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REVIEW OF THE ROLE OF BRACHYTHERAPY IN THE MANAGEMENT OF ORAL CAVITY CANCERS

Radiotherapy

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ABSTRACT

From the day of invention of Radium, brachytherapy has been practised worldwide. Can any technological advancement in external beam radiotherapy replace brachytherapy? Answer probably no, especially in Gynaecological cancers as categorically stated by GEC-ESTRO experts. External beam radiation therapy using contemporary conformal techniques and brachytherapy play a significant role in the management of oral cavity cancer. Small sized tumors in most of the oral cavity sites can be managed with brachytherapy alone either with intraoral cone or interstitial brachytherapy in order to minimize exposure of normal tissue. As these techniques do not treat regional lymph node basins, they are only appropriate to use as a single modality in selected stage I and II patients. The risk of occult nodal involvement in stage I and II is very low. External beam radiation therapy to the draining lymph node regions is used as the primary mode of irradiation when regional lymph nodes are at significant risk for subclinical involvement, and brachytherapy may be added as a boost to the primary tumor. Since head and neck cancers are Surgeons domain, number of patients reporting to Radiation Oncology department is too low to carry out large randomized trial. Most of the patients report to Radiation Oncology department in either in late stage or in an early stage with poor general condition. This paves the way for selection bias and, of course, inferior results when compared with other modality. To evaluate the role of this therapy in treatment of head and neck cancers, we have reviewed its outcomes with oral cavity cancer. In conclusion, brachytherapy with or without EBRT can be an alternative to surgery in early and locally advanced oral cavity cancers although concrete evidence is yet to be produced with a sophisticated study in a reproducible manner.

KEYWORDS

brachytherapy, oral cavity cancer, high dose rate

INTRODUCTION

The aim of the treatment of oral cavity is to eradicate the disease with less or no morbidity, giving better quality of life. Surgery alone, radiotherapy alone, surgery with radiotherapy (with or without chemotherapy) or concurrent chemo-radiotherapy is the treatment modalities currently available. Successful outcome and better quality of life depends on the comprehensive management of various departments including surgery, radiotherapy, chemotherapy, dental and prosthetic support, psycho-social support, rehabilitation services.[1] Physiologic functions of the oral cavity constitute speech (articulation), swallowing (oral and preparatory phase) and mastication. If the surgery is extensive, these functions will be compromised. For early lesions (T1, T2, N0 stages) of anterior 2/3rd of tongue, floor of mouth and buccal mucosa, surgery with wide local excision and selective neck dissection for lymph nodes is sufficient. Mandibulotomy approach is required for adequate visualization of the lesion and acquisition of the margins for advanced lesions (T3, T4, node positive). Marginal mandibulectomy has to be done for lesions which are close to the mandible (less than 1 cm) or reaching the alveolar margins. Segmental mandibulectomy is indicated for lesions invading bone either by clinical examination or by imaging studies.[1]

Post-operative Radiotherapy

Outcomes are almost similar for surgery and radiotherapy for stage I and II. Postoperative chemo radiotherapy is necessary for advanced lesions to improve the survival outcome. Postoperative radiation therapy is recommended for patients with T3, T4 disease, close or positive surgical margins, presence of perineural invasion, multiple involved lymph nodes, extra capsular extension. Extra capsular extension and positive margins are the two high risk features where postoperative chemo radiation is indicated. Surgical tumor bed and dissected lymph node region are the target areas for irradiation. If primary tumor alone were operated, elective nodal irradiation should be considered in node negative cases.[2,3]

Meta-analysis by Blanchard et al. reported 0.85 Hazard Ratio (HR) of death with surgery and radiotherapy compared to surgery alone in head and neck cancers.[4] Outcomes are better in terms of HR for EFS and OS in post-operative radiotherapy group. The recommended post-operative radiotherapy dose is 60Gy in negative margins and those with intermediate risk, 66Gy for patients with positive margins and 50 - 54Gy for uninvolved neck nodes.[5]

Ang et al. reported a study on adjuvant radiotherapy in 213 patients having squamous cell carcinoma of the oral cavity, oropharynx and hypopharynx. Most of them were advanced stages, 48% had stage III and 38% had stage IV cancers. Patients were classified into three risk groups after surgery as low risk, intermediate risk and high risk. Low risk included patients without any adverse pathologic factors. High risk included patients with extra capsular extension with or without ≥2 adverse pathologic factors. Local control and survival rates were decreased for high risk patients for whom radiotherapy was delayed. The 5-year local control rates were 90% for low risk (without radiotherapy), 94% for intermediate risk (with radiotherapy) and 68% for high risk disease. The 5-year overall survival rates were 83% for low risk, 66% for intermediate risk and 42% for high risk.[6]

P freundner et al. conducted a study on 257 patients who were treated with surgery and adjuvant RT. Median dose of 56 Gy was given. The 5-year loco regional control was 100% for negative margins, 92% for close margins, 87% for R1 resection, 69% for R2 resection. The 5-year overall survival was 67% for negative margins, 59% for close margins, 26% for R1 resection, 27% for R2 resection. They concluded that resected margins and high radiation dose were the two factors which influence locoregional control. Total dose, resected margin status, T stage, N stage were the factors associated significantly with overall survival.[7]

