Original paper

# Dose-volume analysis of target volume and critical structures in computed tomography image-based multicatheter high-dose-rate interstitial brachytherapy for head and neck cancer

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## Abstract

**Purpose:** To evaluate dose-volume relationships of target volume and critical structures in computed tomography (CT) image-based brachytherapy for head and neck cancer.

**Material and methods:** Thirty-seven patients with mobile tongue, floor of mouth, and base of tongue cancer treated with brachytherapy (post-operative alone and as a boost after external beam radiotherapy [EBRT], or definitive alone or as a boost after EBRT) were selected. Treatment plans were made using post-implant CT images. The fractionation schedule was 7-15 × 3-5 Gy for post-operative (with or without EBRT), 14-15 × 3 Gy for definitive alone, and 5-10 × 3 Gy for boost treatments. For the target volume, $V_{100}$, $D_{90}$, and dose non-uniformity ratio (DNR) were calculated. For the mandible, spinal cord and salivary glands doses to specified volumes were reported.

**Results:** The median values of $V_{100}$ and $D_{90}$ were 89.9% and 99.9%, respectively; the median values of DNR was 0.46. The median $D_{2cm^3}$ of the mandible and spinal cord were 48.3% and 5.8%, respectively. The ipsilateral median $D_{2cm^3}$ of parotid and submandibular glands were 6.4% and 12.5%, whereas on the contralateral side, the corresponding values were 5.3% and 7.0%, respectively.

**Conclusions:** Using conformal treatment planning, it was desirable to keep the dose to the mandible, spinal cord, and salivary glands at an acceptable level. The quantitative plan evaluation may help us find correlations between dosimetric parameters and clinical outcome, which may lead to improve the quality of the treatment, but it requires longer follow-up and results from other studies.

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**Key words:** brachytherapy, CT, dosimetry, head and neck, HDR.

## Purpose

The goal of any technology developed for radiation therapy is to deliver lethal doses to the target volume defined by radiation oncologists, while keeping doses to adjacent normal tissue as low as possible. Advancements in brachytherapy (BT) have been characterized by delivering a total dose, which cannot be safely given by external beam radiotherapy (EBRT) alone, and the rapid dose fall-off that allows relative sparing of critical and normal tissues [1]. In this respect, BT alone or as a boost is used for the management of malignancies in head and neck, gynecological, and other regions [2,3]. Especially for head and neck malignancies, BT is difficult because this region has complex anatomical structures with functional and cosmetic importance. Low-dose-rate (LDR) BT for head and neck malignancies has long been in use, and it is an established method. However, it has some shortcomings, such as radiation exposure to medical staff, isolation of patients for a long time in a shielded room with limited time of nursing care due to radiation exposure, and without dose optimization after implantation. Remote after-loading high-dose-rate (HDR) stepping source system has been introduced to eliminate some defects of LDR BT [4,5].

Recently, with the development of imaging modalities, such as computed tomography (CT), magnetic resonance imaging (MRI), and ultrasonography, image-based HDR BT has been implemented. Using three-dimensional (3D) cross-sectional image sets, radiation oncologists and medical physicists can depict the target volume and critical structures, and calculate the volumetric doses delivered

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to these organs [5,6,7,8,9,10,11,12]. In the gynecological region, there are recommendations about image-based BT, where authors referring to concepts and terms in 3D image-based treatment planning, 3D dose volume parameters, aspects of 3D image-based anatomy, radiation physics and radiobiology [13,14]. However, as to the head and neck region, the recommendations of the Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) define that it is too early for precise suggestion regarding the use of 3D imaging and optimization in BT of head and neck tumors [1] and in its 1st update, the authors reported that standardized organ at risk dose-volume constraints in head and neck BT are lacking [15]. In this study, we present the dosimetric data of 3D image-based HDR BT in patients with head and neck cancers by applying dose-volume analysis of the target volume and critical structures. The dosimetry of BT with EBRT was not compared.

## Material and methods

### *Patients' characteristics*

Between January 2013 and January 2017, thirty-seven patients with mobile tongue ($n$ = 15, left side: right side = 12 : 3, T1 : T2: T3: T4 = 6 : 5 : 2 : 2), floor of mouth ($n$ = 9, left side: right side: middle = 3 : 3 : 3, T1 : T2 = 8 : 1), and base of tongue ($n$ = 13, left side: right side = 3 : 10; T1 : T2 : T3 : T4 = 3 : 3 : 4 : 3) cancer treated with multicatheter HDR BT were selected for this study at our institute (post-operative ± EBRT, $n$ = 14, or definitive alone, $n$ = 3, or as a boost after EBRT, $n$ = 20). The mean follow-up period was 24 months (range, 3-53 months) (Table 1).

