# High-dose-rate interstitial brachytherapy in head and neck cancer: do we need a look back into a forgotten art – a single institute experience

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#### Abstract

**Purpose:** To evaluate the treatment outcomes with high-dose-rate (HDR) interstitial brachytherapy (HDR-BRT) in head and neck cancers (HNC).

**Material and methods:** Fifty-eight patients with HNC as per American Joint Committee on Cancer (AJCC) TNM staging criteria were analyzed retrospectively between 2008 and 2015. Forty-two patients received external beam radiotherapy (EBRT) with HDR-BRT and 16 patients received BRT alone. The survival was calculated with respect to median biological equivalent doses (BED) and median 2 Gy equivalent dose (EQD<sub>2</sub>), keeping  $\alpha/\beta$  = 10 for tumor. Loco-regional control and disease free survival was assessed.

**Results:** The median follow-up period was 25 months (2-84 months). The disease-free survival (DFS) probability at year 1 was 82.7%, and 68% at year 7. The overall survival probability was 91.3% at year 1 and 85.8% at year 7. The local control rate was 70%. The rate of recurrence was 30%. Distant metastasis rate was 17.2%. The median BED and EQD<sub>2</sub>, respectively, were 86.78 Gy and 71.6 Gy. The DFS was 74.1% and 75.9% in patients receiving a dose more than median BED and EQD<sub>2</sub>, respectively, and was 64.8% and 61.5% for less than the median dose.

Conclusions: The overall outcome was good with implementation of HDR-BRT used alone or as boost, and shows DFS as better when the dose received is more than the median BED and median  $EQD_2$ . The role of HDR-BRT in HNC is a proven, effective, and safe treatment method with excellent long term outcome as seen in this study, which reflects the need for reviving the forgotten art and science of interstitial brachytherapy in HNC.

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Key words: BED, EQD<sub>2</sub>, HDR, head and neck cancer, interstitial brachytherapy.

## Purpose

Head and neck cancer (HNC) is the most common cancer in India, and consists of about one-third of all cancers [1,2,3]. According to the Indian Council of Medical Research (ICMR), approximately 0.2 to 0.25 million new HNC patients are diagnosed each year [4]. The majority of patients with HNC have a locally advanced stage at diagnosis, and presently, multimodality treatment remains the main stay i.e., radiotherapy in combination with surgery, chemotherapy, and/or biological therapy. Small percentage of patients with early stage (T1N0) is offered radical brachytherapy (BRT) alone or radical external beam radiation (rEBRT) alone, or combination of moderate dose external beam radiotherapy (mEBRT), followed/preceded by BRT boost similar to radical surgery i.e., wide local excision (WLE). Larger lesions (T2N0) with high nodal spread potential are offered rEBRT or mEBRT + BRT similar to radical surgery WLE with neck dissection i.e.,

modified neck dissection, which could be either ipsilateral or bilateral (WLE + MND [B/L or IL]). Advances in chemotherapy and its concurrent use with radiation in LAD (T3N + excluding N2a/3) has allowed to reduce the tumor size (primary and/or nodes), and allowed to boost the primary using BRT with increase in local control (LC) rates.

Brachytherapy remains best conformal form in the radiation armamentarium. With the advent of high-doserate brachytherapy (HDR-BRT), having an advantage of avoiding radiation exposure to health care providers and with fractionated radiation scheme, HDR-BRT has replaced low-dose-rate (LDR) and even pulse-dose-rate (PDR) (practiced at few centers) in most centers where BRT is commonly used, as sole or adjunct therapeutic measure, and the use of BRT has been proven in various other sites [5,6]. The advantage of BRT is that it provides a localized high dose of radiation, with rapid fall-off beyond planning treatment volume or implant treatment

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Received: 05.11.2016 Accepted: 04.03.2017 Published: 28.04.2017 volume (PTV/ITV), sparing normal surrounding tissue, and short overall treatment time [7]. Brachytherapy is an important alternative to 'conventional full/radical dose' EBRT, since rEBRT is known to have detrimental effect on adjacent normal tissues, such as the parotids, salivary glands, mandible, and muscles of mastication. With advent of stepping source technology, there is an advantage of optimizing dose distribution by varying dwell times and dwell positions with graphical representation of dose volume histogram (DVH), which has been able to help us know the dose received by clinical target volume (CTV) and organs at risk (OAR), and has resolved the complicated dosimetry concerns.

