The Laryngoscope

Postoperative ^{125}I Brachytherapy Delivered by Digital Model Obturators for Recurrent or Locally Advanced Maxillary Cancers

Ming-wei Huang, PhD; Jian-guo Zhang, BSMed; Dai Tong, MD; Jie Zhang, PhD; Lei Zheng, PhD; Yi Zhang, PhD; Guang-yan Yu, PhD

Objectives/Hypothesis: We aimed to evaluate the feasibility and effectiveness of postoperative ^{125}I brachytherapy delivered by use of digital model obturators for recurrent or locally advanced maxillary cancers.

Study Design: Retrospective study.

Methods: From 2006 to 2008, 12 patients (seven females; median age, 65 years; range, 22–86 years) with recurrent or locally advanced maxillary cancers showing positive margins after surgery underwent ^{125}I brachytherapy by use of digital model obturators and interstitial implants. The radioactivity was 18.5 to 33.3 MBq per seed, and the prescription dose was 80 to 160 Gy. Functional outcome of patients was evaluated by the Performance Status Scale (PSS) for head and neck cancer before and after brachytherapy.

Results: The ^{125}I seeds and dosages were well distributed in the radiation fields, and all patients had higher PSS scores after than before treatment with obturators. During a median follow-up of 53 months (range, 28–62 months), local control at 3 and 5 years was 83.3% and 66.7%, respectively, with a mean local control time of 53.5 $\pm$ 3.79 months. Overall survival at 3 and 5 years was 91.7% and 71.4%, respectively, with a mean survival time of 56.6 $\pm$ 2.99 months. Two patients died due to local recurrence, and one patient died due to lung metastasis. No patient had severe complications during follow-up.

Conclusions: ^{125}I brachytherapy delivered by digital model obturator is effective in treating maxillary cancers with positive margins after maxillectomy for advanced or recurrent cancer. The method may improve the quality of life of patients with maxillary defects.

Key Words: Brachytherapy, obturator, maxillary cancer.

Level of Evidence: 4.

***Laryngoscope,* 122:2461–2467, 2012**

INTRODUCTION

Cancers involving the maxilla can originate from primary tumors of the maxilla or tumors of adjacent structures such as the palate, upper gingiva, and paranasal sinuses.[1] These tumors, especially recurrent or advanced ones, may represent significant treatment challenges[1–3] because the maxilla is located near many important tissues, including major blood vessels, nerves, eyes, and organs of speech and swallowing, which may compromise radical resection or wide local excision and the delivery of radiation.[1,2,4,5]

Although negative margins are difficult to achieve in these cancers, surgery is traditionally a recommended treatment for resectable malignant maxillary tumors that are primary or recurrent.[1,4] However, the postoperative recurrence rate of head and neck tumors is 31.7% for patients with negative margins but is markedly higher (71%) for patients with positive or close margins.[6] Therefore, surgery combined with postoperative adjuvant radiotherapy is often recommended for maxillary cancers,[1,7–9] especially for patients with positive or close resection margins.[10–13] However, radiotherapy for patients with maxillary cancers may lead to orofacial complications[5,10,14–16] and detrimental impact on quality of life,[14,17–19] especially for patients with recurrent tumors who previously received radiation.

Brachytherapy can deliver a high radiation dose to a tumor while sparing surrounding normal vital tissues.[20,21] The low dose rate of ^{125}I irradiation can enhance the tolerance of normal tissues.[22] Several reports have analyzed the benefits of ^{125}I brachytherapy used alone or combined with surgery for head and neck cancers.[21–25]

In this study, we evaluated the feasibility and effectiveness of postoperative ^{125}I brachytherapy for patients with positive margins after surgery for recurrent or locally advanced maxillary cancers. We used computed tomography (CT) images to design digital model obturators to reconstruct the defective maxilla for each patient to deliver ^{125}I brachytherapy to target areas where soft tissues are too thin to contain ^{125}I seeds. In addition, the digital model method could resolve the difficulty in making impressions for patients with postoperative temporary inability to open the mouth.