### *Implantation and treatment planning*

Plastic catheters (Elekta, Brachytherapy, Veenendaal, The Netherlands) (median 7, range 3-12) were implanted into the region of the target volume in surgical act under visual guidance. After catheter implantation, all patients underwent CT imaging. The images were transferred to Oncentra Brachy v. 4.3 (Elekta, Brachytherapy, Veenendaal, The Netherlands) planning system, which uses the TG-43 calculation formalism without taking into consideration the tissue heterogeneities. Based on CT image sets, the planning target volume (PTV) and critical structures as the mandible, spinal cord, and salivary glands (parotid and submandibular glands) on both sides were delineated by the same person (HA). Because tumor or tumor bed were sometimes not visible on CT images, positions of the inserted catheters, inspection, palpation, and MR images could help in determination of the PTV contour. After catheter reconstruction, treatment plans were made with geometrical optimization. Then, we adjusted the isodose curve with graphical optimization in order to cover the PTV appropriately by the prescribed dose (PD), and maintain the doses to critical structures as low as possible. Dose non-uniformity ratio (DNR) was defined as the ratio of volume receiving 1.5 times of the PD and the PD ($V_{150}/V_{100}$). Our aim was to gain DNR ≤ 0.40 [16]. The fractionation schedule was 7-15 x 3-5 Gy (total dose of 21-48 Gy) for post-operative, 14-15 x 3 Gy (total dose of 42-45 Gy) for definitive alone, and 5-10 x 3 Gy (total dose of 15-30 Gy) for boost treatments [1].

**Table 1.** Treatment characteristics

| Factor | $n$ | Fractionation schedule |
|---|---|---|
| Postoperative w/o EBRT | 14 | 7-15 × 3-5 Gy (total dose of 21-48 Gy) |
| Definitive alone | 3 | 14-15 × 3 Gy (total dose of 42-45 Gy) |
| Boost after EBRT | 20 | 5-10 × 3 Gy (total dose of 15-30 Gy) |
| Implant location | | |
| Left side | 18 | |
| Right side | 16 | |
| Middle | 3 | |

*n – number of patients for analysis, w/o – with or without, EBRT – external beam radiotherapy*

### *Target volume evaluation*

For quantitative estimation of doses for the target volume coverage, the following dose-volume parameters were calculated using dose-volume histograms (DVH): percentage volume of the PTV receiving more than 100% and 150% of the PD ($V_{100}$ and $V_{150}$); minimum percentage dose of the PD that was given to 90% and 100% of the PTV ($D_{90}$ and $D_{100}$). To analyze homogeneity and conformity of dose distributions, we calculated dose non-uniformity ratio (DNR), dose homogeneity index (DHI), and conformal index (COIN). Their definitions were as follows: DNR = $V_{150}/V_{100}$; DHI = $(V_{100} - V_{150})/V_{100}$; COIN = $(PTV_{100}/V_{PTV}) \times (PTV_{100}/V_{100})$.

The $PTV_{100}$ and $V_{PTV}$ are indicated as absolute partial volume of the PTV, receiving 100% of the PD and absolute volume of the PTV, respectively.

### *Critical structures evaluation*

As critical structures, we selected the mandible, spinal cord, and salivary glands (parotid and submandibular glands) on both sides. For the mandible and spinal cord, minimum percentage doses of the PD that was given to maximally irradiated 0.1 $cm^3$, 1 $cm^3$, and 2 $cm^3$ volumes ($D_{0.1cm^3}$, $D_{1cm^3}$, and $D_{2cm^3}$) were calculated from DVH. Salivary glands were divided into two groups: ipsilateral and contralateral, based on the implant location. Three patients had centrally located tumor and were excluded from salivary gland analysis. The following dose-volume parameters of each group such as ipsilateral and contralateral side were calculated using DVH: mean dose in percentage of the PD ($D_{mean}$), percentage volume of each salivary gland receiving more than 10%, 30%, and 50% of the PD ($V_{10}$, $V_{30}$, and $V_{50}$), and minimum percentage dose of the PD that was given to 10%, 30%, and 50% of each salivary gland ($D_{10}$, $D_{30}$, and $D_{50}$) fully detected with CT images (some salivary glands were not adequately represented on the CT because of having been removed by operation, atrophy by EBRT, and patients' position during CT), minimum percentage dose of the PD that was given to maximally irradiated 0.1 $cm^3$, 1 $cm^3$, and 2 $cm^3$

**Table 2.** Evaluation of implant-related dosimetric parameters

| Parameters | All, $n$ = 37 | | Mobile tongue, floor of mouth, $n$ = 24 | | Base of tongue, $n$ = 13 | | $p$ value |
|---|---|---|---|---|---|---|---|
| | Median | Range | Median | Range | Median | Range | |
| $V_{100}$ (cm$^3$) | 16.8 | 6.5-43.8 | 16.0 | 6.5-43.8 | 18.0 | 9.9-32.9 | > 0.05 |
| $V_{150}$ (cm$^3$) | 7.0 | 2.9-21.0 | 6.6 | 2.9-21.0 | 7.6 | 4.3-15.6 | > 0.05 |
| DNR | 0.46 | 0.34-0.58 | 0.45 | 0.34-0.57 | 0.47 | 0.36-0.58 | > 0.05 |

*n – number of patients for analysis, $V_{100}$, $V_{150}$ – volume receiving 100% and 150% or more of the prescribed dose, DNR – dose nonuniformity ratio*