Post-operative Chemo Radiotherapy

Bernier et al. did a randomized trial on 334 operable stage III and stage IV cancers of oral cavity, oropharynx, larynx, hypopharynx. All patients underwent surgery. Patients, after surgery were randomized to receive either radiotherapy alone with 66 Gy or chemoradiotherapy with 66 Gy along with Injection Cisplatin 100 mg/m^2 on day 1, 22 and 43. Patients included were pT3-4N0/Node positive, T1-2 N2-3, and T1-2 N0-1 with extra capsular extension, margin positive or perineural invasion. Chemoradiation improved 5-year DFS (36 versus 47%), 5-year OS (40 versus 53%) and 5-year loco regional control (69 versus 82%), but increased grade 3 and 4 complications (21versus 41%).[2]

Cooper et al. randomized 459 patients with cancer of the oral cavity, oropharynx, larynx, or hypopharynx which are operable and who had two or more involved lymph nodes, nodal extra capsular extension, or a positive margin to post-op RT (60–66 Gy) versus post-op chemoradiotherapy (60–66 Gy and Cisplatin100mg/m^2×3cycles, 3 weekly). Chemoradiotherapy improved 2-year disease free survival (43 versus 54%), locoregional control (72 versus 82%) and had an increasing trend for overall survival (57 versus 63%) and with increased grade 3–4 complications (34 versus 77%).[3]

Radiotherapy

Dose recommended for definitive radiotherapy is 66 to 70Gy for 7 weeks to the primary and gross lymphadenopathy in conventional 2Gy per fraction for 5 days per week. Accelerated fractionation can be either 2Gy/fraction for 6 days/week to total dose of 66 to 74Gy or as concomitant boost of 72Gy in 1.8Gy per fraction/day to the large field

and 1.5Gy per fraction/day to the boost volume as second daily fraction during last 12 days of treatment. Dose of 81.6Gy in 1.2Gy per fraction twice daily for 7 weeks is delivered in case of hyper fractionated radiotherapy.[5]

Brachytherapy

While considering the treatment of oral cavity squamous cell cancer, brachytherapy is an important option in the armamentarium of a radiation oncologist. It plays a significant role in organ and function sparing strategies which influences patient's quality of life functionally, psychologically and cosmetically. The prefix for brachytherapy is derived from the Greek word "brachy", refers to "short". The application refers to the use of sealed radioisotopes near or within the tumor volume. Moreover it involves the implantation of radioisotopes into tumors to allow high dose conformity with dose intensification to areas of high volume disease and rapid inverse square falloff to the surrounding normal tissue. Main advantage is due its high tumor to normal tissue ratio and decrease in steep gradients within the tumor. The ICRU report 38 defined LDR as radiation dose delivered at 0.4 to 2.0 Gy per hour and HDR of >12.0 Gy per hour.[8,9]

Types

Brachytherapy can be divided into multiple categories: Interstitial, intracavitary, intraluminal and surface applicator techniques in terms of approach to the target volume. In addition, the application can be further subdivided based on loading technique (preloading or after loading), the dose rate (low dose rate [LDR] or high dose rate [HDR]) and duration of the implant (temporary or permanent). In interstitial brachytherapy, the radioisotope is placed either temporarily or permanently into the tumor site or bed.[10]

Temporary Implants

The radioactive sources are loaded through implanted catheters into the tumor volume in the temporary implant technique which allows for a more accurate and deliberate placement without the risk of radiation exposure that is associated with permanent implants during implantation. In addition, the implant dosimetry can be optimized using various planning systems with three-dimensional (3D) reconstruction of the implant geometry.[192] It is the most common temporary radioisotope used with t1/2 of 74.2 days. It undergoes beta-decay emitting polyenergetic gamma rays having mean energy of 380 keV.[11,12]

In the 1930s, a method was devised by Ralston Paterson and Herbert Parker for implantation of radioactive source to have a homogenous dose distribution throughout the target volume, designated as the Paterson-Parker system or the Manchester system. The development was later followed with a system of rules and tables with respect to the sources placement in a uniform grid, achieving more doses at the centre in comparison to the periphery of the tumor by Edith Quimby of Memorial Sloan-Kettering in New York. Paris system is devised for implantation which is used mainly for temporary interstitial technique.[13-18] Usage of computers, imaging technologies, dose-calculating algorithms has changed the radiation treatment planning to significantly evolve in optimal and accurate radiation delivery.

Remote after loading Technique

Iridium 192 seeds and ribbons were used in the implantation of tumors with the help of plastic catheters. In the 1960s, Henshke et al. introduced the after loading technique (in comparison to preloading, where radioactive sources are implanted during the initial procedure), where the sources were inserted into the previously implanted applicators or catheters within the tumor thus minimizing the potential exposure of radiation to medical personnel.[19]

HDR after loading system comprises of a computer-guided remote source after loading machine, ^{192}Ir source, transfer tubes/applicators, a computer treatment planning system, and a control console. Fractionated high-dose RT can be delivered with a single high activity ^{192}Ir source that is fixed to a computer-controlled sliding guide wire using a transfer tube into the placed catheter. The source then positions itself for a predetermined length of time at various dwell positions that are 5-mm apart. Each dwell position contributes various amounts of radiation dose that depends on the dwell time calculated by the TPS in order to achieve conformal isodose coverage of the target volume.[19]

Techniques In Brachytherapy Interstitial Implant

Radioactive sources have to be placed meticulously in the planned tumor volume which determines a successful brachytherapy. There are various techniques with many modifications over the years. Currently, most interstitial head and neck implants are based on an after loading system with a computerized treatment planning system.