From the Department of Oral and Maxillofacial Surgery (M.-W.H., J.-G.Z., J.Z., L.Z., Y.Z., G.-Y.Y.) and Department of Prosthodontics (D.T.), Peking University School and Hospital of Stomatology, Beijing, China.

Editor's Note: This Manuscript was accepted for publication May 29, 2012.

The authors have no funding, financial relationships, or conflicts of interest to disclose.

Send correspondence to Jian-guo Zhang, BSMed, or Guang-yan Yu, PhD, Department of Oral and Maxillofacial Surgery, Peking University School and Hospital of Stomatology, Beijing, 100081, China. E-mail: rszhang@126.com or gyyu@263.net

DOI: 10.1002/lary.23527

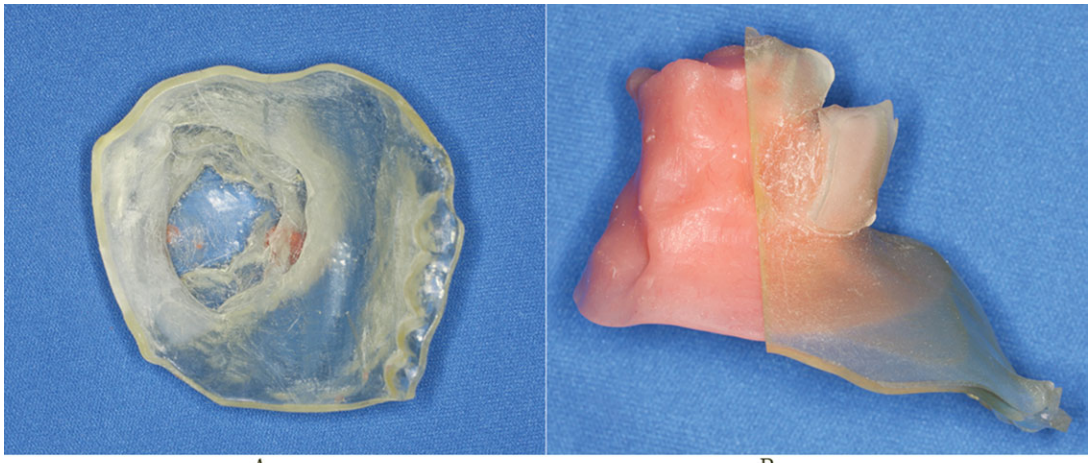

Fig. 1. (A) Computed tomography-designed model of the defective part of the maxilla. (B) The obturator constructed from denture soft-liner elastic material. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

MATERIALS AND METHODS

Patients

From October 2006 to January 2008, 12 patients (seven females; median age, 65 years; range, 22–86 years) with cancers involving the maxilla underwent surgery and postoperative ^{125}I brachytherapy. This study was approved by the ethics committee of Peking University, and all patients gave their informed consent for use of their data. Six cases were recurrent after previous surgery and external radiotherapy. One case was a second primary tumor in the maxillary area that had previously been irradiated. The previous median dose of external radiation in these cases was 60 Gy (range, 50–66 Gy; conventional fractionation, 2 Gy/d). The other five cases were primary locally advanced tumors. All 12 patients underwent wide local excision (with half or partial maxillectomy). Postoperative histopathology revealed six cases of adenoid cystic carcinoma (ACC) (three recurrent tumors), two mucoepidermoid carcinoma (MEC) (one moderate grade and one high grade, both recurrent tumors), two squamous cell carcinoma (SCC) (one recurrent and one second primary tumor), and two adenocarcinoma and polymorphous low-grade adenocarcinoma, respectively. The resection margins were positive for all patients. The seven patients with recurrent or second primary tumors had undergone neck dissection or radiation in previous treatments. Only the patient with adenocarcinoma underwent elective neck dissection, with no cervical lymph node metastasis on postoperative histopathology. All other patients with negative findings for necks did not receive treatment to the neck.