**Table 3.** Evaluation of the PTV-related parameters

| Parameters | All, $n$ = 37 | | Mobile tongue, floor of mouth, $n$ = 24 | | Base of tongue, $n$ = 13 | | $p$ value |
|---|---|---|---|---|---|---|---|
| | Median | Range | Median | Range | Median | Range | |
| $V_{PTV}$ (cm$^3$) | 12.9 | 5.2-42.3 | 12.7 | 5.2-42.3 | 13.7 | 6.9-35.0 | > 0.05 |
| $PTV_{100}$ (cm$^3$) | 11.2 | 4.6-32.9 | 11.1 | 4.6-32.9 | 12.4 | 6.2-29.4 | > 0.05 |
| Coverage (%) | | | | | | | |
| $V_{100}$ | 89.9 | 77.8-93.5 | 90.0 | 77.8-93.5 | 90.0 | 79.9-90.9 | > 0.05 |
| $V_{150}$ | 44.1 | 36.3-63.6 | 43.9 | 36.3-54.3 | 45.5 | 37.6-63.6 | > 0.05 |
| $D_{90}$ | 99.9 | 83.4-105.2 | 99.9 | 83.4-105.2 | 100.0 | 87.2-101.1 | > 0.05 |
| $D_{100}$ | 57.0 | 37.6-73.4 | 57.9 | 37.6-73.4 | 56.9 | 48.0-68.6 | > 0.05 |
| Homogeneity | | | | | | | |
| DHI | 0.50 | 0.29-0.61 | 0.50 | 0.37-0.61 | 0.48 | 0.29-0.59 | > 0.05 |
| Conformity | | | | | | | |
| COIN | 0.64 | 0.51-0.77 | 0.64 | 0.58-0.77 | 0.66 | 0.51-0.75 | > 0.05 |

*n – number of patients for analysis, PTV – planning target volume, PD – prescribed dose, VPTV – volume of the PTV, $PTV_{100}$ – partial volume of the PTV receiving the PD, $V_{100}$, $V_{150}$ – percentage volume of the PTV receiving 100% and 150% or more of the PD, $D_{90}$, $D_{100}$ – minimum percentage dose of the PD that was given to 90% and 100% of the PTV, DHI – dose homogeneity index, COIN – conformal index*

volumes of each salivary gland ($D_{0.1cm^3}$, $D_{1cm^3}$, and $D_{2cm^3}$). In those cases, where the full volume of parotid glands was not visible on the CT, only $D_{0.1cm^3}$, $D_{1cm^3}$, and $D_{2cm^3}$ parameters were calculated.

### *Statistical analysis*

We presented the results as the median and ranges according to each subdivided site such as mobile tongue (including floor of mouth) and base of tongue. We compared these parameters by using non-parametric Mann-Whitney *U* test. To examine the relationships of $V_{100}$ and $D_{90}$, $V_{PTV}$ and $V_{100}$, $D_{2cm^3}$ and $D_{1cm^3}$, and $D_{1cm^3}$ and $D_{0.1cm^3}$, linear regression analysis was performed. We considered the level of statistical significance as $p \leq 0.05$. For statistical analysis we used GraphPad Prism version 5.01 for Windows (GraphPad Software, San Diego, CA, USA).

## Results

Generally, mobile tongue and floor of mouth cancer patients were operated, and then received HDR BT in case of positive or close margin. A few patients were treated with HDR BT alone without surgery. Base of tongue cancer patients received EBRT followed by HDR BT with or without operation. During the follow-up period, 15 patients had local and/or regional relapse and 24 patients were alive. One patient had soft tissue necrosis as a late adverse events.

Tables 2-7 shows parameters analyzed in this study. The respective values are given below.

### *Dosimetric evaluation of implant*

The characteristics of implant related dosimetric parameters are shown in Table 2. The median volume receiving 100% or more of the PD ($V_{100}$) for all primary sites was 16.8 cm$^3$ (range, 6.5-43.8 cm$^3$). The DNR slightly surpassed 0.40, with the median of 0.46 (range, 0.34-0.58) for all primary sites. There were no significant differences in the parameters between mobile tongue (including floor of mouth) and base of tongue tumors.

### *Dosimetric evaluation of the PTV*

The characteristics of the PTV related parameters are illustrated in Table 3. For all primary sites, the median $V_{PTV}$ was 12.9 cm$^3$ (range, 5.2-42.3 cm$^3$). The median dose coverage of the PTV was characterized with $V_{100}$ of 89.9% (range, 77.8-93.5%), $V_{150}$ of 44.1% (range, 36.3-63.6%), $D_{90}$ of 99.9% (range, 83.4-105.2%), and $D_{100}$ of 57.0% (range, 37.6-73.4%), respectively. The median DHI and COIN were 0.50 (range, 0.29-0.61) and 0.64 (range, 0.51-0.77). There were no significant differences in the parameters

