumor, typically under general anesthesia. These catheters are later used to