There has been a rise in use of HDR-BRT in other forms of cancers, especially gynecological malignancies; however, HDR usage for HNC is decreased in Group I institutes (those in countries with the highest GDP) from 5% (2002) to 2% (2007) [8], and because of low incidence of HNC in those countries. Brachytherapy as a treatment option is not used commonly by different centers and is linked to availability of appropriate infrastructure, cost of isotope, expertise etc. The other reasons for reduced acceptability are lack of experience/expertise, complex application (fear of injuring close vital vessels), and curved anatomical structure or shape, complicated dosimetry, and biological concerns [9,10]. There have been recent reports of HDR/LDR brachytherapy employed as a therapeutic modality for HNC [11,12,13].

With lack of substantial uniform literature related to HDR-BT in HNC, we present data from our Institute in regards to the disease free and survival benefits in various sites of HNC using interstitial implants.

#### Material and methods

#### **Patients**

This study consists of consecutive retrospective patients, and was completed to evaluate the benefit of using EBRT and interstitial BRT, or radical BRT in various HNC since the beginning of the department at our center. Fifty-eight patients were treated with interstitial HDR-BRT for various sites of HNC between December 2008 and August 2015. The study population included 41 males and 17 females, with a median age of 56 years (range, 27-81 years). Squamous cell carcinoma was confirmed in all patients. All patients had a Karnofsky Performance Status of at least 70, and their disease was staged based on the clinical, endoscopic, and radiologic findings using AJCC 2010 staging. Forty-two patients underwent EBRT (median dose 46 Gy) followed by BRT, whereas 16 patients received BRT alone. Patient characteristics are shown in Table 1.

#### External beam radiation therapy

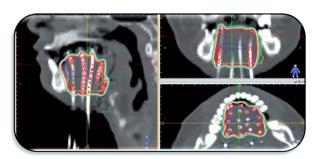
External beam radiation therapy was delivered using multiple beams encompassing the primary tumor and bilateral upper neck nodes using photon beams with Linear Accelerator (Siemens Oncor Expression, Germany) with 6 MV energy with either 3DCRT or IMRT. External beam radiation therapy planning target volume included gross tumor volume (GTV), and CTV 1 (CTV with adequate

Table 1. Patient characteristics

Characteristics	No. of patients				
Sex					
Male	41 (70	.69%)			
Females	17 (29.31%)				
Age					
Median	56.1 (range, 27-81 years)				
Treatment method					
EBRT + brachytherapy	42 (72.41%)				
Brachytherapy alone	16 (27.59%)				
Tumor size (cm)					
Median	3.0 cm (range	e, 1.5-5.5 cm)			
Primary/treatment site	EBRT + BRT	BRT alone			
Oral cavity	16	5			
Lip	2	1			
Buccal mucosa	1	0			
Lateral border of tongue	12	2			
Hard palate	1	2			
Oropharynx	20	3			
Base of tongue	11	1			
GE fold/vallecula	2	0			
Tonsil	5	0			
Soft palate	2	2			
Nasopharynx	1	1			
Miscellaneous	1	1			
Recurrent	4	6			
Tumor and nodal stage					
T1	8 (1	7%)			
T2	21 (44	1.7%)			
T3	11 (23	3.4%)			
	7 (14	.9%)			
NO	31 (66%)				
N1	9 (19.1%)				
N2	7 (14.9%)				
Follow-up duration					
Median	25 months (rang	ge, 6-84 months			
Adjuvant chemotherapy					
Time to relapse					
Median	12 months (rang	e, 3-60 months)			

 $\it EBRT-external\ beam\ radiation\ the rapy,\ BRT-brachy the rapy,\ GE\ fold-glosso-epiglottic\ fold$ 