**Table 4.** Evaluation of the mandible- and spinal cord-related parameters

| Parameters | All | | | Mobile tongue, floor of mouth | | | Base of tongue | | | *p* value |
|---|---|---|---|---|---|---|---|---|---|---|
| | *n* | Median | Range | *n* | Median | Range | *n** | Median | Range | |
| Mandible | | | | | | | | | | |
| $D_{0.1cm^3}$ (%) | 37 | 81.8 | 25.1-134.1 | 24 | 84.1 | 61.2-134.1 | 13 | 66.2 | 25.1-101.5 | < 0.05 |
| $D_{1cm^3}$ (%) | 37 | 57.8 | 19.6-81.6 | 24 | 58.6 | 46.4-81.6 | 13 | 44.2 | 19.6-65.2 | < 0.05 |
| $D_{2cm^3}$ (%) | 37 | 48.3 | 17.5-73.2 | 24 | 50.3 | 38.3-73.2 | 13 | 36.2 | 17.5-55.9 | < 0.05 |
| Spinal cord | | | | | | | | | | |
| $D_{0.1cm^3}$ (%) | 36 | 10.0 | 4.9-15.4 | 24 | 9.6 | 4.9-13.3 | 12 | 11.3 | 8-15.4 | < 0.05 |
| $D_{1cm^3}$ (%) | 36 | 6.8 | 3.3-11.8 | 24 | 6.0 | 3.3-9.8 | 12 | 7.8 | 4.9-11.8 | < 0.05 |
| $D_{2cm^3}$ (%) | 36 | 5.8 | 2.8-10.8 | 24 | 5.3 | 2.8-8.9 | 12 | 7.0 | 3.8-10.8 | < 0.05 |

*n – number of patients for analysis, $D_{0.1cm^3}$, $D_{1cm^3}$, $D_{2cm^3}$ – minimum percentage dose of the prescribed dose that was given to maximally irradiated 0.1 cm³, 1 cm³, 2 cm³ volume of the organs, * – in one patient spinal cord was not detected on planning CT images because it was out of field of view*

**Table 5.** Evaluation of ipsilateral salivary glands-related parameters

| Parameters | All | | | Mobile tongue, floor of mouth | | | Base of tongue | | | *p* value |
|---|---|---|---|---|---|---|---|---|---|---|
| | *n* | Median | Range | *n* | Median | Range | *n* | Median | Range | |
| Parotid gland | | | | | | | | | | |
| $D_{mean}$ (%) | 15 | 4.1 | 2.0-6.5 | 12 | 3.7 | 2.0-6.1 | 3 | 5.8 | 4.1-6.5 | > 0.05 |
| $D_{0.1cm^3}$ (%) | 33 | 10.8 | 5.9-17.1 | 20 | 10.8 | 5.9-14.0 | 13 | 11.4 | 9.7-17.1 | > 0.05 |
| $D_{1cm^3}$ (%) | 33 | 7.5 | 4.2-13.4 | 20 | 7.5 | 4.3-10.1 | 13 | 7.7 | 6.2-13.3 | > 0.05 |
| $D_{2cm^3}$ (%) | 33 | 6.4 | 3.8-11.8 | 20 | 6.3 | 3.8-9.4 | 13 | 6.5 | 4.6-11.8 | > 0.05 |
| $D_{10}$ (%) | 15 | 6.7 | 3.5-99 | 12 | 6.3 | 3.5-9.1 | 3 | 8.8 | 6.7-9.9 | > 0.05 |
| $D_{30}$ (%) | 15 | 5.1 | 2.6-7.6 | 12 | 4.8 | 2.6-7.1 | 3 | 6.9 | 5.1-7.6 | > 0.05 |
| $D_{50}$ (%) | 15 | 4.1 | 2.0-6.3 | 12 | 3.7 | 2.0-5.9 | 3 | 5.6 | 4.1-6.3 | > 0.05 |
| $V_{10}$ (%) | 15 | 0.8 | 0.0-9.1 | 12 | 0.7 | 0.0-5.0 | 3 | 3.7 | 0.8-9.1 | > 0.05 |
| Submandibular gland | | | | | | | | | | |
| $D_{mean}$ (%) | 22 | 12.3 | 5.9-41.8 | 13 | 9.4 | 6.0-28.0 | 9 | 21.0 | 5.9-41.8 | < 0.05 |
| $D_{0.1cm^3}$ (%) | 22 | 20.6 | 11.4-62.5 | 13 | 19.7 | 11.8-43.5 | 9 | 32.7 | 11.4-62.5 | > 0.05 |
| $D_{1cm^3}$ (%) | 20 | 15.1 | 7.7-42.2 | 13 | 13.5 | 9.6-34.3 | 7 | 25.7 | 7.7-42.2 | > 0.05 |
| $D_{2cm^3}$ (%) | 19 | 12.5 | 6.3-34.7 | 13 | 11.6 | 8.2-30.4 | 6 | 20.0 | 6.3-34.7 | > 0.05 |
| $D_{10}$ (%) | 22 | 17.5 | 8.9-51.3 | 13 | 13.9 | 9.0-38.8 | 9 | 28.1 | 8.9-51.3 | < 0.05 |
| $D_{30}$ (%) | 22 | 13.8 | 7.0-45.2 | 13 | 10.7 | 7.0-32.1 | 9 | 23.4 | 7.0-45.2 | < 0.05 |
| $D_{50}$ (%) | 22 | 11.8 | 5.7-40.7 | 13 | 8.9 | 5.7-27.4 | 9 | 20.4 | 5.7-40.7 | < 0.05 |
| $V_{10}$ (%) | 22 | 68.6 | 4.1-100.0 | 13 | 36.3 | 4.7-100.0 | 9 | 100.0 | 4.1-100.0 | < 0.05 |
| $V_{30}$ (%) | 22 | 0.0 | 0.0-97.9 | 13 | 0.0 | 0.0-38.8 | 9 | 5.2 | 0.0-97.9 | < 0.05 |
| $V_{50}$ (%) | 22 | 0.0 | 0.0-13.2 | 13 | 0.0 | 0.0-0.1 | 9 | 0.0 | 0.0-13.2 | > 0.05 |

