Case report

Edema worsens target coverage in high-dose-rate interstitial brachytherapy of mobile tongue cancer: a report of two cases

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Abstract

Purpose: We report our study on two patients to highlight the risk of underdosage of the clinical target volume (CTV) due to edema during high-dose-rate interstitial brachytherapy (HDR-ISBT) of mobile tongue cancer.

Material and methods: To treat the lateral side of the CTV, flexible applicator tubes were implanted on the mouth floor. Two-dimensional planning was performed using X-ray images for Case 1, and three-dimensional (3D) planning was performed using computed tomography (CT) for Case 2. Prescribed doses for both cases were 54 Gy in nine fractions.

Case reports: Case 1 was treated for cancer of the right lateral border of the tongue in 2005. Tongue edema occurred after implantation, and part of the lateral border of the tongue protruded between the applicator tubes. Acute mucosal reaction abated in the protruded area earlier than in the other parts of the CTV. In this case, the tumor recurred in this area 5 months after the treatment. Case 2 was treated for cancer of the left lateral border of the tongue. Because tongue edema occurred in this case also, plastic splints were inserted between the applicator tubes to push the edematous region into the irradiated area. The mucosal surface of the CTV was covered by the 70% isodose, and 100% isodose line for before and after splint insertion. Local control of the tumor was achieved 4 years after treatment.

Discussion and conclusions: To ensure sufficient target coverage, 3D image-based planning using CT should be performed, followed by re-planning using repeated CT as needed. Also, the development of devices to prevent protrusion of the edematous tissue outside the target area will help to ensure the full dosing of CTV.

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Key words: edema, HDR, target coverage, tongue cancer.

Purpose

Radiotherapy is one of the standard treatment modalities for anterior mobile tongue cancer. Low-dose-rate (LDR) and high-dose-rate (HDR) interstitial brachytherapy (ISBT), with or without external beam radiotherapy (EBRT), shows a high rate of local control that is nearly equivalent to that of radical surgery [1,2,3,4,5,6,7,8,9,10]. We also showed that local control rates using HDR-ISBT for early mobile tongue cancer is an effective alternative treatment [7,8].

In most institutes, a single treatment plan for dose optimization of mobile tongue brachytherapy is developed just after implantation. However, the dosimetry will change if there is any change in the geometry between the applicator positions and the clinical target volume (CTV) following treatment planning. In prostate brachytherapy, both edema and applicator displacement are considered as causes of underdosage or overdosage to the CTV and organs at risk (OAR) [11,12,13,14]. In case of prostate implants, the end of the applicator tip is inside the body and is not in a fixed position. Such that, the geometry between the applicator positions and CTV location will often change during treatment. However, applicator displacement in tongue brachytherapy is less of an issue because the applicator tip is fixed inside the oral cavity; thus, the geometry between the applicator and the CTV during

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treatment will not change. Tongue edema is a problem that is often observed during ISBT of the tongue because applicator implantation by itself can cause tongue edema [15,16]. Tongue edema can reduce target coverage because the treatment margin of brachytherapy is only 5-10 mm from gross tumor volume (GTV) [10,17].

We report on how tongue edema in one case affected dosimetry to such an extent that local tumor recurrence occurred. We also describe a second case, in which tongue edema led to reduced tumor coverage, which was quantified using three-dimensional (3D) CT-based treatment planning.

Case reports

Applicator implantation

Implantation of applicators was performed under general anesthesia in both cases at National Hospital Organization Osaka National Hospital. To treat the lateral side of the CTV, a metallic open-ended needle (Bevel Needle®, Elekta AB, Stockholm, Sweden) was inserted from the submandibular region and was implanted on the mouth floor or the lateral border of the tongue. Next, the needle was inserted into the vinyl template. After insertion of the needle, it was replaced by a flexible applicator tube (Flexible implant tube, 6F, single leader®; Elekta AB). To treat the medial side of the tongue, the open-ended needle was implanted to the dorsal surface of the tongue and inserted into the hole of the vinyl template. After that, a flexible applicator tube was replaced.