One of the most popular techniques with various modifications is the Henschke's plastic tube technique. Rigid metal hollow guide needles are implanted into the tumor volume by free hand. It is then followed with the threading of plastic tubes into these rigid hollow needles and held in position. Metal needles are subsequently removed.[20]

Through and through technique is used for tumor volumes when both sides are accessible for implantation. The first step is to identify the target volume and the entry points for catheters. With the help of metal needle or trocar, the skin is pierced at the entry site and coursed along in the tumour volume, exiting at the marked skin site at the other end. The trocar is threaded with an afterloading catheter followed with the subsequent removal of trocar. The above series of steps are repeated to form a parallel distribution of catheters.

The technical aspects of loop technique are similar to the through-and-through technique. The catheters will exit along the same side of the entry points, forming a loop.[21]

Brachytherapy can be used as a single modality or in combination with EBRT. It is used as a single treatment modality in small primary tumors and in the recurrent disease. In advanced diseases, it can be used as palliative procedure to decrease symptoms like dysphagia in cancer oesophagus. No phase III randomized studies comparing brachytherapy with EBRT in head and neck malignancies are there but there is ample evidence in support of brachytherapy as part of the optimal treatment strategy for various head and neck sites.[21-23]

HDR Brachytherapy In Oral Cavity Cancer

Brachytherapy alone can be used in T1N0 and T2N0 tumors of oral cavity which is currently being evaluated. Mohanti et al. compared the results of HDR brachytherapy with previously reported results on LDR brachytherapy in cancers of the head and neck region. They included 84 patients, out of which 70 were oral cavity and 14 were oropharynx. 78 patients were of early stage. 42 patients received brachytherapy alone with 40 Gy as median dose in 10 fractions. 42 patients received EBRT (median dose of 50 Gy in 25 fractions) and brachytherapy (median dose of 15 Gy in 5 fractions). The local control rate at 5-year was 62% and DFS was 52%. For T1 tumors, local control was 84% and for T2, it was 42%. The primary site relapse rates were 23.8% in brachytherapy alone group and 68.4% in combination group. They concluded that the rates of DFS were similar for both HDR and LDR brachytherapy.[24]

Patra et al. reported the results of the effect of the HDR interstitial brachytherapy after EBRT in head and neck cancer. 33 patients having oral cavity and oropharynx carcinomas received HDR-interstitial brachytherapy after external beam radiation therapy. 45% had early stage disease and 55% had advanced stage disease. Median dose of 50 Gy EBRT was given. Dose of brachytherapy ranged from 14–21 Gy. 79% of patients achieved complete response and 21% achieved partial response with 100% control rates for early disease and 78% for advanced disease. 9% had local failure after complete response. 12% of patients developed grade 3 mucositis, 9% had transient haemorrhage, 3% had local infection, 3% had severe dysphagia and 15% had grade 3/4 xerostomia. The study showed excellent local control and acceptable complication rates could be achieved with brachytherapy boost after EBRT.[22]

Rudoltz et al. reported the results of HDR interstitial brachytherapy in patients with cancers of the oral cavity and oropharynx. 55 patients were included with 29% T1, 47.5% T2, 14.5% T3 and 9% T4. Patients received EBRT followed by HDR brachytherapy. Electron boost was given to the patients with cervical adenopathy. Brachytherapy was well tolerated in all patients.7% had osteoradionecrosis and 9% had soft tissue necrosis. Local control rates were 87% for T1 and T2 tumors and 47% for T3 and T4 tumors. The actuarial 2-year local control was 79%. They concluded that HDR – Interstitial brachytherapy as a boost for patients with primary squamous cell carcinomas of the oral cavity and oropharynx is feasible.[25]

Wadsley et al. reviewed the results of Iridium implantation in T1 and T2a carcinoma of the tongue and floor of mouth. 24 patients received

brachytherapy alone as primary treatment. Four patients were treated after surgery due to close or positive margins. Median follow up period was 42 months. Dose delivered was 65 Gy LDR brachytherapy. 2 year OS was 81%, DSS about 91%, local recurrence free survival rate 85% and nodal relapse free survival rate was 76%. Only one patient developed osteoradionecrosis after 7 years. The study concluded that early stage oral cavity cancers can be treated with high local control rate and minimal toxicity using brachytherapy.[26]