*n – number of patients for analysis, PD – prescribed dose, $D_{mean}$ – mean percentage dose of the PD that was given to the organs, $D_{0.1cm^3}$, $D_{1cm^3}$, $D_{2cm^3}$ – minimum percentage dose of the PD that was given to maximally irradiated 0.1 cm³, 1 cm³, 2 cm³ volume of the organs; $D_{10}$, $D_{30}$, $D_{50}$ – minimum percentage dose of the PD that was given to 10%, 30%, 50% of the organs; $V_{10}$, $V_{30}$, $V_{50}$ – percentage volume of the organs receiving 10%, 30%, 50% or more of the PD*

between mobile tongue (including floor of mouth) and base of tongue tumors.

### *Dosimetric evaluation of critical structures*

#### *Mandible and spinal cord*

As to the mandible, the median $D_{0.1cm^3}$, $D_{1cm^3}$, and $D_{2cm^3}$ were 81.8% (range, 25.1-134.1%), 57.8% (range, 19.6-81.6%), and 48.3% (range, 17.5-73.2%), respectively, whereas with regard to the spinal cord, corresponding values were 10.0% (range, 4.9-15.4%), 6.8% (range, 3.3-11.8%), and 5.8% (range, 2.8-10.8%) for all cases, respectively (Table 4). Comparing the 2 location groups (patients with base of tongue and patients with mobile tongue, including floor of mouth), the latter received significantly higher doses for the mandible (median $D_{2cm^3}$: 50.3% vs. 36.2%), while, on the other hand, significantly lower doses for the spinal cord (median $D_{2cm^3}$: 5.3% vs. 7.0%).

#### *Ipsilateral salivary glands*

Table 5 shows the evaluation of ipsilateral salivary glands related parameters. For all cases, the median $D_{mean}$,

**Table 6.** Evaluation of contralateral salivary glands-related parameters

| Parameters | All | | | Mobile tongue, floor of mouth | | | Base of tongue | | | *p* value |
|---|---|---|---|---|---|---|---|---|---|---|
| | *n* | Median | Range | *n* | Median | Range | *n* | Median | Range | |
| Parotid gland | | | | | | | | | | |
| $D_{mean}$ (%) | 15 | 3.1 | 1.1-4.1 | 12 | 2.7 | 1.1-4.0 | 3 | 4.0 | 2.6-4.1 | > 0.05 |
| $D_{0.1cm^3}$ (%) | 34 | 9.5 | 4.9-11.9 | 21 | 9.6 | 4.9-11.9 | 13 | 9.5 | 6.8-11.2 | > 0.05 |
| $D_{1cm^3}$ (%) | 34 | 6.0 | 3.3-8.8 | 21 | 6.0 | 3.3-8.8 | 13 | 5.9 | 3.5-7.8 | > 0.05 |
| $D_{2cm^3}$ (%) | 34 | 5.3 | 2.3-7.7 | 21 | 5.3 | 2.8-7.7 | 13 | 5.2 | 2.3-6.9 | > 0.05 |
| $D_{10}$ (%) | 15 | 5.7 | 2.5-6.7 | 12 | 5.5 | 2.5-6.5 | 3 | 6.6 | 5.5-6.7 | > 0.05 |
| $D_{30}$ (%) | 15 | 4.0 | 1.7-5.1 | 12 | 3.8 | 1.7-5.1 | 3 | 5.0 | 3.8-5.1 | > 0.05 |
| $D_{50}$ (%) | 15 | 3.4 | 1.3-4.1 | 12 | 3.1 | 1.3-4.0 | 3 | 3.9 | 3.2-4.1 | > 0.05 |
| $V_{10}$ (%) | 15 | 0.5 | 0.0-0.9 | 12 | 0.4 | 0.0-0.8 | 3 | 0.8 | 0.4-0.9 | > 0.05 |
| Submandibular gland | | | | | | | | | | |
| $D_{mean}$ (%) | 33 | 6.8 | 2.9-29.3 | 20 | 5.8 | 2.9-11.2 | 13 | 9.9 | 4.4-29.3 | < 0.05 |
| $D_{0.1cm^3}$ (%) | 33 | 11.7 | 5.8-34.5 | 20 | 11.2 | 5.8-17.1 | 13 | 15.8 | 9.3-34.5 | < 0.05 |
| $D_{1cm^3}$ (%) | 31 | 8.0 | 4.1-13.8 | 20 | 7.7 | 4.1-13.5 | 11 | 11.2 | 5.8-13.8 | > 0.05 |
| $D_{2cm^3}$ (%) | 31 | 7.0 | 3.6-12.4 | 20 | 6.7 | 3.6-11.9 | 11 | 9.5 | 4.6-12.4 | > 0.05 |
| $D_{10}$ (%) | 33 | 9.6 | 4.2-35.1 | 20 | 8.3 | 4.2-14.4 | 13 | 13.3 | 7.0-35.1 | < 0.05 |
| $D_{30}$ (%) | 33 | 7.7 | 3.4-31.5 | 20 | 6.7 | 3.4-12.4 | 13 | 11.2 | 5.3-31.5 | < 0.05 |
| $D_{50}$ (%) | 33 | 6.8 | 2.8-29.0 | 20 | 5.6 | 2.8-11.1 | 13 | 9.7 | 4.4-29.0 | < 0.05 |
| $V_{10}$ (%) | 33 | 6.0 | 0.0-100.0 | 20 | 2.8 | 0.0-67.3 | 13 | 45.1 | 1.0-100.0 | < 0.05 |
| $V_{30}$ (%) | 33 | 0.0 | 0.0-41.0 | 20 | 0.0 | 0.0-0.0 | 13 | 0.0 | 0.0-41.0 | NA |