Treatment planning and treatment

For Case 1, we performed two-dimensional treatment planning using two orthogonal X-ray images to confirm applicator positions. Prescribed doses were delivered to 5 mm from the applicator. Titanium markers were implanted at the edge of the tumor to help draw the tumor contour and position on treatment planning software (PLATO, Elekta AB). For Case 2, treatment planning was conducted using 3D CT. We drew the contour of the tongue and mandible in CT. The contour of the CTV was identified using not only CT but also by employing titanium markers and perioperative examinations (inspection, palpation, and intraoral ultrasonography). The extent of the tumor on the tongue's surface was also evaluated by staining with Lugol's iodine during implantation and by placement of metal markers.

We defined the CTV as an equivalent to GTV. We used a modified Paris system with computer optimization (geometrical optimization) and delivered prescribed doses to 85% of the basal dose at first. Subsequently, we always modified the isodose shape manually and sometimes changed the % basal dose to adequately cover the CTV by isodose lines of the prescribed dose (PD) without excessive doses to OARs [18]. Prescribed dose was 54 Gy per nine fractions in 7 days. Biological effective dose ($\alpha/\beta = 10$) was 86.4 Gy, and equivalent total dose in 2 Gy fractions (EQD_2) was 72 Gy. Our planning aim was that the CTV was covered by 100% of PD. We used microSelectron-HDR® (Elekta AB) with an ^{192}Ir source. Source strength was 249.2 GBq and 282.6 GBq for Case 1 and Case 2, respectively.

Case 1

A 55-year-old female patient had a squamous cell carcinoma on the right lateral border of her tongue that was staged cT2N0M0 using the 2002 UICC classification (Figure 1A). She underwent HDR-ISBT as monotherapy. Two plane implantation with 8 flexible applicator tubes was performed in November 2005. Tongue edema developed the day after implantation, and a part of the lateral border of the tongue protruded between two of the applicator tubes (Figure 1B). She had an acute mucosal reaction to the therapy, with exudative mucositis peaking 13 days after treatment; however, a part of the protruding area had no white coating (Figure 1C). After 23 days of treatment, the coating disappeared from nearly all the protruding area (Figure 1D). Five months after the treatment, the tumor recurred in this area (Figure 1E). Biopsy was performed and histological finding showed squamous cell carcinoma. She received salvage surgery and tumor was controlled until she died by intercurrent disease 122 months after salvage surgery.

Case 2

A 47-year-old male patient had a squamous cell carcinoma on the left lateral border that was staged cT2N0M0 using the 2002 UICC classification (Figure 2A). Two plane implantation with 9 flexible applicator tubes was performed in October 2010. We performed 3D CT-planning and delivered 6 Gy as D_{100} (CTV = GTV). D_{90} (CTV) was 6.9 Gy. If 5 mm margin will add to the CTV, D_{100} (CTV) and D_{90} (CTV) were 4.8 Gy and 6.5 Gy, respectively. If 10 mm margin will add to the CTV, D_{100} (CTV) and D_{90} (CTV) were 3.5 Gy and 5.3 Gy, respectively. This patient also developed tongue edema the day after implantation (Figure 2B); therefore, two plastic splints were inserted between applicator tubes to push the edematous tongue into the irradiated area (Figure 2C).

Figures 2D and 2E show the isodose distribution curves before and after splint insertion. The mucosal surface of the CTV was covered by the 70% isodose line before splint insertion, but it was covered by the 100% isodose line after splint insertion. Local control of tumor recurrence was achieved until the patient's death by neck metastasis 4 years after the treatment.

Discussion

Because ISBT can deliver higher doses of radiation to more localized regions than EBRT, better rates of local control in cases of mobile tongue carcinoma were expected, and the rapid dose fall-off from applicators could maintain complication rates within tolerable levels. However, if unexpected tongue edema occurs, dose fall-off will become a cause of underdosage to the CTV. Schultze *et al*. [15] investigated tongue edema in 51 patients with head and neck cancers (most patients had a base of tongue cancer and mobile tongue cancer was not included), and found that applicator-induced edem-

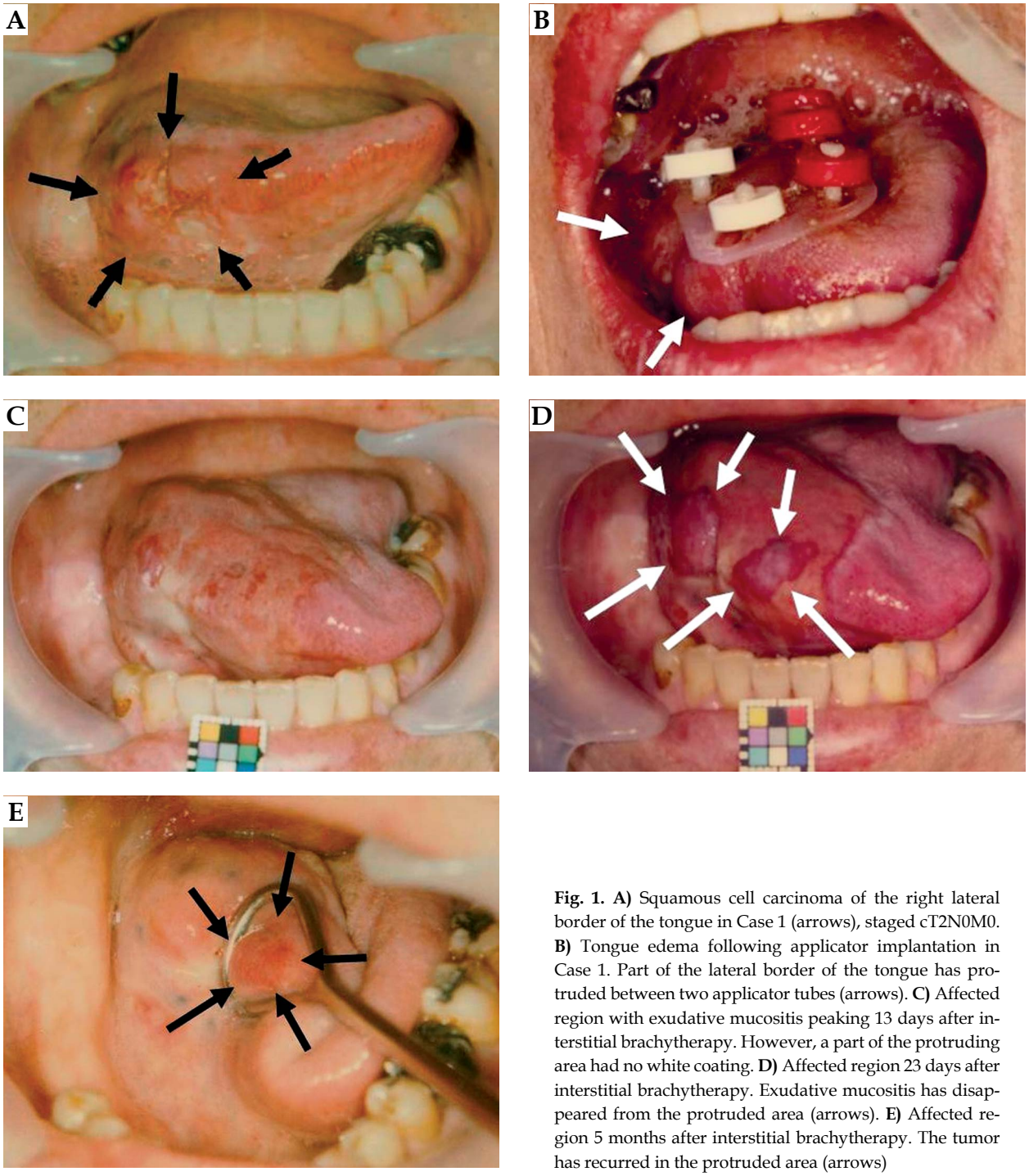

Fig. 1. A) Squamous cell carcinoma of the right lateral border of the tongue in Case 1 (arrows), staged cT2N0M0. **B)** Tongue edema following applicator implantation in Case 1. Part of the lateral border of the tongue has protruded between two applicator tubes (arrows). **C)** Affected region with exudative mucositis peaking 13 days after interstitial brachytherapy. However, a part of the protruding area had no white coating. **D)** Affected region 23 days after interstitial brachytherapy. Exudative mucositis has disappeared from the protruded area (arrows). **E)** Affected region 5 months after interstitial brachytherapy. The tumor has recurred in the protruded area (arrows)

atous deviation of tongue width was 6 mm, measured using magnetic resonance imaging (MRI). American Brachytherapy Society (ABS) recommendations showed that a smaller dose per fraction may be reduced normal tissue injury. Our single fraction doses were 6 Gy and D_{100} (CTV) was 6 Gy. However, D_{90} (CTV) was 6.9 Gy. Furthermore, D_{90} (CTV) and D_{100} (CTV) change 3.5-6.5 Gy if CTV margin of 5-10 mm was added. In future, we should investigate which DVH value showed the highest correlation with tongue edema. Our total prescribed doses were 54 Gy and EQD_2 ($\alpha/\beta = 10$) was 72 Gy. It is relatively higher than 54-80 Gy for the other series [16]. However, it is also a same problem showing above. Implant volume may also be a risk factor of tongue edema. If implant volume becomes larger, both traumatic and irradiation damages become larger. We implanted two plane implantations for these 2 cases, and it led to not much implant volume because our standard technique was two or more plane implantations [19]. Further investigation will also be necessary.

American Brachytherapy Society recommendations also showed that corticosteroids may be used to reduce

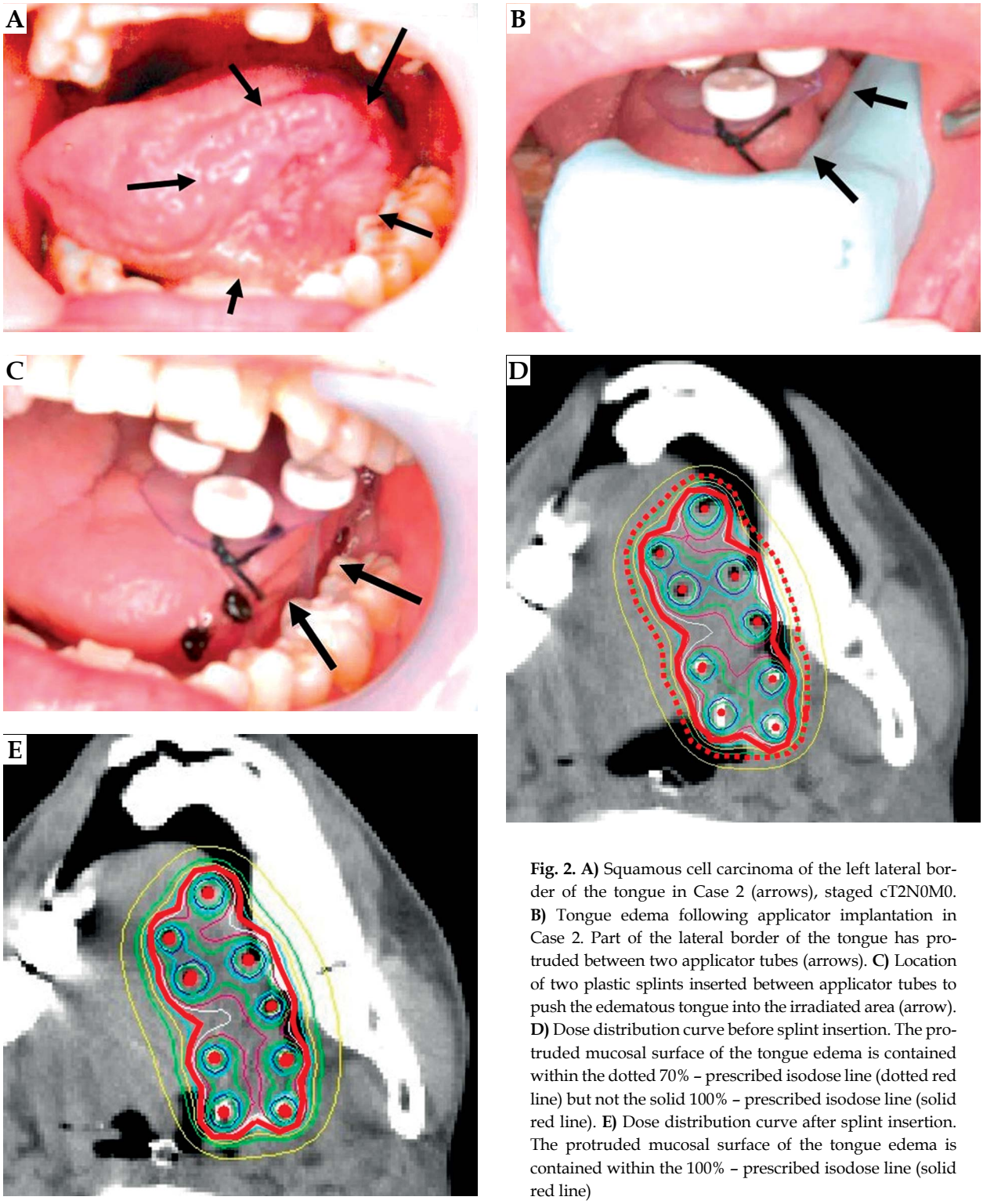

Fig. 2. A) Squamous cell carcinoma of the left lateral border of the tongue in Case 2 (arrows), staged cT2N0M0. **B)** Tongue edema following applicator implantation in Case 2. Part of the lateral border of the tongue has protruded between two applicator tubes (arrows). **C)** Location of two plastic splints inserted between applicator tubes to push the edematous tongue into the irradiated area (arrow). **D)** Dose distribution curve before splint insertion. The protruded mucosal surface of the tongue edema is contained within the dotted 70% – prescribed isodose line (dotted red line) but not the solid 100% – prescribed isodose line (solid red line). **E)** Dose distribution curve after splint insertion. The protruded mucosal surface of the tongue edema is contained within the 100% – prescribed isodose line (solid red line)

postoperative swelling. We infused dexamethasone sodium phostate (8 mg) intravenously to prevent tongue edema during implantation. However, severe tongue edema sometimes occurred. And so, we must consider the way to solve this problem.

To prevent underdosing related to edema, 3D image-based planning using CT should be performed to evaluate the dose distribution of the CTV and OARs [20,21]. Because edematous changes of the tongue may occur after first CT planning, CT should be repeated every day during the treatment period. And, re-planning should be performed to keep adequate dose coverage for the CTV. However, because treatment re-planning is time consuming, it would be desirable to have a device that could

counter edema-related protrusion of tissues outside the target area. We contrived a means, by which edematous tissue could be contained between the applicator tubes by using a splint insertion for Case 2. We are in the process of developing a specific device for this purpose and will report on it in the near future.

Conclusions

To ensure sufficient target coverage, 3D image-based planning using CT should be performed, followed by re-planning using repeated CT as needed. Also, the development of devices to prevent protrusion of the edematous tissue outside the target area will help ensure full dosing of the CTV.

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Disclosure

Authors report no conflict of interest.

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