Miscellaneous includes basal cell carcinoma of skin and external auditory meatus



**Fig. 1.** Computed tomography image of catheter implantation in case of floor of mouth

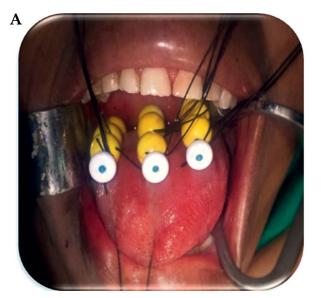
margins around GTV) and CTV 2 (neck nodes). Patients were treated with 2 Gy per fraction; 5 d/week. External beam radiotherapy dose is kept low whenever possible to salvage salivary gland without jeopardizing the risk of LR control or survival. All these patients were reviewed closely during the course of EBRT for BRT boost plan. The patient response was assessed prior to planning for BRT in form of disease regression by clinical evaluation, and when needed, with radiological evaluation in form of computed tomography of head and neck.

## Brachytherapy

The implant procedure was performed under general anesthesia. A nasogastric tube was placed for feeding during treatment. A straight stainless-steel needle was introduced through the sub-mental skin with respect to the site, and traversed through the floor of mouth or implanting organ, exited at the other end of operative bed. Subsequent needles passed next to the first one as needed with respect to number of lines and planes in order to keep interval distance of 14-16 mm between them, according to the need to cover the target. A plastic catheter was threaded through each needle, and then the needle was removed, leaving the catheter in place. The number of

catheters varied according to the dimension of the target. The plastic catheters were placed in the operative bed as near parallel as possible at 14 to 16 mm intervals, taking care of peripheral fall-off with a security margin of 10 mm in all directions about the target, using the modified technique. The catheters were held to the skin exit points with plastic buttons [11,14]. This implantation technique was used for the various HNC sites. Prophylactic tracheostomy was not done routinely, except for one patient where lingual surface of epiglottis was involved. After the implant procedure, all patients underwent a computed tomography (CT) scan with a slice thickness of 3 mm for three-dimensional (3D) treatment planning. Intravenous contrast was used when necessary to visualize the carotid vessels. The CT study was transferred to the Flexiplan system (Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden), and PTV and OAR were contoured and catheters were reconstructed. The treatment planning process was done by computer assisted dose optimization (Figure 1). The prescribed dose was in the range of 3.5-4.5 Gy per fraction, depending on the site and status of the disease. The median fractions numbers of fractions were 10 and were given twice a day fractions 6 hours apart. The dose parameters were assessed through DVH in percentage. Prescribed and reported doses were specified by D<sub>90</sub>, as determined by DVH. The implant was planned after 2-3 weeks of completion of EBRT. Median gap between external and implant was 21 days. Figure 2A and 2B show the elastic bead placement using Bhalavat's technique, and CT image of the implant with catheter reconstruction and planning, respectively.

The implant tubes were removed after the planned BRT doses were delivered. Total dose (EBRT/BRT) is kept within tolerance levels and has been assessed by estimating biologically equivalent doses (BED). We attempted to calculate the delivered BED (EBRT/BRT/total) from given radiation doses using a formula suggested by Jones *et al.* [15] and to correlate the outcome in terms of various control rates. The BED of the EBRT + BRT and BRT alone



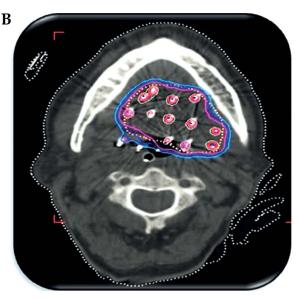


Fig. 2. A) Plastic bead placement using Bhalavat's technique. B) Computed tomography image of the implant with catheter reconstruction and planning

are mentioned in Table 2, keeping  $\alpha/\beta = 10$ . For case of hard palate, surface mould BRT was applied and intranasal BRT used for a case of nasopharynx.

#### Follow-up

Patients underwent follow-up evaluation at every 4 weeks for the first 6 months, every 3 months for the next 6 months, every 6 months for the next 3 years, and annually thereafter. Biopsy was avoided unless it was essential to confirm residual/recurrent disease. Overall, follow-up ranged from 6 to 84 months (median, 25 months) for all the patients. Twenty-nine patients reached the two-year follow-up, and of these, 8 patients reached the five-year follow-up; these patients were alive at the time of reporting in December 2015. The patients were followed-up with routine investigations including complete blood counts, chest X-ray, and ultrasonography of the neck. In suspicious cases, CT of the neck was done.