*n – number of patients for analysis, PD – prescribed dose, Dmean – mean percentage dose of the PD that was given to the organs, $D_{0.1cm^3}$, $D_{1cm^3}$, $D_{2cm^3}$ – minimum percentage dose of the PD that was given to maximally irradiated 0.1 cm³, 1 cm³, 2 cm volume of the organs; $D_{10}$, $D_{30}$, $D_{50}$ – minimum percentage dose of the PD that was given to 10%,30%, 50% of the organs; V10, V30, V50 - percentage volume of the organs receiving 10%, 30%, 50% or more of the PD, NA – not available*

**Table 7.** Correlation coefficient (R2) between parameters

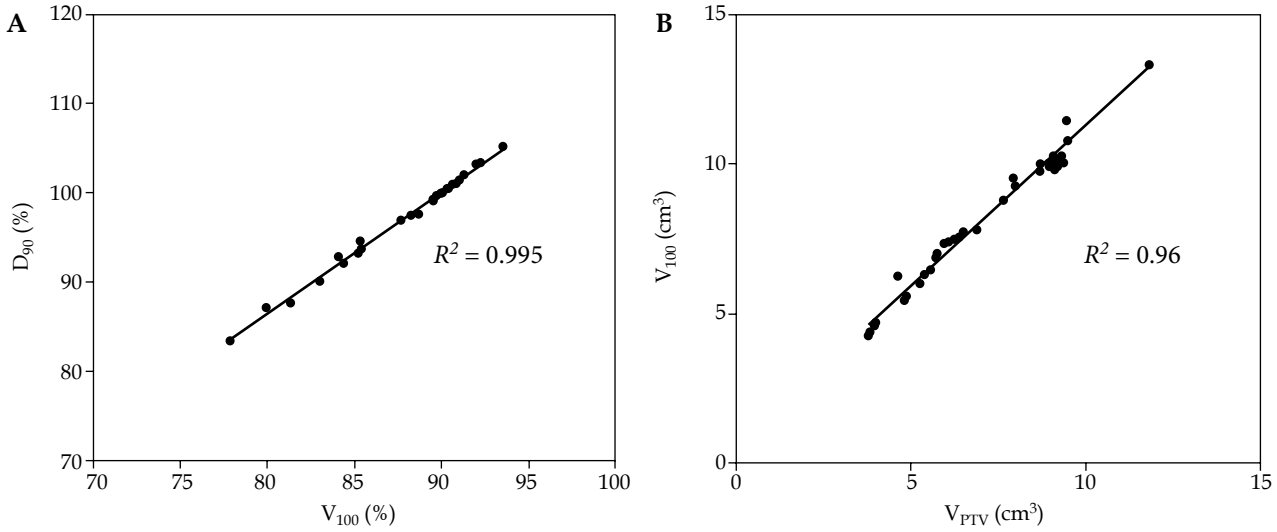
| Target volume | | Critical structures | | | | | |
|---|---|---|---|---|---|---|---|
| $V_{100}$ and $D_{90}$ | VPTV and $V_{100}$ | $D_{1cm^3}$ and $D_{0.1cm^3}$ | | | | | |
| | | Mandible | Spinal cord | Ipsilateral parotid gland | Contralateral parotid gland | Ipsilateral submandibular gland | Contralateral submandibular gland |
| *0.995 | *0.960 | 0.554 | *0.964 | *0.966 | *0.940 | *0.976 | *0.972 |

** – high correlation, PTV – planning target volume, PD – prescribed dose, $V_{100}$ – percentage volume of the PTV receiving 100% or more of the PD; $D_{90}$ – minimum percentage dose of the PD that was given to 90% of the PTV, VPTV – volume of the PTV, $V_{100}$ – volume of the PTV receiving 100% or more of the PD; $D_{1cm^3}$, $D_{0.1cm^3}$ – minimum percentage dose of the PD that was given to maximally irradiated 1 cm³, 0.1 cm³ volume of organs*

$D_{2cm^3}$, $D_{30}$ of parotid glands were 4.1% (range, 2.0-6.5%), 6.4% (range, 3.8-11.8%), and 5.1% (range, 2.6-7.6%), whereas those of submandibular glands were 12.3% (range, 5.9-41.8%), 12.5% (range, 6.3-34.7%) and 13.8% (range, 7.0-45.2%), respectively. The median percentage volume of parotid glands and submandibular glands receiving 10% or more of the PD ($V_{10}$) were 0.8% (range, 0.0-9.1%) and 68.6% (range, 4.1-100.0%), respectively. Both $V_{30}$ and $V_{50}$ of parotid glands were 0.0% for each patient, whereas the median $V_{30}$ and $V_{50}$ of submandibular glands were 0.0% (range, 0.0-97.9%) and 0.0% (range, 0.0-13.2%), respectively. For parotid glands, there were no significant differences in the parameters between mobile tongue (including floor of mouth) and base of tongue cancer patients. On the other hand, for submandibular glands, 6 parameters ($D_{mean}$, $D_{10}$, $D_{30}$, $D_{50}$, $V_{10}$, and $V_{30}$) of base of tongue cancer patients were significantly higher than those of mobile tongue (including floor of mouth) cancer patients.