All 12 patients underwent postoperative ^{125}I brachytherapy using digital model obturators designed by CT to reconstruct the defective maxilla.

^{125}I Brachytherapy Plan System and ^{125}I Radioactive Seeds

The brachytherapy treatment planning system (BTPS) (Beijing Atom and High Technique Industries, Beijing, China) was used to develop the ^{125}I brachytherapy plan. The ^{125}I seed (model 6711; China Institute of Atomic Energy, Beijing, China) was 4.5 mm long and 0.8 mm in diameter and had a half-life of 59.4 days with radioactivity of 18.5 to 33.3 MBq per seed. The photon energy emitted by ^{125}I is low (27–35 keV), and the dose is greatly reduced with distance so it minimizes the dose to adjacent structures and attending staff.[26]

^{125}I Brachytherapy Method

Design of obturators. All patients underwent CT scanning at about 2 to 4 weeks after surgery, when the operative wounds were almost healed. Then the model of the defective maxilla was manufactured by using a three-dimensional reconstruction technique and rapid prototyping technology (Fig. 1A). The obturators were constructed from denture soft-liner elastic material and were >1 mm thick to contain the radioactive seeds (Fig. 1B). They were designed with a hollow center to allow greater stability and elasticity when inserting into the undercut.

Brachytherapy plan. Steel wires (4.5 mm long, 0.8 mm in diameter) without radioactivity, used as markers, were temporarily implanted into the obturators in the front, back, top, and sides. Then all patients wearing these obturators underwent CT again to confirm that the obturators fit the maxilla defects and to determine the relative position of adjacent tissues and wires, to guide placement of radioactive seeds close to the target area. Using this CT images, the brachytherapy plan was made by the BTPS. In the plan, the obturator was used to place seeds to the area where it is just covered by thin mucosa (like maxillary sinus). If there is enough soft tissue (maybe residual tumors or adjacent tissues) to locate the ^{125}I seeds, we can use interstitial implantation. After CT, the steel wires in the obturator were removed.

The planning target volume was designed to cover the residual tumor with a 0.5- to 1-cm margin. The prescription dose (peripheral matching dose) was 80 to 120 Gy for recurrent tumors in areas that had previously received radiotherapy and 120 to 160 Gy for primary tumors. The dose distribution involved adjusting the available seed activities and seed positions if necessary.

Placement of radioactive seeds. According to the implantation plan, part of the radioactive seeds were placed in the obturators and sealed with acrylic resin (Fig. 2A). The relative position between the steel wires and the planned seeds in the obturator were helped to locate the position of ^{125}I seeds in the obturator. Other radioactive seeds were interstitially implanted into soft tissue with the patient under local or general anesthesia by intra- or extra-oral puncture with implantation needles under CT guidance (Fig. 2B).[21] After interstitial implantation, the digital model obturator containing ^{125}I radioactive seeds was inserted.

Verification and quality assurance of treatment. After implantation of obturators, patients immediately underwent