Hosokawa et al reported the importance of total treatment time in oral tongue carcinoma treated with brachytherapy and external irradiation. 94 patients were included in the study having stage T1-T2N0. EBRT dose delivered was 35-40 Gy. Brachytherapy dose was 35-40 Gy. The time period for the start of brachytherapy after EBRT was 25.3 days (mean) with standard deviation of 3.5 days. Median follow up period was 59.1 months. The 5-year actuarial survival rate was 78.4%. The local control rate at 5-year was 92.8% for T1 and 62.7% for T2. The local control rate was lower when the total treatment time was more than 43 days (statistically significant). The total treatment time was an important factor influencing local control rate in oral cavity cancers and the estimated loss of local control was 2% per day of treatment exceeding more than 30 days.[27]

Vikram et al. studied the feasibility of brachytherapy in 32 patients, of which, 16 were males and 16 were females. Median age was 60 years. 37.5% had primary in the oral cavity, 31.5% in oropharynx, 12.5% in nasal cavity, 12.5% on the skin, and 6% unknown. 69% received both EBRT (median dose of 52 Gy) and brachytherapy (median dose of 20 Gy), 31% received brachytherapy alone (median dose of 41 Gy). Median follow up period was 22 months. The 2-5 year actuarial local control rate was 77%. 5 patients developed local recurrence. Overall treatment durations including both radiotherapy and brachytherapy over twelve weeks and the time period between EBRT and brachytherapy over five weeks were the two important factors associated with local recurrence. Four patients had osteonecrosis and one had soft tissue necrosis with 25% actuarial complication rate. Complication rates were more with the site of implant as oral tongue. Brachytherapy, as a treatment modality was safe and effective with excellent local control rate but the treatment duration should not be unduly prolonged. Careful patient selection with particular attention to oral – dental hygiene and the positioning of mechanical shields between the implant and the mandible is required to reduce the compliations.[28]

HDR Brachytherapy In Oral Tongue Cancer

Early stage oral tongue cancer can be treated with either surgery or RT with comparable rate of local control. Brachytherapy alone can be used to treat most T1 or T2 lesions. For larger lesions, utilization of both EBRT and brachytherapy is preferred.

Brachytherapy alone is recommended for T1N0 and T2N0 tumors <4 cm. The local control rate is higher than 90% for T1 and T2N0 tumors treated with brachytherapy alone. The local control rate is lower in patients with larger tumors. Approximately 10–30% of patients may develop soft tissue necrosis within the implant volume. Osteoradionecrosis may occur in 5–10% of cases. The vast majority of necroses heal spontaneously after medical treatment. Only 1–2% of patients require surgical intervention.[29]

Mazeron et al. reported on 166 patients with T1-2 lesions who received interstitial brachytherapy. 5-year local control rate of 87% was seen in 155 node negative patients. This compares favourably with a surgical series from MSKCC in New York with local control rate of 85%, 77%, and 50% for T1, T2, T3 lesions, respectively. Additional reports suggest better local control when a brachytherapy was used. Mazeron et al. performed a retrospective analysis and found that the lesions had an increase in local control from 73% to 92% for a dose level from 50-60 Gy to 65-75 Gy associated with the increase in the risk of soft tissue necrosis from 16% to 33%. The authors recommend that dose of 65Gy is sufficient to achieve good local control and a more acceptable soft tissue necrosis level.[30,31]

Guinot et al. studied in 50 patients with oral cancer who were treated with brachytherapy. 84% had Stage T1/2 tumors and16% Stage T3 tumors. 32% had Stage N1, 68% had Stage N0. Interstitial brachytherapy alone was given to 34% (T1/2N0) and 66% received interstitial brachytherapy with EBRT. Median dose of 44 Gy was given in patients treated with brachytherapy alone in 4 Gy per fraction and 18 Gy in 3 Gy/fraction when combined with 50 Gy of EBRT. 3 year and 5 year actual DFS were 81% and 74%. 3 year and 5 year local control rates were 87% and 79% (T1/2); 94.5% and 91% (T3), respectively. 3 year and 5 year local control rate who received both was 80% and 69%. 16% had soft tissue necrosis, 4% had bone necrosis. HDR brachytherapy when given in 3–4 Gy per fraction produced similar results as LDR brachytherapy.[32]

Kakimoto et al. studied role of HDR and LDR brachytherapy in T3 tumors and reported local control rate of 67% after 3 years in patients treated with LDR-interstitial brachytherapy. Whereas local control rate after 3 years with HDR-interstitial brachytherapy was 71%. They concluded that patients treated with HDR-interstitial brachytherapy had similar local control rates to those treated with LDR-interstitial brachytherapy. Kakimoto et al and Yamazaki et al. reported in their retrospective analysis that the local control for T3 mobile tongue was similar for both HDR and LDR, with a majority receiving a combined treatment with EBRT.[33]

HDR Brachytherapy In Floor Of Mouth Cancer

Early stage floor of mouth cancers can be treated with either RT or surgery. Brachytherapy alone can be given for stages T1N0 and T2N0 with less than 3 cm size and greater than 5mm from the mandible. Tumors >3 cm and <4 cm size and >5mm from the mandible can be treated either with brachytherapy or surgery. Surgery is recommended for lesions more than 4 cm size and less than 5mm from the mandible. When compared to oral tongue, the risk of injury to normal tissues for floor of mouth lesions close to mandible is higher which poses a significant risk of osteoradionecrosis, requiring greater care. Floor of mouth implants are essentially similar in approach to oral tongue implants. A Lead mandibular shield should be placed to minimize the risk. However, caution must be taken regarding the size and placement of the shield to avoid obstruction of the implant and unintended protection of the tumor.