*Contralateral salivary glands*

Table 6 shows the evaluation of contralateral salivary glands related parameters. For all cases, the median $D_{mean}$, $D_{2cm^3}$, $D_{30}$ of parotid glands were 3.1% (range, 1.1-4.1%), 5.3% (range, 2.3-7.7%), and 4.0% (range, 1.7-5.1%), whereas those of submandibular glands were 6.8% (range, 2.9-29.3%), 7.0% (range, 3.6-12.4%) and 7.7% (range, 3.4-31.5%), respectively. The median percentage volume of parotid glands and submandibular glands receiving 10% or more of the PD ($V_{10}$) were 0.5% (range, 0.0-0.9%) and 6.0% (range, 0.0-100.0%), respectively. Both $V_{30}$ and $V_{50}$ of parotid glands were 0.0% for each patient, whereas the median $V_{30}$ of submandibular glands was




*PTV – planning target volume, PD – prescribed dose, $D_{90}$ (%) – minimum percentage dose of the PD that was given to 90% of the PTV, $V_{100}$ (%) – percentage volume of the PTV receiving 100% or more of the PD, $V_{100}$ – volume receiving 100% or more of the PD, $V_{PTV}$ – volume of the PTV, $R^2$ – correlation coefficient*

**Fig. 1.** Correlation between $D_{90}$ and $V_{100}$ **(A)**, and $V_{100}$ and $V_{PTV}$ **(B)**

0.0% (range, 0.0-41.0%) and $V_{50}$ was 0.0% for each patient. For parotid glands, there were no significant differences in the parameters between mobile tongue (including floor of mouth) and base of tongue cancer patients. For submandibular glands, 6 parameters ($D_{mean}$, $D_{0.1cm^3}$, $D_{10}$, $D_{30}$, $D_{50}$, and $V_{10}$) of base of tongue cancer patients were significantly higher than those of mobile tongue (including floor of mouth) cancer patients.

### *Correlation analysis*

The results are shown in Table 7. Good correlation was seen between $V_{100}$ and $D_{90}$, and $V_{PTV}$ and $V_{100}$ (Figure 1). $D_{2cm^3}$ correlated well with $D_{1cm^3}$ for all critical structures with $R^2 > 0.96$. $D_{1cm^3}$ also showed good correlation with $D_{0.1cm^3}$ for all critical structures except for the mandible (Table 7).

## Discussion

Development in BT planning makes it possible also in the head and neck region to evaluate dose-volume relationships concerning the target volume and critical structures. Compared with the conventional implant-based 2D treatment planning for mobile tongue cancer, 3D image-based BT planning may decrease irradiated doses to the mandible without compromising clinical target volume coverage [12]. At our institute, post-implantation CT image sets have been successfully used for HDR head and neck BT. For high quality image-based BT, 3D tomographic image sets of target and critical structures are highly recommended. Therefore, the dose plan evaluation for implant, PTV, and critical structures using DVH data have great significance. Although the software we applied in this study did not take into account the exact patient dimension and tissue heterogeneities, our results are not affected by the small inaccuracies in dose calculation [17]. In this study, we did not consider the indications of HDR BT, only the dosimetric analysis of interstitial therapy. Previously, there were only a few data available about the exact dose prescription of HDR BT, so fractionation schedule of our study was inhomogeneous.

### *Implant related parameters*

There is no agreement on what degree of dose non-uniformity is permitted in the image-based head and neck HDR BT. Systematic collection and documentation of implant quality measures (COIN, DNR, etc.) for future evaluation are advisable [16]. Strnad *et al*. [16] reported that DNR should be equal to or lower than 0.36 and in IMBT (intensity modulated brachytherapy), this value should be 0.42. Guinot *et al*. [18] did not allow a hot spot joining two tubes in order to keep DNR under 0.35. In small gross tumor volumes (few cm$^3$ and applicator spacing is less than 10 mm), the DNR may be as high as 0.50-0.52 [15]. For all our patients, the median DNR was 0.46. Our results are slightly worse compared with the literature data. However, more dosimetric studies would be needed because there is no clear consensus for the acceptable value of DNR. It is to be noted that the DNR can depend considerably on the number of catheters. The higher their number, the better the DNR, but on the other hand, great number of catheters can cause inconvenience to the patients.