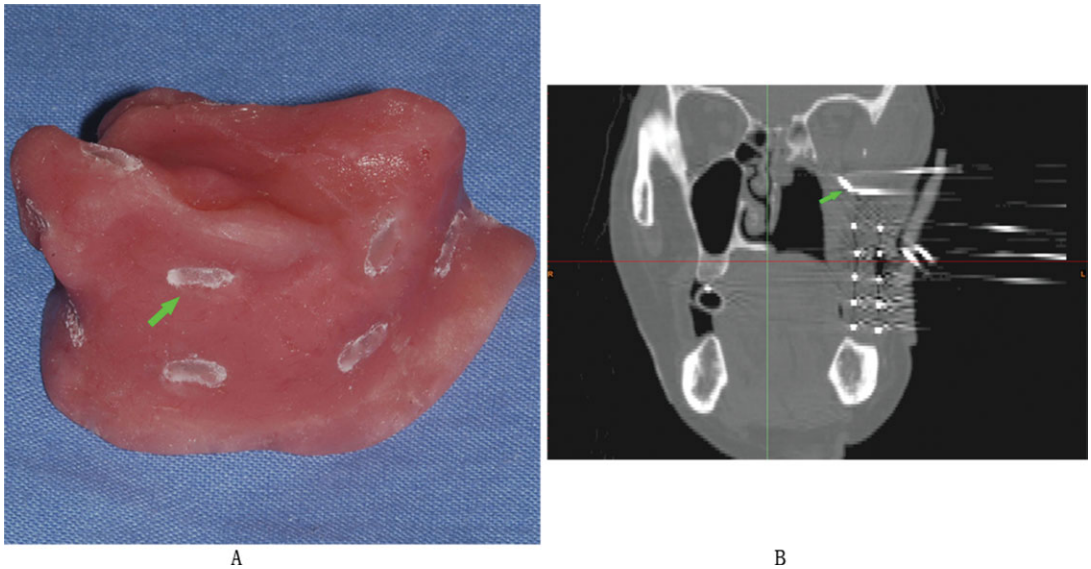

Fig. 2. (A) Radioactive seeds were implanted in the obturator and sealed with acrylic resin (the arrow indicates the position of ^{125}I seed). (B) Computed tomography-guided interstitial implantation of radioactive seeds from different directions (the arrow indicates the implant needles). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

CT examination. The CT images and BTPS were used to confirm the position, number and distribution of seeds, as well as radiation dosage in the target areas and organs at risk.

Follow-up

Patients wore the obturators for 6 to 8 months, removing them only for cleaning. CT or positron-emission tomography/computed tomography scan was performed 6 and 12 months after implantation or if necessary. Before and after brachytherapy, patients completed the Performance Status Scale (PSS) questionnaire for head and neck cancer patients, which includes questions about three functions: eating in public, understandability of speech, and normalcy of diet.[27] Total scores are from 0 to 100, lower scores representing worse functioning. Complications were evaluated according to the Radiation Therapy Oncology Group (RTOG)/European Organization for Research and Treatment of Cancer grading system.[28]

Statistical Analysis

SPSS 13.0 for Windows (SPSS Inc., Chicago, IL) was used for data analysis. Paired t test was used to evaluate the dose distribution and Wilcoxon signed ranks test to analyze PSS scores before and after brachytherapy. Two-sided $P < .05$ was considered significant. The Kaplan-Meier test was used to assess overall survival, disease-free survival and local control. Follow-up data were obtained until December 2011. Data for all patients who survived until this date were censored for overall survival analysis, data for all patients who survived without local or distant treatment failure were censored for disease-free survival analysis, and data for all patients without local recurrence until this date or death were censored for local control analysis.

RESULTS

Obturators

The obturators were designed from CT digital reconstructive models. On average, patients could open their mouths 2.3 cm, and two patients could open their mouths only 1.5 and 1.8 cm. In all cases, CT scans allowed for the successful creation of a digital model. The insertion of the obturators closed the oronasal fistula and allowed for normal impressions to be taken for denture construction.

Distribution of Radiation Seeds and Postimplant Dosimetry

The mean number of seeds in the obturators was 19.6 ± 3.4 and was 22.3 ± 2.8 for seeds implanted in surrounding tissues. All CT images showed stable seed distribution without migration and no loss of seeds in the obturators. The D_{90} (the doses delivered to 90% of the target volume) without radioactive seeds in obturators was 52.6 ± 3.5 Gy. The actuarial D_{90} with obturators was 121.8 ± 10.7 Gy (range, 86.3–176.8 Gy) and was higher than the prescribed dose for all patients.[29] The actuarial V_{100} (the percentage target volume that receive at least the prescribed dose) was >95% for each patient (mean, 98.6% ± 0.5%), and the V_{150} was <50% for all.[29] Figure 3 shows the distribution of seeds and doses with use of obturators. The mean dose measured in the carotid artery and jugular veins, eyes, and external auditory canals was 35.4 ± 3.57, 12.8 ± 2.39, and 10.4 ± 2.40 Gy, respectively, all within the tolerance limit.