Mazeron et al. reported their experience in treating with brachytherapy alone in cancers of floor of mouth and a primary local control rate of 93.5%, 74% for T1N0 and T2N0 was obtained. Factors like tumor size and gingival extension were found to negatively affect local control.[34] Matsumoto et al. reported similar results with brachytherapy using ^{198}Au grains with the local control rate of 89% for T1, 76% for T2 (< = 3 cm), 56% for T2 (>3 cm), respectively. The local control rate for T1-2N0 disease without gingival extension was 82% and with gingival involvement it was 55%.[35]

Marsiglia et al. showed patients with floor of mouth who underwent definitive brachytherapy with local control rate of 93% and 88%, for T1 and T2 lesions, respectively. 18% of patients had bone necrosis that was mostly treated with conservative medical measures. Patients with poor oral hygiene and lack of dental shield were more likely affected with bone complications.[36] Pernot et al. reported the outcomes of carcinoma of the floor of the mouth treated with radiation therapy. 105 patients received EBRT and brachytherapy. 102 patients received brachytherapy alone. The local control rate at 5 year was 97% forT1, 72% forT2, 51% forT3. T1 /T2 N0 patients, particularly T2 N0 had a better prognosis with brachytherapy alone with increased local control and specific survival rates. 6% had severe complication rate with one fatality.[37]

Morrish et al. found that dose and post radiation extractions are the two factors which play an important role in the development of osteoradionecrosis. 50% or higher rates of osteoradionecrosis were reported with doses of >75 Gy. Beumer et al. reviewed 83 cases of osteoradionecrosis with 78 involving the mandible and found out that post radiation extractions and periodontal diseases were the most common precipitating factors. 44% of those cases who received doses greater than 70 Gy need to undergo mandibular resection. Dental care shielding, patient selection, brachytherapy technique and dose should be given proper attention to minimize this complication.[38]

HDR Brachytherapy In Buccal Mucosal Cancer

Incidence of cancer in the buccal mucosa is high in Southeast Asian countries due to common use of chewing tobacco and areca nut containing products. This can lead to oral sub mucous fibrosis a precancerous lesion in the mouth which may progress to frank malignancy in due course of time. Interstitial brachytherapy alone may be an option for these lesions. For advanced lesions either surgery or a combination of EBRT and brachytherapy may be considered.

Brachytherapy alone can be given for tumors which are <4 cm in diameter and less than 1.5 cm in thickness. It is not indicated when the tumor involves intermaxillary commissure or the bucco-alveolar sulcus. Various techniques are available for implant. Lapeyre et al. described two techniques in the treatment of buccal mucosa, either a parallel wire technique or a loop technique. Loop technique constitutes radioactive wires or loop to encircle the tumor posteriorly. Lesions less than 1 cm in thickness, a single parallel plane implant is sufficient. Otherwise, a multiplane implant, most commonly double plane implant may be required. Mandible must be 5mm away from the nearest implanted catheters. To protect the surrounding structures including the mandible, customized mandibular lead-lined shields should be used along the buccoalveolar sulcus.[39]

Lapeyre et al. compared the two techniques in 36 patients. Stage T1-3 was included. Median dose of 65 Gy was given. Parallel wire technique was used in 14 patients and loop technique in 22 patients. Seven patients had local failure. Six patients had local failure with the parallel wire technique whereas only one patient with loop technique. The actuarial local control rate at 5 years was 91% for loop and 58% for parallel wire techniques. 17% rate of incidence of complications was reported and among them soft tissue necrosis was the most common complication.[39]

One of the largest reviews of buccal mucosa cancers was done by the European Group of Curie therapy, where 226 patients were received brachytherapy alone, 80 patients were received brachytherapy and EBRT and 273 patients were received EBRT alone. Brachytherapy alone patients had 81% local control, combined treatment arm had 65% and EBRT alone arm had 66%.[40]

Kotsuma et al. retrospectively reviewed data for 36 patients with buccal mucosa carcinoma treated with brachytherapy alone or with EBRT. Among them 25 were males, 11 were females.12 patients had nodal disease. Median dose of 70 Gy LDR interstitial brachytherapy was used in 15 cases and 48 Gy HDR- interstitial brachytherapy was used in 14 cases. 7 patients received brachytherapy with mold technique with 15 Gy median dose. 31 patients also received 24-48 Gy EBRT. Median follow up period was 75.5 months.

The local control and PFS rate at 5year was 75.7% and 67.7%. The local control rate for T1 was 100%, T2 was 85.6%, T3 was 53.6% and T4 was 33.4%. Good local control was achieved with HDR-interstitial brachytherapy. Patients with early-stage lesions achieved higher local control rate. 2 patients who were treated with LDR interstitial brachytherapy developed Grade 3 or higher late complications.[41]

HDR Surface Mold Therapy In Oral Cancer

Nishimura et al. reported the effectiveness of HDR brachytherapy using molds. Sites included were buccal mucosa, floor of mouth and gingiva. Two of the buccal mucosa patients had retromolar extension. Eight patients were treated using molds. A customized mold was prepared for each patient with two to four catheters. Patients received 40-60 Gy EBRT in 2 Gy per fraction. Four to seven fractions of 3–4 Gy were given after external radiation. HDR total dose ranged from 16–28 Gy. Four had local recurrence in spite of initial 88% complete response. There were no serious late complications like ulcer or bone exposure.[42]

Matsuzaki et al treated 5 patients. Sites included were buccal mucosa (4) and lip (1) using mold technique after external radiation. Follow-up period was 2–40 months. One patient developed local recurrence, others were disease free. The study concluded that customized mold can be a viable alternative to other therapeutic modalities in lip and buccal mucosa carcinoma.[43]

Comparison Of EBRT Alone With EBRT And Brachytherapy Boost

The efficacy of treatment with external beam radiotherapy alone in comparison with EBRT and brachytherapy is controversial. Housset et al. concluded that brachytherapy boost was superior to external radiation alone for T1 and T2 tumors.[44] The size of the tumor is a significant predictor of local control. The results of HDR brachytherapy for oral tongue, buccal mucosa and floor of mouth cancers based on T-stage/anatomical site are shown in the Tables 1 and 2 below.

CONCLUSION:

HDR Interstitial brachytherapy used as a boost to EBRT in oral cavity cancers provides results comparable to that of surgery, with the advantages of organ preservation, better functional and cosmetic outcomes. Toxicity is much lesser in normal tissue as dose received by them is minimal to comprehend any complication. Toxicities can be minimized with better tumor control by good brachytherapy techniques and meticulous planning. From the various studies and literature quotes, brachytherapy with or without EBRT can be considered an alternative to surgery in early and locally advanced oral cavity cancers. HDR brachytherapy remains an important option for treatment of oral cavity cancer.

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Table 1: Results Of HDR Brachytherapy For Oral Tongue Cancer Based On T-stage

Study	Patra et al [22]	Guinot et al [32]	Yamazaki et al [23]			Kakimoto et al [33]	
¶n	13OPC, Oral tongue-18, FM-2	50 oral	80HDR	217 Ra-226	351 Ir-192	14 HDR	61 LDR Ir–192
T category	Earlystage(I,II)15, Advanced (III,IV) 18	42early stage, 8T3 16N+	24T1, 47T2, 9T3	77T1, 103T2, 37T3	111T1, 202T2, 38T3	All T3	
§Schedule	EBRT: 50Gy (46–66Gy)+ Bx: 3–3.5Gy × 4–7 (14–21Gy)	33 EBRT:50Gy+ Bx:3Gy×6 (12–24.5Gy) 17Bx only: 4Gy×11 (42–49Gy)	EBRT:37Gy± Bx: 6Gy× 6–10	EBRT:29Gy±Bx: 72Gy (59–94Gy)	EBRT:30Gy±Bx: 72Gy (59–94Gy)	EBRT: 30Gy (12.5–60 Gy) ± Bx: 6Gy×10	EBRT: 30Gy (12.5–60Gy) ± Bx: 72Gy (50–94Gy)
†Local control	79%CR+21%PR	Bx100% vsEBRT+Bx 69%				71%(2y)	67%(2y)
T1	100%early	94%	87%	85%	79%		
T2		84%	79%	75%	73%		
T3	78% Advanced disease**	0%	89%	62%	64%		
T4							

n=number of patients, EBRT = External Beam Radiotherapy,Bx= Brachytherapy, OPC=Oropharyngeal cancer, ia=intra-arterial infusion, CR=complete response, PR=partial response, LRC=locoregional control, CRT=chemoradiotherapy, **including surgical salvage, ¶HDR unless otherwise stated, §twice a day unles sotherwise stated, † 5y unless otherwise stated, HDR = High Dose Rate, LDR = Low Dose Rate, N+ = Node positive, Ra= Radium, Ir = Iridium.

Table 2: Results Of HDR Brachytherapy For Oral Cancer Based On T-stage

Author	InoueT et al [45]		Chu et al [46]	Pernot et al [37]	Rudoltz et al [25]	Kotsuma et al [41]	
¶n-Subsite	16 HDR FM	41 LDR^{198} Au–FM	FM	207 FM	55various 16 oral (FM-9, BM-1, 6Oral tongue) + 39OPC	36BM 14HDR, 15LDR*, 7Mold**	
T category	4T1, 11T2, 1T3	22T1, 19T2	N/A	N/A	16T1, 26T2, 8T3, 5T4	3T1, 23T2, 7T3, 3T4, 12N+	
§Schedule	EBRT: 30–40Gy ± Bx: 6Gy×6–8	EBRT: 30–40Gy ± Bx: 65–85Gy	EBRT: 50Gy+ Bx: 30Gy	105 EBRT + Bx, 102 Bx only	EBRT: 55.2Gy (45–70.2Gy) Bx: 16.8Gy (12–30Gy) 1.2–5Gy/fx	LDR*: EBRT+ Bx: 70Gy (42.8-110Gy)	HDR: EBRT+ Bx: 6Gy×8fr (24–60Gy)
†Local control	94%	69%			79% (2y)	80% HDR Vs. 65% LDR	
T1	100%	85%	98%	97%	87%	100%	
T2	100%	67%	88.5%	72%		85.6%	
T3				51%	47%	53.6%	
T4						33.3%	

Abbreviations: n = number of patients, Bx = brachytherapy, EBRT = external beam radiotherapy, OPC = oropharyngeal cancer, LP = lip, BM = Buccal mucosa, FM = floor of mouth, *LDR–10Ra–226, Ir–192,2Au–198 and 1I–125, **Mold=LDR Ir–192 and Cs–137, †5y unless otherwise stated, ¶HDR unless otherwise stated, §bid unless otherwise stated, N/A=not available

REFERENCES

1. Shah JP, Gil Z. Current concepts in management of oral cancer – Surgery. Oral Oncol 2009;45:394–401.
2. Bernier J, Domenge C, Ozsahin M, et al. Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. N Engl J Med 2004;350:1945-52.
3. Cooper JS, Pajak TF, Forastiere AA, et al. Postoperative concurrent radiotherapy and chemo-therapy for high-risk squamous-cell carcinoma of the head and neck. N Engl J Med 2004;350:1937-44.
4. Blanchard P, Baujat B, Holostenco V, et al. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): A comprehensive analysis by tumour site. Radiother Oncol 2011;100:33–40.
5. National Comprehensive Cancer Network (2012) NCCN guidelines for Head and Neck cancers. Available:http://www.nccn.org/professionals/physician_gls/f_guidelines.asp as accessed on 05-01- 2013.
6. Ang KK, Trotti A, Brown BW, et al. Randomized trial addressing risk features and time factors of surgery plus radiotherapy in advanced head-and-neck cancer. Int J Radiat Oncol Biol Phys 2001; 51:571–8.
7. Pfreundner L, Willner J, Marx A, et al. The influence of the radicality of resection and dose of postoperative radiation therapy on local control and survival in carcinomas of the upper aerodigestive tract. Int J Radiat Oncol Biol Phys 2000;47:1287-97.
8. Brucer M. Brachytherapy. Am J Roentgenol Radium Ther Nucl Med 1958;79:1080-90.
9. International Commission on Radiation Units and measurements (ICRU), "Dose and volume specification for reporting intracavitary therapy in gynecology", ICRU Report 38, ICRU, Bethesda, Maryland, USA:1985.
10. Han P, Hu KS, Shankar RA, et al. Head and Neck Brachytherapy. In: Devlin P, editor. Brachytherapy: Applications and Techniques. Philadelphia, PA: Lippincott, Williams and Wilkins; 2007. p.223–68.
11. Vikram B, Mishra S. Permanent iodine-125 implants in postoperative radiotherapy for head and neck cancer with positive surgical margins. Head Neck 1994;16:155-7.
12. Clarke DH, Edmundson GK, Martinez A, et al. The utilization of I-125 seeds as a substitute for Ir-192 seeds in temporary interstitial implants: an overview and a description of the William Beaumont Hospital technique. Int J Radiat Oncol Biol Phys 1988;15:1027-33.
13. Paterson R, Parker HMA. A dosage system for gamma ray therapy. Br J Radiol 1934; 7:592-612.
14. Quimby EQ. Dosage tables for linear radium sources. Radiology. 1944;43:572.
15. Quimby EQ. The grouping of radium tubes in packs on plaques to produce the desired distribution of radiation. Am J Roengenol. 1932;27:18.
16. Glasser O, Quimby EH, Taylor LS. Physical foundations of radiology, New York: Harper & Row; 1961.
17. Pierquin B, Dutreix A, Paine C. The Paris system in interstitial radiation therapy. Acta Radiol Oncol 1978;13:33.
18. Dutreix A, and Marinello G. The Paris system in Modern brachytherapy. Pierquin B, Wilson JF, Chassagne D.(Eds). New York: Masson; 1987. p.25-42.
19. Henschke U, Hilaris BS, Mahan GD. Afterloading in interstitial and intracavitary radiation therapy. Am J Roentgenol 1963;90:386-95.
20. Pierquin B, Marinello G. Palatal tonsillar region. In: Wilson F, editor. A practical manual of brachytherapy. Madison: Medical Physics Publishing; 1997. p.108-9.
21. Nag S, Cano ER, Demanes DJ, et al. American Brachytherapy Society. The American Brachytherapy Society recommendations for high-dose-rate brachytherapy for head-and-neck carcinoma. Int J Radiat Oncol Biol Phys 2001; 50:1190-8.
22. Patra NB, Goswami J, Basu S, et al. Outcomes of high dose rate interstitial boost brachytherapy after external beam radiation therapy in head and neck cancer--an Indian (single institutional) learning experience. Brachytherapy 2009; 8:248-54.
23. Yamazaki H, Yoshida K, Yoshioka Y, et al. High dose rate brachytherapy for oral cancer. J Radiat Res 2013;54:1–17.
24. Mohanti BK, Sahai P, Thakar A et al. Institutional Experience of Interstitial Brachytherapy for Head and Neck Cancer with a Comparison of High- and Low Dose Rate Practice. Asian Pac J Cancer Prev 2014;15(2):813-8.
25. Rudoltz MS, Perkins RS, Luthmann RW, et al. High-dose-rate brachytherapy for primary carcinomas of the oral cavity and oropharynx. Laryngoscope1999;109:1967–73.
26. Wadsley JC, Patel M, Tomlin SC, et al. Iridium-192 implantation for T1 and T2a carcinoma of the tongue and floor of mouth: retrospective study of the results of treatment at the Royal Berkshire Hospital. Brit J Radiol 2003;76:414–7.
27. Hosokawa Y, Shirato H, Nishioka T, et al. Effect of treatment time on outcome of radiotherapy for oral tongue carcinoma. Int. J. Radiation Oncology Biol. Phys 2003;57:71–8.
28. Vikram B, Beitler JJ, Sood BM, et al. High dose rate brachytherapy with or without external beam radiation therapy in previously untreated cancers of the head and neck region. Int. J. Radiation Oncology Biol. Phys 1999;45(3):378.
29. Mazeron JJ, Ardiet JM, Haie-Méder C, et al. GEC-ESTRO recommendations for brachytherapy for head and neck squamous cell carcinomas. Radiother Oncol 2009;91:150–6.
30. Spiro RH, Strong EW. Epidermoid carcinoma of the mobile tongue. Treatment by partial glossectomy alone. Am J Surg 1971;122:707-10.
31. Mazeron JJ, Crook JM, Benck V, et al. Iridium 192 implantation of T1 and T2 carcinomas of the mobile tongue. Int J Radiat Oncol Biol Phys 1990;19:1369-76.
32. Guinot JL, Santos M, Tortajada MI, et al. Efficacy of high-dose-rate interstitial brachytherapy in patients with oral tongue carcinoma. Brachytherapy 2010;9:227–34.
33. Kakimoto N, Inoue T, Inoue T, et al. Results of low and high–dose-rate interstitial brachytherapy for T3 mobile tongue cancer. Radiother Oncol 2003;68:123–8.
34. Mazeron JJ, Grimard L, Raynal M, et al. Iridium-192 curietherapy for T1 and T2 epidermoid carcinomas of the floor of mouth. Int J Radiat Oncol Biol Phys 1990;18:1299-306.
35. Matsumoto S, Takeda M, Shibuya H, et al. T1 and T2 squamous cell carcinomas of the floor of the mouth: Results of brachytherapy mainly using 198Au grains. Int J Radiat Oncol Biol Phys 1996;34:833-41.
36. Marsiglia H, Haie-Meder C, Sasso G, et al. Brachytherapy for T1-T2 floor-of-the-mouth cancers: The Gustave-Roussy Institute experience. Int J Radiat Oncol Biol Phys 2002;52:1257-63.
37. Pernot M, Hoffstetter S, Peiffert D, et al. Epidermoid carcinomas of the floor of mouth treated by exclusive irradiation: Statistical study of a series of 207 cases. Radiother Oncol 1995;35:177-85.
38. Morrish RB Jr, Chan E, Silverman S Jr, et al. Osteonecrosis in patients irradiated for head and neck carcinoma. Cancer 1981;47:1980-3.
39. Lapeyre M, Peiffert D, Malissard L, et al. An original technique of brachytherapy in the treatment of epidermoid carcinomas of buccal mucosa. Int J Radiat Oncol Biol Phys 1995;33:447-54.
40. Gerbaulet A, Pernot A. Cancer of the buccal mucosa-proceedings of the 20th annual meeting of the European Curietherapy Group. J Eur Radiother 1985;6:1-4.
41. Kotsuma T, Yoshida K, Yoshida M. Brachytherapy for buccal cancer: evaluation of HDR-ISBT. 2008;20:141.
42. Nishimura Y, Yoshihiko Yokoe Y. High-dose-rate brachytherapy using molds for oral cavity cancer: The technique and its limitations. Int J Clin Oncol 1998;3:351–6.
43. Matsuzaki H, Takemoto M, Hara M, et al. Two-piece customized mold technique for high-dose-rate brachytherapy on cancers of the buccal mucosa and lip. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2012; 113:118–25.
44. Housset M, Baillet F, Dessard-Diana B, et al. A retrospective study of three treatment techniques for T1-T2 base of tongue lesions: surgery plus postoperative radiation, external radiation plus interstitial implantation and external radiation alone. Int J Radiat Oncol Biol Phys 1987;13:511-6.
45. Inoue T, Inoue T, Yamazaki H, et al. High dose rate versus LDR interstitial radiotherapy for carcinoma of the floor of mouth. Int J Radiat Oncol Biol Phys 1998;41:53–8.
46. Chu A, Fletcher GH. Incidences and causes of failure to control by irradiation the primary lesion in squamous cell carcinomas of the anterior two thirds of the tongue and floor of mouth. Am J Roentgenol 1973;117:502-8.
47. Kotsuma T, Yoshida K, Yoshida M. Brachytherapy for buccal cancer: evaluation of HDR-ISBT. 2008;20:141.