### Statistical analysis

Statistical analysis was performed using SPSS 17.0 (Statistical Package for Social Sciences 17.0 for Windows) statistical software. Survival results were calculated using the Kaplan-Meier method and log-rank test. The time origin was the date of the first HDR-BRT procedure. The endpoint of overall survival (OS) was death from any cause. The endpoint of DFS was any type of recurrence (e.g. failure at the primary site or regional lymph nodes, distant metastasis). The endpoint of interest from local control (LC) was defined as tumor regrowth in the treated area with BRT or in an adjacent region (e.g. failure at the primary site or regional lymph nodes). The patient DFS and OS was calculated from the last date of their follow-up.

#### Results

#### Patient and disease characteristics

The study consists of 58 patient with 41 males and 17 females, with age ranging from 27-81 years (median age, 56). Twenty-one patients had T2 and 11 had T3 tumor. Nodal status showed that 31 patients were node negative, and 9 had N1 disease and 7 had N2 disease. Other characteristics are mentioned in Table 1.

The median time from the end of primary treatment to recurrence was 12 months (range, 3-60 months).

### Treatment and dose characteristics

Forty-two patients received EBRT followed by BRT (including 4 recurrent cases), and 16 patients received radical BRT alone (including 6 recurrent cases). All patients received a total dose of 21-65 Gy (mean, 47.6 Gy; median, 46 Gy) as EBRT, followed by BRT 9-41 Gy (mean, 22.9 Gy; median, 22.5 Gy), and the total dose of 16-53 Gy (mean, 40.7 Gy; median, 44.5 Gy) in cases receiving radical BRT. The median implant volume was 41 cm³ (range, 25-82 cm³). Of the 4 recurrence patients who underwent EBRT followed by BRT, the median dose for EBRT was 56 Gy and for BRT was 22.5 Gy, and the median total dose in 6 recurrent cases receiving radical BRT was 40.5 Gy (range, 31.5-53 Gy).

**Table 2.** Biological equivalent dose and other parameters in external beam radiation therapy and brachytherapy

Dose parameters	EBRT + BRT (Gy)	Brachytherapy alone (Gy)
BED (Gy)	Mean, 89.5	Mean, 58.2
	Median, 88.9	Median, 63.1
EQD <sub>2</sub> (Gy)	Mean, 74.5	Mean, 48.4
	Median, 74.1	Median, 52.5

BED-biological equivalent dose, Gy - Gray,  $EQD_2-2$  Gy equivalent dose, EBRT-external beam radiation therapy, BRT-brachytherapy

#### Local control

Post-external beam radiation therapy complete response was observed in 81.2% and partial response was seen in 18.8%. After BRT, all patients had complete response. Local control rate was 70% and recurrence rate was 30%. There was no neck relapse in any cases treated with combination radiation, whereas one patient of soft palate treated with radical BRT developed a node, which was treated with modified neck dissection (MND) plus post-operative radiation, and remained loco-regionally controlled till the last follow-up.

#### Radiobiological characteristics and survival

The BED and 2 Gy equivalent dose (EQD<sub>2</sub>) were calculated keeping  $\alpha/\beta=10$  (tumors). The resultant doses are mentioned in Table 2 for both treatment modalities. The median BED for EBRT + BRT was 88.9 Gy, and median BED for BRT alone was 63.1 Gy. The median BED was taken as the cut-off value, and patients were subsequently evaluated for the DFS. The median BED for EBRT + BRT was 88.9 Gy, and for radical BRT was 63.1 Gy; median EQD<sub>2</sub> was 74.1 Gy and 52.5 Gy, respectively. The DFS was 73.7% for EBRT + BRT with dose more than median BED, and 65% for less than the median BED. Similarly, the DFS was 87.5% for BRT alone with dose more than median BED, and 37.5% less than the median BED.

## Brachytherapy dosimetric characteristics and parameters

The dose parameters were evaluated and optimization assessed. Dose heterogeneity was specified by  $V_{100}$  (the percentage of implant volume receiving 100% of the prescribed dose),  $V_{150}$  (the percentage of implant volume receiving 150% of the prescribed dose), and  $V_{200}$  (the percentage of implant volume receiving 200% of the prescribed dose) [16]. In our series, the mean values were:  $D_{90} = 4.07$  Gy (range, 3.9-4.5 Gy), equivalent to 90.4% of the reference dose of 4.5 Gy;  $V_{100} = 93.33\%$  (range, 92-95%);  $V_{150} = 23.7\%$  (range, 18-41%);  $V_{200} = 12.52\%$  (range, 11-25%). The mean values of homogeneity index (HI) and dose non-uniformity ratio (DNR) were estimated to be 0.69 (range, 0.61-0.75) and 0.37 (range, 0.29-0.41), respectively.

**Table 3.** Local control in T1, T2 and recurrence case

Presentation	EBRT + BRT	Brachytherapy alone
LC T1	3 (100%)	5 (100%)
LC T2	16 (84.2%)	2 (100%)
Recurrence	2 (50%)	2 (33.3%)

LC – local control, EBRT – external beam radiation therapy, BRT – brachytherapy

#### Follow-up and survival evaluation

The various outcomes in the form of LC, local relapse, regional recurrence, and distant metastasis for both the treatment modalities are illustrated in Table 3. The overall LC rate in EBRT + BRT was 66.7% and in BRT alone was 56.3%. Distant metastasis with loco-regional failure was seen in 32.3%, and 43.75% patients undergoing EBRT + BRT and BRT alone, respectively. Three patients were lost to follow-up. In early stage of disease, the LC rate were 100% in T1 lesion in both treatment modalities, and 84.21% in EBRT + BRT and 100% in BRT alone in T2 lesions. In cases of recurrences alone, i.e., 4 patients receiving EBRT followed by BRT and 6 patients receiving BRT alone, the local control was 50% and 33.33%, respectively. The details are illustrated in Table 4. A case of floor of mouth cancer has been depicted in Figure 3 before treatment and after treatment with BRT.

The local control as per the site and stage are mentioned in Table 5 and Table 6. The results shows that the outcomes are better for the early stage tumors, and propensity for distant metastases increases with growing stage of the disease (p < 0.01). The site wise results showed no significant statistical significance (p < 0.56). Similarly, the results of disease outcomes are mentioned in Table 7 for BRT alone, which show similar results as

**Table 4.** Disease free survival in relation to biological equivalent dose

Radiobiological parameter	Treatment modality and DFS		
	EBRT + BRT	BRT alone	
Less than median BED	13/20 (65%)	3/8 (37.5%)	
More than median BED	14/19 (73.7%)	7/8 (87.5%)	
Less than median EQD <sub>2</sub>	12/20 (60%)	3/8 (37.5%)	
More than median EQD <sub>2</sub>	15/19 (78.9%)	7/8 (87.5%)	

BED – biological equivalent dose, Gy – Gray,  $EQD_2$  – 2 Gy equivalent dose, EBRT – external beam radiation therapy, BRT – brachytherapy, DFS – disease free survival

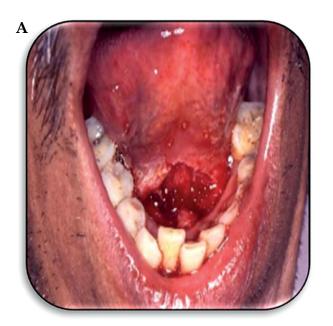
those for EBRT + BRT. The 2-year OS probability was 91.4%, and DFS was 80.9%. At 5-years, OS was 85.6% and DFS was 68.1%.

#### Acute and late toxicity

Among all the patients, only one patient developed osteoradionecrosis (ORN); no other significant late toxicities were noted. Acute toxicity was assessed using RTOG toxicity scales, and acute toxicity in the form of infection was seen in 2 patients and managed conservatively. Bleeding was not seen in any of the patients. Late toxicity in the form of soft tissue necrosis (STN/STF) was seen in 2 patients (3.44%).

## Discussion

Head and neck cancers form a large percentage in India, and are responsible for one-third of total malignancies. Most of them are presented in advanced stages (80-85%). Oral cavity and oropharynx are essential in coordinating the complex functions of deglutition, phona-



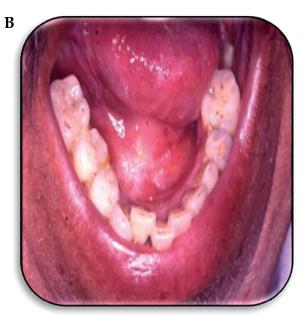


Fig. 3. A) Case of cancer of floor of mouth before treatment. B) After brachytherapy treatment

tion, and respiration (airway fluency), and preserving its function is a difficult challenge when treating carcinoma in this anatomical region. Oral cavity and oropharynx are responsible for 50% of total HNC. Association of dysphagia is extremely common with these locations.

The treatment modalities available include surgery, EBRT, BRT, chemotherapy, and various combinations. The goal of treatment is to remain improved LC/DFS/ OS with acceptable sequel from the treatment offered with acceptable quality of life for longer survivors. Good loco-regional control rates with surgery for oral tongue and oropharynx have been reported at the expense of functional outcome, and the placement of permanent gastrostomy tubes and/or tracheostomy to support nutrition and prevent aspiration, respectively, are not uncommon. Nonsurgical treatments with combined radio-chemotherapy significantly improved tumor control and DFS, but are reported to be associated with a substantial increase in adverse effects. Although the patients do not complain as being narrated, it may be partly an effect of the philosophy of the treating physician and/or psychological preservation of organ. However, a significantly lower incidence (9%) was reported by List and Bilir [16] in a summary article on toxicity of chemo-radiation in the HNC population.

Preservation of 'organ with an acceptable quality of life' is an important aspect while dealing with various head and neck sites. The practice today in oncology, despite the implementation of the latest technological advances (by any methods), is a plateau achieved in the procedures available for the treatment. Radical radiation therapy with its ability of organ and function preservation, either by EBRT followed by BRT or BRT alone, forms an important aspect in this regard compared to radical surgery. Literature reviews suggests that the treatment of head and neck tumors with radiotherapy needs a high tumor dose to achieve local control [17]. Brachytherapy, an important tool in the armamentarium of radiotherapy, is known to deliver high dose to the target area, because

**Table 5.** Local control rate based on different sites

Site	EBRT + BRT (%)	BRT alone (%)
Oral cavity		
Lip	100	100
Buccal mucosa	0	-
Lateral border of tongue	75	100
Hard palate	100	100
Oropharynx		
Base of tongue	80	0
GE fold/vallecula	50	-
Tonsil	60	-
Soft palate	100	100
Nasopharynx	100	0
Miscellaneous	100	100
Recurrent	50	33.3

 $\it EBRT-external\ beam\ radiation\ the rapy,\ BRT-brachy the rapy,\ GE\ fold-glosso-epiglottic\ fold$ 

of its 'conformal' delivery capacity and with its ability in protection of OAR, despite peaks and troughs (since its discovery) for its implementation. It is an improved method in the treatment of HNC resulting in preservation of functions/organ to a great extent when used as alone for early stage, and when used suitably and carefully in borderline advanced disease with moderate dose EBRT, without jeopardizing the ultimate improved local control and survival rates.

The article presents author's experience in use of BRT in HNC in different sites and for different clinical presentation of early (T1-2N0) and late (other than T1-N0) stage, and as re-irradiation for recurrences/second primary in

**Table 6.** Survival outcomes as per size and stage of tumor in external beam radiation therapy with brachytherapy boost

	Mean BED (Gy)	LC	LR	R	L + R	Distant metastases
Stage						
T1	80.0	3	0	0	0	0
T2	88.7	16	0	0	1	2
T3	90.3	4	2	0	0	2
T4	91.8	3	0	0	0	3
Recurrence	94.2	2	1	1	0	0
Stage I	76.8	2	0	0	0	0
Stage II	88.1	13	0	0	0	2
Stage III	90.8	5	1	0	1	1
Stage IV	90.8	8	1	0	0	4

 $BED-biological\ equivalent\ dose,\ Gy-Gray,\ LC-local\ control,\ LR-local\ recurrence,\ R-regional\ recurrence,\ L+R-local\ recurrence$ 

	Mean BED (Gy)	LC	LR	R	L + R	Distant metastases
Stage						
T1	65.4	5	0	0	0	0
T2	67.7	2	0	0	0	0
T3	22.7	0	1	0	0	1
T4	-	_	-	-	-	_
Recurrence	59.6	2	1	0	1	2
Stage I	65.4	5	0	0	0	0
Stage II	67.7	2	0	0	0	0
Stage III	19.2	0	1	0	0	0
Stage IV	26.1	0	0	0	0	1

**Table 7.** Survival outcomes as per size and stage of tumor in brachytherapy alone

BED – biological equivalent dose, Gy – Gray, LC – local control, LR – local recurrence, R – regional recurrence; L + R – loco-regional recurrence

the same site in the private hospital. Forty-seven of fifty-eight cases (81%) were of oral tongue and oropharynx, including 10 recurrences (Table 1). The complex anatomy and various subsites of head and neck region require individual approaches as per the specific sites, also uses different fractionation and different total dose, subject to clinical requirement. Our current <sup>192</sup>Ir implantation technique is modified to suit local conditions, uses different HDR dose (radical or boost) delivered in divided fractions, ranged 3-4.5 Gy delivered by 2 fractions per day, 6 hours apart after acceptable optimized isodose distribution.

Radical BRT is advocated for early T1 lesion having low potential for nodal spread and is possible for small/ T1N0 lesion of oral cavity and oropharynx excluding base of tongue (BOT). Discussing about BOT and oropharynx, the literature reports higher nodal micro-metastasis rates with 70% or more ipsilateral and 30% bilateral nodes, and imprecise incidence but definite involvement retropharyngeal lymph nodes [18,19], disallows the use of radical BRT alone. Most patients are treated with combination of EBRT followed by local boost whenever possible, except early tonsillar/soft/hard palate lesions (T1N0), which can be attempted with radical curative BRT alone with fair success and chances of nodal relapse. The local control rates for T1 and T2 tumors were excellent, i.e., 100% and 90%, respectively. The 5-year OS/DFS probability in tongue, lip, oral cavity, and oropharynx was found to be in par with reported case series in the literature [16,20,21,22,23,24].

Brachytherapy series reported for BOT, although small, have shown excellent outcome in terms of control rates, survivals, complications, and late sequelae [11,14]. In our study, BOT showed loco regional control rate of 80% (Table 6), with preservation of organ function and acceptable quality of life. The loco-regional control rates of different sites are mentioned in Table 6, which are found to be consistent with other series. Out of the 10 recurrent cases treated with BRT, our study had a local control rate of 40% (4 out of 10 patients), which was better than the

results in the comparative series by Glatzel et al. and Bartochowska et al. [12,25].

Acute complications of BRT reported by Gibbs et al. [26] were transient bleeding (5%), infection (8%), and late toxicities in the form of soft-tissue necrosis/ulceration (7%), osteoradionecrosis (5%), and xerostomia. In our study, acute toxicity in the form of possible infection managed conservatively was observed in 2 patients and none of them showed episodes of bleeding. Late toxicity was seen in 2 of 58 cases (3.44%), in the form of STN/ STF, and in one another case (1/58) in the form of ORN. These toxicities were observed in patient with median BED more than 88.95 Gy, and reflect that a higher dose delivered to achieve higher local control rates is associated with additional toxicities. These toxicities were managed conservatively and healed within 6 months, and were disease free at the time of last follow-up. This late sequel with BRT outweighed by excellent LC with good organ and function preservation rates.

#### Conclusions

High-dose-rate interstitial BRT is a favorable option for patients with HNC as primary radical/curative, or as boost or salvage treatment. The combination treatment using boost with interstitial BRT is effective and seems a viable alternative to surgery and radical EBRT. Interstitial BRT boost should be attempted and integrated with external radiation whenever possible, depending on the clinical response after moderate dose external beam radiation and availability of expertise. Although, within a retrospective series using a small number of patients, our study showed that HDR interstitial BRT demonstrates a better local control probability with an acceptable toxicity in diverse treatment settings. Interstitial BRT, though complex, can be well executed with some experience, and is well tolerated with acceptable toxicity and function preservation. This study reflects the need for reviving the forgotten art and science of interstitial BRT in HNC and using BRT where suitable.

#### Disclosure

Authors report no conflict of interest.

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