Local Control Rate and Overall Survival Rate

Patients were followed for a minimum of 28 months after treatment (median, 53 months; range, 28–62 months). The 3- and 5-year local control was 83.3% and 66.7%, respectively, with a mean local control time of 53.5 months (95% confidence interval, 46.1-60.9 months; Fig. 4). Local recurrence occurred in four patients at 22, 36, 42, and 46 months (median, 39 months).

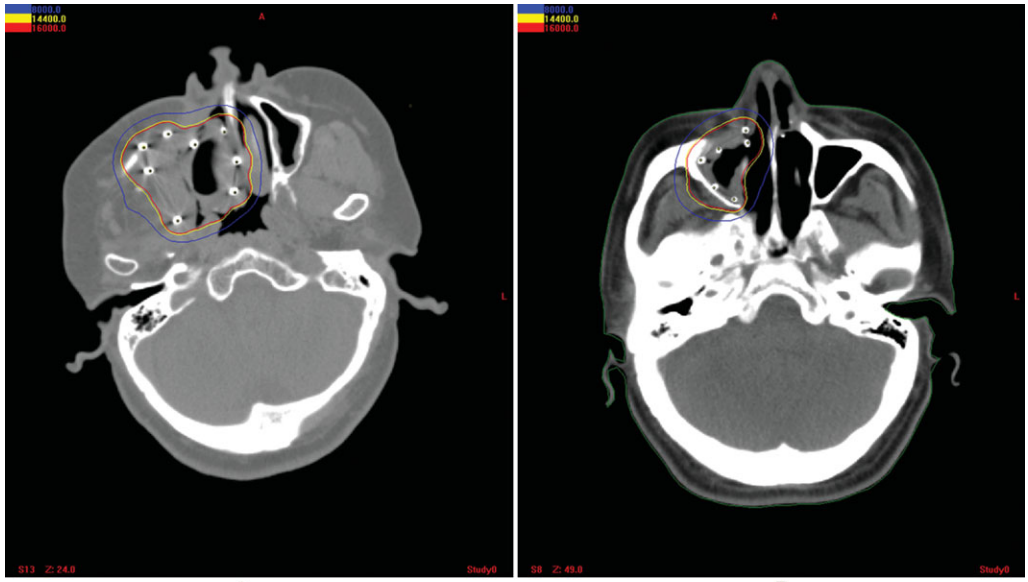

Fig. 3. Computed tomography and brachytherapy treatment planning system analysis of radioactive seed and dose distribution with obturators. Radioactive seeds in obturators delivered doses to tissues of (A) nasal cavity and (B) residual maxillary sinus. The red line is the 100% dose isodose line (160 Gy), yellow is the 90% dose isodose line (144 Gy), and blue is the 50% dose isodose line (80 Gy).

Overall survival at 3 and 5 years was 91.7% and 71.4%, respectively, with a mean overall survival time of 56.6 months (range, 50.7–62.4 months; Fig. 5). The 3- and 5-year disease-free survival was 83.3% and 58.3%, respectively, with a mean disease-free survival time of 51.7 months (range, 44.1–59.2 months; Fig. 6). Distant metastasis occurred in two patients with ACC. Two patients were alive with disease (one with local failure, one with local and distant failure). Two patients (one with SCC and one with MEC) died of local recurrence, and one patient with ACC died of lung metastasis.

Complications

Nearly all patients experienced temporary, minor side effects (RTOG grades 1 and 2) during the treatment, including mild pain and mucositis. These symptoms lasted 0.5 to 2 months and healed without treatment. One patient presented a mucosa ulcer, 1.0 × 0.8 cm, in the target area, with mild pain 2 weeks after implantation. The ulcer was treated conservatively and healed within 4 weeks. We observed no severe late complications.

PSS Scores

PSS scores for all separated areas of functioning were greater after brachytherapy with obturators than before brachytherapy ($P < .05$; Table I). The mean scores for eating in public, understandability of speech, and normalcy of diet were 29.2 ± 9.7, 20.8 ± 9.7, and 39.2 ± 2.9 without obturators, and 60.4 ± 12.9, 56.3 ± 11.3,

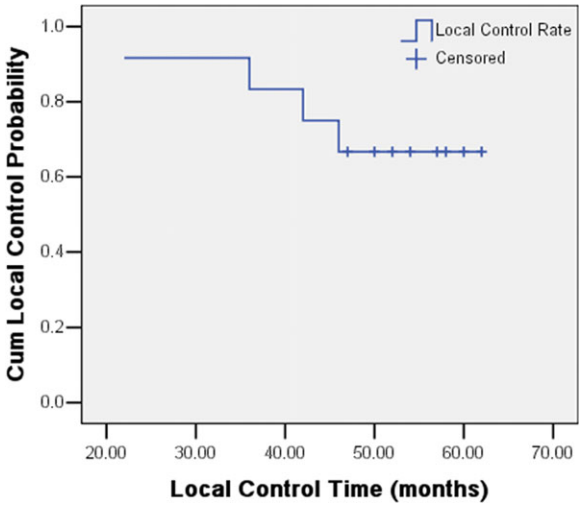

Fig. 4. Kaplan-Meier estimates showing local control after ^{125}I brachytherapy. Cum = cumulative. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

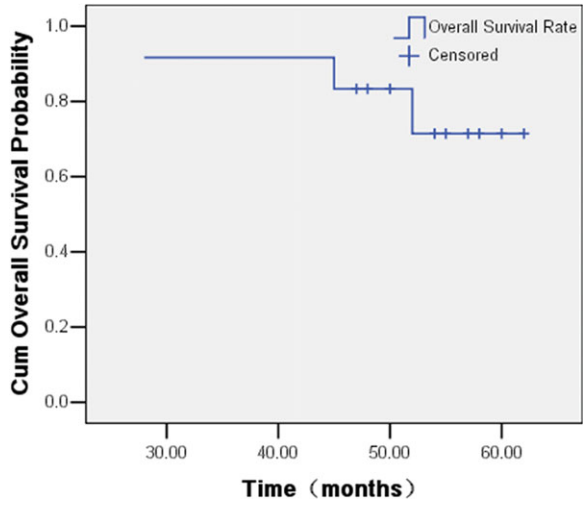

Fig. 5. Kaplan-Meier estimates showing overall survival after ^{125}I brachytherapy. Cum = cumulative. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

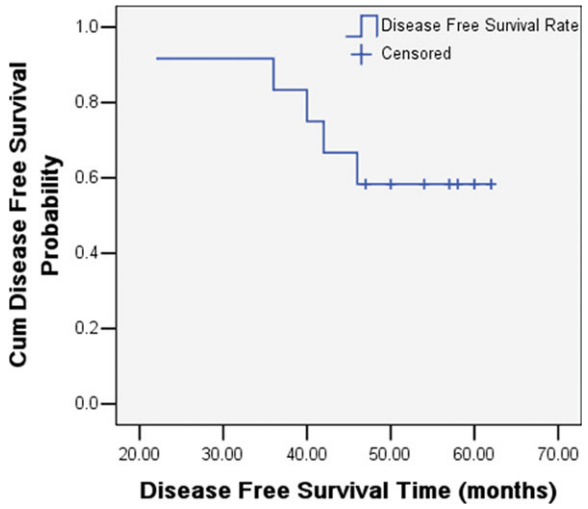

Fig. 6. Kaplan-Meier estimates showing disease-free survival after ^{125}I brachytherapy. Cum = cumulative. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

and 55 ± 5.2 with obturators, respectively. Scores for understandability of speech were especially higher; for two patients the scores improved from 0 (never understandable, may use written communication) to 50 (usually understandable, need face-to-face contact).

DISCUSSION

In our study we used ^{125}I brachytherapy as the treatment modality for advanced or recurrent maxillary cancers with positive resection margins after surgery and prior radiotherapy, and designed a digital modal obturator to accurately deliver the ^{125}I radioactive seeds. Use of the digital modal obturator achieved good seed and dose distribution and improved the quality of life of patients with maxillectomy. The computer-aided design helped in making impressions of maxillary defective areas for patients with postoperative difficulty in opening the mouth. Our results, albeit with a small sample, demonstrate good local control and functional outcome.

Radiotherapy can enhance the local control of head and neck carcinomas with positive or close margins after surgery.[30–32] It can be administered by external beam radiotherapy or brachytherapy.[30,31,33,34] External radiotherapy can enhance local control but has some problems. Some of the patients in our study refused external beam radiotherapy because of poor medical conditions or potential severe complications such as xerostomia, difficulty in opening the mouth, osteoradionecrosis, and arterial hemorrhage.[10,15–17,19,35] For patients with recurrent tumors after external radiation therapy, the redelivery of curative doses of external radiation is difficult because of the limited tolerance of normal critical structures. Brachytherapy addresses this problem by delivering a high dose directly to the tumor and a lower dose to the adjacent normal structures.[21,34] Jiang et al. concluded in a retrospective study that ^{125}I seed implantation was feasible and safe for patients with recurrent head and neck cancers and found a 5-year local control of 39% with no severe late complications.[21]

Postoperative ^{125}I brachytherapy is increasingly being found effective for patients with head and neck malignant tumors after surgery and in improving local control and patient survival.[21–26,36–38] Goffinet et al. found a local control rate of 70% for patients with recurrent or advanced head and neck cancer who underwent surgery with permanent ^{125}I implant.[38] Glaser et al. found rates of 89% and 53% for 2- and 5-year disease-free survival, respectively, for cases of recurrent head and neck cancers after surgery and ^{125}I implant, and that ^{125}I implant did not result in added complications.[22] Zhang et al. found 100% local control and no complications (median follow-up, 66 months; range, 50–74 months) for patients with postoperative residual parotid malignant tumors who received ^{125}I brachytherapy alone.[26] Some case reports showed good results with brachytherapy with different applicators for malignant tumors of the head and neck.[25,39,40] Stannard et al.

TABLE I.
Performance Status Scale Scores Before Brachytherapy (Without Obturators) and After Brachytherapy (With Obturators).

	Patient No.												
	1	2	3	4	5	6	7	8	9	10	11	12	Total
Without obturator													
A	25	25	25	25	50	25	25	25	25	25	50	25	29.2 ± 9.7*
B	25	25	25	0	25	25	0	25	25	25	25	25	20.8 ± 9.7†
C	40	40	40	30	40	40	40	40	40	40	40	40	39.2 ± 2.9†
With obturator													
A	50	75	50	50	75	50	50	75	50	50	75	75	60.4 ± 12.9
B	50	50	50	50	50	50	50	75	50	50	75	75	56.3 ± 11.3
C	50	50	60	50	60	50	50	60	50	60	60	60	55 ± 5.2

Data are number or mean ± standard deviation. The Performance Status Scale evaluated three criteria: A, eating in public; B, understandability of speech; and C, normalcy of diet. *P* values are Wilcoxon signed ranks test comparing before (without obturators) and after (with obturators) brachytherapy for the same functional area.

*$P = .001$.

†$P = .002$.

found 100% local control and no severe complications with ^{125}I brachytherapy, in the form of a temporary applicator or implant for malignant tumors in the palate with bone erosion and positive or close margins after surgery, during a median follow-up of 50 months (range, 32–158 months).[25]

Local control and overall survival for maxillary cancers has been traditionally poor, and surgery combined with radiotherapy has better results than radiotherapy or surgery alone.[1,8] Katz et al. found that 88% recurrence of maxillary cancers occurred within 5 years.[32] During the follow-up in our series (median, 53 months), there were four local recurrences, and they occurred after a median of 39 months, which is similar to other studies (median, 11–35 months).[41,42] The reported 5-year local control and survival rates for advanced maxillary cancers (T3-T4) are 57% to 60% and 28.9% to 56%, respectively.[1,8,32] Although SCC and ACC are the most common malignancy of the maxillary,[41] the distribution of cancers among our cases may have influenced the local control and survival results. We had two cases of SCC, and the others arose from salivary glands, including six cases of ACC, which may be associated with better survival than SCC.[8,43] As is known, because of the slow tumor growth rate and tendency to recur even after years clinically free of symptoms, ACC requires long-term (even lifelong) follow-up,[44,45] but maxillary ACC has a worse local control and survival rate than other sites of head and neck.[42,46,47] The median time to recurrence was 35 months for ACC in the maxillary region,[42] and 73% recurrence of ACC occurred within 5 years.[48] Some authors have claimed that overall 5-year survival for maxillary ACC are 40% to 62.9%.[41–43,49,50] The advanced stage and positive surgical margins lead to poor local control and survival rate.[41,43,50,51] In our study, the stage of cancers (maxillary recurrent cancers after prior surgery and radiotherapy or locally advanced cancers) and positive resection margins were high risks of recurrence. The 5-year local control and overall survival we achieved were 66.7% and 80%, respectively, for the six patients of ACC, and they were 66.7% and 71.4%, respectively, for all 12 patients, which shows that the short-term effects are encouraging. But the long-term effects of ^{125}I brachytherapy for maxillary cancers may need further study.

We successfully achieved the expected dose distribution in the target areas with the aid of obturators. The use of obturators can facilitate delivery of brachytherapy to areas that are covered by only a thin layer of soft tissue (such as the maxillary sinus, nasal cavity, skull base, orbital floor) and some structures that are enveloped by bone. The radioactive seeds contained in the digital model obturators play an indispensable role in administering brachytherapy to targets. With ^{125}I seeds in obturators, the target volume received a significantly higher dose than without ^{125}I seeds in obturators ($P < .01$). In addition, the obturators fit the adjacent tissues accurately, thus allowing the radioactive seeds to effectively and precisely treat their targets.

The use of obturators designed by use of CT images significantly improved the quality of life for all of our patients. The obturator filled in areas with bone and soft tissue defects and improved the appearance of patients. It also closed the oronasal fistula, which helped the ability to eat and speak. Use of the obturator allowed dentists to make impressions for designing dentures, which enhanced masticatory efficiency. Their use may not have the difficulties of aspiration and swallowing as with the use of conventional impression material. The soft lining material and hollow center are elastic enough for entering undercuts, which provides retention force and stabilizes seeds during treatment.

CONCLUSION

^{125}I brachytherapy is an effective alternative for treating patients with positive resection margins after maxillectomy for locally advanced or recurrent maxillary cancers after prior surgery and radiotherapy. Using digital model obturators as an applicator is a feasible way to deliver ^{125}I brachytherapy and may improve the quality of life of patients with maxillary defects. The preliminary short-term results of this study demonstrated good local control as well as functional outcomes. An increasing number of patients and longer follow-up should provide further data concerning the efficacy of ^{125}I brachytherapy.

Acknowledgments

The authors thank Shu-ming Liu (Department of Oral and Maxillofacial Surgery, Peking University School and Hospital of Stomatology) for valuable discussion, and Mr. Bo Yu for modifying the manuscript.

BIBLIOGRAPHY

1. Stavrianos SD, Camilleri IG, Mclean NR, Piggot TA, Kelly CG, Soames JV. Malignant tumors of the maxillary complex: an 18-year review. *Br J Plast Surg* 1998;51:584–588.
2. Jiang GL, Ang KK, Peters L J, Wendt CD, Oswald M J, Goepfert H. Maxillary sinus carcinomas: natural history and results of postoperative radiotherapy. *Radiother Oncol* 1991;21:193–200.
3. Tufano RP, Mokadam NA, Montone KT, et al. Malignant tumors of the nose and paranasal sinuses: hospital of the university of Pennsylvania experience 1990–1997. *Am J Rhinol* 1999;13:117–123.
4. