

TPS-guided interstitial Iodine-125 implantation in patients with oral cavity and maxillofacial carcinomas

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Abstract. – OBJECTIVE: To investigate the efficacy as well as the complications involved in the use of interstitial Iodine-125 implantation for the treatment of oral cavity and maxillofacial carcinomas.

PATIENTS AND METHODS: Fifteen patients with oral cavity and maxillofacial carcinomas received treatment planning system (TPS)-guided interstitial Iodine-125 implantation. The apparent activity per particle ranged from 0.6 mCi (2.22MBq) to 0.7 mCi (2.59MBq). The matched peripheral dose delivered by radioactive seeds ranged from 90 to 120 Gy. The efficacy of the treatment and the postoperative complications were evaluated during follow-up.

RESULTS: The seeds were implanted successfully in all 15 patients and median number of seeds implanted was 36.53. CT scans were performed in all patients at 1-6 months postoperatively. During follow-up at 6-27 months, seed migration occurred and a good local tumor control was achieved with an overall response of 86.7%. No severe side effects were observed.

CONCLUSIONS: TPS-guided interstitial Iodine-125 implantation is an effective and safe procedure with minimal invasiveness for the treatment of oral cavity and maxillofacial carcinomas, and it effectively prevents the recurrence of cancer and short-term lymphatic metastasis.

Key Words:

Malignant tumor, Oral cavity and maxillofacial, Radioactive iodine-125 seed, Treatment planning system (TPS).

Introduction

Oral cavity and maxillofacial carcinomas can be effectively treated or even cured by conventional surgery combined with chemotherapy and radiotherapy. However, these traditional treatments often affect the appearance of patients and some patients are inoperable due to the status of

disease. Interstitial Iodine-125 seed implantation is superior to other regimens in managing oral and maxillofacial carcinomas with potential advantages including less invasiveness, fewer complications, safety and high efficacy¹⁻³. In the current study, we report our case load of 15 patients with oral and maxillofacial carcinomas using interstitial Iodine-125 implantation.

Patients and Methods

Patients

Fifteen patients (9 women, 6 men, age range 23-81 yrs) between the period of 2010 and 2012 were admitted in our institution with oral and maxillofacial carcinomas including 10 cases of primary tumors and 5 cases of recurrent tumors and were enrolled in this study. Pathological examination confirmed carcinomas as adenoid cystic carcinomas (n=9), mucoepidermoid carcinomas (n=2), adenocarcinoma (n=2) and malignant mixed tumor (n=2). The sites of tumors included tongue (n=3), gums (n=2), parotid gland (n=5), floor of mouth (n=1), palate (n=2) and mandible and maxilla (n=2). Our study got the approval for clinical research of Independent Ethics Committee of Xuzhou Central Hospital. We have read the Helsinki Declaration and have followed the guidelines in this investigation.

Inclusion Criteria

The inclusion criteria were as follows: (1) Oral cavity and maxillofacial carcinomas were confirmed by imaging examination and histopathological study of biopsy specimens; (2) Both primary and recurrent carcinomas were included; (3) Patients were in good physical condition to tolerate procedures of implantation; (4) The liver, kidney and heart functions were normal.

Chemicals and Devices

Iodine-125 was purchased from Beijing Astro Technology Ltd. Co. (Beijing, China). A 3D computer treatment planning system (TPS) was provided by Imaging Center of Beijing University of Aeronautics and Astronautics (Beijing, China). GEMINI GXL-16 PET/CT system was procured from Philips Medical Solutions (Sittard Geleen, The Netherlands).

Seed Implantation

CT scans on tumors were performed before implantation and the images generated were digitized in the TPS to produce a three-dimensional computerized model of tumors as well as surrounding vital organs, thus, facilitating the treatment plan (Figure 1). The digitized TPS data were used to define the target volume on which basis the D90 of irradiation (the dose delivered to the 90% of the target volume as defined by CT using dose-volume histogram) was prescribed. The number and the position of the Iodine-125 seeds at the target site were determined using the TPS. Patients had to fast 4h prior to implantation and received sedatives 0.5h before the start of procedure. Under general or local infiltration anesthesia, radioactive seeds were implanted in predetermined positions in tumors under CT guidance (Figure 2A). Postoperative CT scans were performed to assess the quality of each implant (Figures 2B, 3). Reimplantations were performed if any "cold spot" were observed. The matched peripheral dose (MPD) calculated by TPS was 90-120 Gy. CT scans were performed at 2, 4, 6 month postoperatively to evaluate the status of tumors, as well as the number and distribution of radioactive seeds (Figure 4).

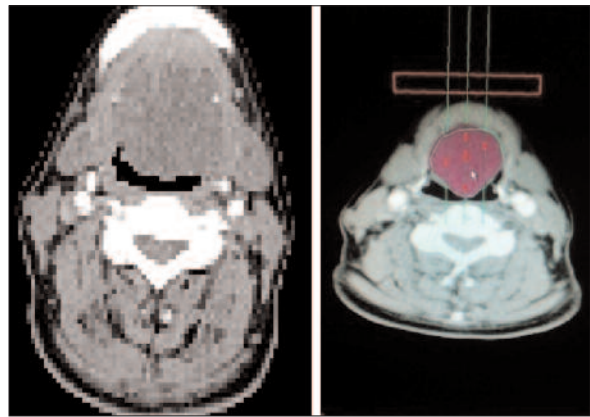


Figure 1. Pretreatment of target volume by CT/TPS.

Outcome Measures

A follow-up CT scan was performed every 2 months postoperatively at 2, 4, 6 month to examine the regression of tumors. Local tumor control was evaluated by CT scan once every postoperative year. The outcome measures included the evaluation of short-term efficacy, efficiency and local tumor control rate. The short-term efficacy was described as the following situations: (1) complete remission (CR), showing complete disappearance of tumor and no evidence of disease on images; (2) partial remission (PR), with the tumor volume reduced $\geq 50\%$ compared to pre-treatment; (3) No change (NC), when tumor volume is either reduced $< 50\%$ or increased $< 25\%$; and (4) progressive disease (PD), with tumor volume increased $\geq 25\%$ or exhibiting new tumor.

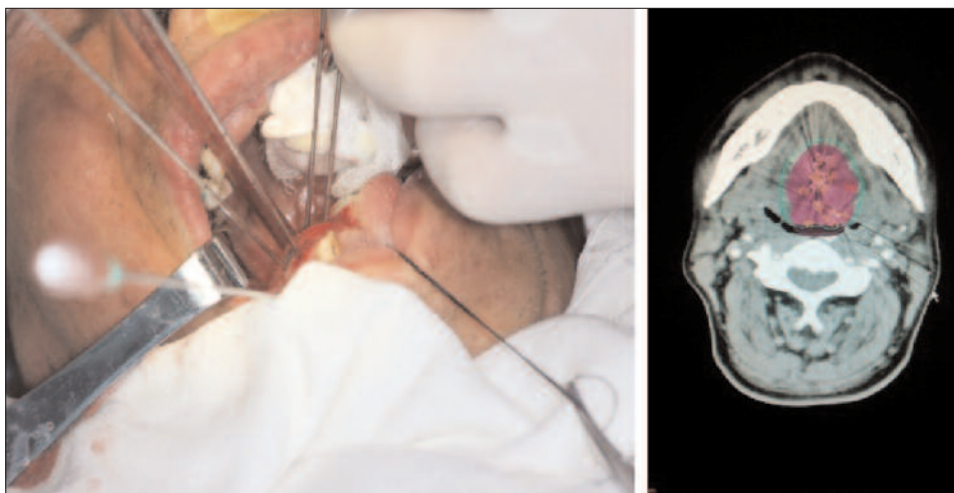


Figure 2. **A**, Implantation of Iodine-125. **B**, Postoperative verification of the distribution of Iodine-125 seeds by TPS.

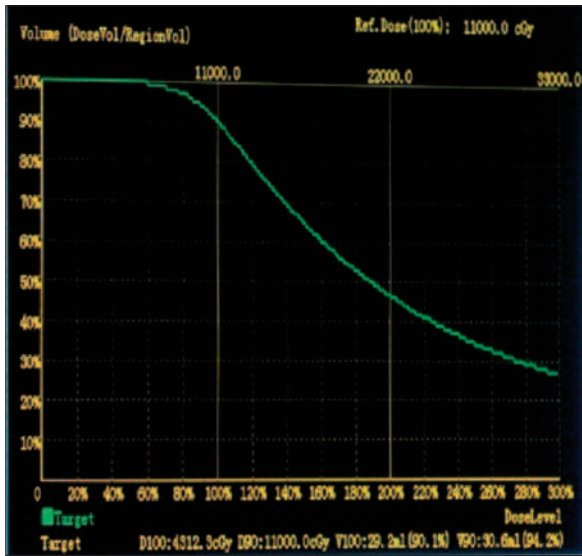


Figure 3. Postoperative dosimetry analysis performed by TPS.



Figure 4. Postoperative CT scan to evaluate changes in tumor volume.

Results

Implantation was achieved in all 15 patients with each patient receiving an average of 36.53 seeds except two patients received reimplantation. Also, four patients experienced transient bleeding and another two patients had mild pain swallowing.

Outcome of Implantation

Overall response rate was 73.3% including 7 patients with CR, 6 patients with PR and 2 pa-

tients with NC while CR and PR reached 86.7% (Table I). During follow-up of 6-27 months, 3 patients developed recurrent tumors outside the target areas. None of the patients developed any long-term complications or damage because of radiation and no mortality was observed.

Table I. Changes in tumor volume in 15 patients with oral cavity and maxillofacial carcinomas.

Gender	Age (years)	Tumor site	Tumor volume (pretreatment)	Tumor response and tumor volume (6 months postoperatively)
Male	81	Right parotid gland	37×29	CR*
Female	28	Right parotid gland	13×10	CR*
Female	42	Left parotid gland	27×17	CR**
Female	62	Palate	16×9	CR*
Female	23	Left parotid gland	20×18	CR*
Female	81	Right upper maxilla	26×15	CR*
Male	77	Left lower gum	22×14	CR*
Male	59	Base of tongue	40×31	PR, 22×13**
Female	44	Left side of tongue	30×25	PR, 13×17**
Male	71	Floor of mouth	38×21	PR, 19×9**
Female	68	Right parotid gland	35×23	PR, 13×12**
Female	55	Left upper maxilla	43×36	PR, 29×21**
Male	77	Right side of tongue	36×33	PR, 16×13**
Male	66	Palate	23×26	NC***
Female	75	Right lower gum	30×22	NC***

*CR = complete remission, **PR = partial remission ***NC = no change.

Discussion

Interstitial permanent iodine-125 implantation is a novel treatment modality for cancer. Radioactive iodine-125 delivers Gamma rays which induce DNA strand breakage in cancer cells; free radicals produced by Gamma-ray-triggered ionization of cellular H₂O cause damage to DNA⁴. Iodine-125 implantation is superior to traditional radiation therapy and display following advantages: (1) Low-energy Iodine-125 seeds have a valid radius of 1.7 cm in tissue, allowing concentration of gamma rays in tumors while sparing normal tissues. (2) Iodine-125 has a longer half-life of 59.6 days, which enables persistent effect of the seeds on tumors. (3) The implantation was demonstrated to be a simple procedure with less damage and mild complications⁵. However, precautions have to be taken when implantation is carried on.

Implantation Eligibility Determination

Despite the fact that Iodine-125 implantation has several advantages over other therapies, surgery remains the first-line treatment option for patients. It has been reported that Iodine-125 implantation was effective in managing the following tumors²⁻⁷ adenoid cystic carcinoma; carcinomas located at tongue, floor of the mouth, oropharynx, parotid gland and parapharyngeal region. In present study, majority of carcinomas were adenoid cystic carcinomas located mainly at the tongue, gum and parotid gland. Consistent with the previous reports, favorable outcomes were achieved in all patients recruited in the current study.

Pretreatment Radiation Dose Determination

The number and distribution of Iodine-125 seeds to be implanted are determined by TPS before the start of the treatment. TPS was developed during the treatment of prostate cancer⁸. It complies with the needs of planning treatment for majority of solid tumors. However, different types of cancers respond to a range of radiation doses as well as cancer cells at various sites or organs tolerate radiation therapy differently. Hence, pretreatment planning has to be individually customized to meet the requirements. In addition, real-time verification, evaluation and adjustment are required to optimize the therapy, ensuring coverage of > 90% target volume with > 90% prescribed radiation dose³. Postoperative

dosimetry analysis is routinely conducted to verify the results. In this study, TPS planning was supplemented with manual planning to assure the precision of radiation dose.

Complications Associated with Implantation

Seed loss and seed migration are most common complications after radioactive seed implantation. With the extension of treatment duration, the change of tumor volume is likely to cause seed loss or migration. Horwitz et al⁹ reported the treatment of tongue cancer using Iodine-125 brachytherapy. Implanted seeds migrated to palate in one patient and seed loss occurred in two other patients during follow-up. In the present study, neither seed loss nor seed migration occurred in any patient; however, precautions have to be taken during further treatment.

Even though Iodine-125 implantation is minimally invasive and the seeds carry low radioactive energy, its impact on surrounding normal tissues cannot be ignored. In some cases, radioactive reactions and some related symptoms such as edema and infections could be developed. In addition, the impact of Iodine seeds on the facial nerve that transverses parotid gland has to be evaluated further. As reported by Zhang et al¹⁰ the brachytherapy with Iodine-125 caused changes in the myelin and axons of facial nerve of rabbit and aggravated damage with increased number of seeds implanted as well as when the seeds remained for longer time in the tissue. Although facial nerve injury did not occur in any patients during this study, precautions have to be taken during further treatment by closely monitoring patient's condition to prevent the occurrence of such complications.

Conclusions

Interstitial Iodine-125 implantation seems to be an effective and feasible procedure for the treatment of patients with oral cavity and maxillofacial carcinomas. The selection of eligible patients, pretreatment planning and prevention of postoperative complications are important issues that need to be considered. Majority of studies on brachytherapy of carcinoma using Iodine-125 were generally based on clinical experience, and not on evidence-based proof. Hence, options of treatment should be considered objectively and chosen very carefully.

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Conflict of Interest

The Authors declare that there are no conflicts of interest.

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