### *PTV related parameters*

According to the GEC-ESTRO recommendation, the prescription dose is usually the minimum dose delivered to the clinical target volume (CTV) or a CTV surrogate (i.e., the $D_{90} > 100$, $V_{100} > 90\%$) [15]. Evaluating 74 patients, in the study of Tselis *et al*. [19], the median $V_{100}$, $V_{150}$, and $D_{90}$ were 88.8%, 58.0%, and 97.7%, respectively. In another study by Yoshida *et al*. [12], the mean $V_{100}$, $D_{90}$, and $D_{100}$ were 98.1%, 112.4%, and 86.7%, respectively. In the current study, for all patients, the median $V_{100}$, $V_{150}$, $D_{90}$, and $D_{100}$ were 89.9%, 44.1%, 99.9%, and 57.0%, respectively. These results are very proximal to the GEC-ESTRO's recommendations. Our results of $D_{100}$

are low, presumably because of the irregular shape of the PTV. $D_{90}$ has shown a good correlation with $V_{100}$, and this means that independently of the shape of the PTV, $D_{90}$ is a good parameter to evaluate the target coverage. The volume of the PTV ($V_{PTV}$) has shown a good correlation with the irradiated volume of 100% PD ($V_{100}$). The reason for this is that in most cases, the coverage ($V_{100}$) was close to 90%. Cisek *et al.* [7] calculated DHI for 4 patients of oropharyngeal, lip, larynx, and maxillary cancer. Their median DHI was 0.31 and in our study, it was 0.50. As regards to conformity, internationally accepted recommendations are not available. Upreti *et al*. [11] found a mean COIN value of 0.52; in our study, we demonstrated 0.64 for all patients. Our somewhat higher value means smaller normal tissue irradiated by the PD.

### *Critical structures related parameters*

No specific tolerance doses to critical structures are given in the GEC-ESTRO recommendations. They only prescribe to keep the doses to organs at risk as low as possible [15].

#### *Mandible and spinal cord*

In an early study, Yoshida *et al*. [12] evaluated 5 mobile tongue cancer patients treated by image-based HDR BT (CT and MRI used). They indicated that the mean $D_{0.1cm^3}$, $D_{1cm^3}$, and $D_{2cm^3}$ of the mandible were 80.1%, 62.5%, and 55.7%, respectively. In our study for mobile tongue (including floor of mouth) cancer patients, the median $D_{0.1cm^3}$, $D_{1cm^3}$, and $D_{2cm^3}$ were 84.1%, 58.6%, and 50.3%, respectively. From these results, the acceptable level of $D_{0.1cm^3}$, $D_{1cm^3}$, and $D_{2cm^3}$ of the mandible for mobile tongue cancer may be roughly 80%, 60%, and 55%, respectively. For the mandible, high correlation was found between $D_{2cm^3}$ and $D_{1cm^3}$, whereas no correlation was found between $D_{1cm^3}$ and $D_{0.1cm^3}$ (Table 7). The explanation for this latter observation is that $D_{0.1cm^3}$ parameter is very sensitive to the distance between the mandible and the PTV. If the PTV is close to the mandible, the 100% isodose line can cover a small volume ($D_{0.1cm^3}$) of the mandible, but if the PTV is far from it, the 100% isodose line does not reach the mandible. However, volumes irradiated by lower doses are not influenced significantly by the distance. That is the reason for good correlation between $D_{1cm^3}$ and $D_{2cm^3}$. Therefore, it is necessary to report $D_{2cm^3}$, $D_{1cm^3}$, and $D_{0.1cm^3}$ parameters and the relationships between these data and late complications of the mandible. No former investigation has been found in the literature about minimum percentage dose of the PD received by the maximally irradiated small volumes for the spinal cord.

#### *Salivary glands*

In our study, the doses delivered to the ipsilateral or contralateral salivary glands with respect to each primary site are compared to the results of an early study. Bhalavat *et al*. [6] estimated the doses for mobile tongue and base of tongue implantations. For ipsilateral parotid glands (our results are in parenthesis), they found that the mean $D_{mean}$ and $D_{30}$ were 5.7% (3.7%) and 6.5% (4.8%) for mobile tongue lesion, and 8.6% (5.8%) and 9% (6.9%) for base of tongue lesion, and for ipsilateral submandibular glands those were 18.4% (9.4%) and 17% (10.7%) for mobile tongue lesion, and 45.9% (21.0%) and 48.9% (23.4%) for base of tongue lesion, respectively. For contralateral parotid glands, the mean $D_{mean}$ and $D_{30}$ were 2.3% (2.7%) and 4.4% (3.8%) for mobile tongue lesion and 5.7% (4.0%) and 8.1% (5.0%) for base of tongue lesion, and for contralateral submandibular glands those were 11.1% (5.8%) and 9.3% (6.7%) for mobile tongue lesion, and 23.6% (9.9%) and 26.5% (11.2%) for base of tongue lesion, respectively. An almost identical dosimetric pattern was observed between these two studies, emphasizing that the doses received by the ipsilateral submandibular glands were about twice as large as the doses received by the contralateral submandibular glands. In our study, almost all values were lower than in the above-mentioned study. We think that one reason for this observation may be our smaller implant volumes compared to theirs (16 $cm^3$ vs. 33 $cm^3$ for mobile tongue lesion).

## Conclusions

This study presented dosimetric characteristics for target volume and critical structures in CT image-based multicatheter HDR interstitial BT for head and neck cancer. By conformal treatment planning, it was possible to maintain the dose to the mandible at an acceptable level, while the doses to the spinal cord and contralateral salivary glands were generally low. The quantitative plan evaluation may help us find correlations between dosimetric parameters and clinical outcome, and may lead to improve the quality of the treatment, but it requires longer follow-up and results from other studies.

## Disclosure

Authors report no conflict of interest.

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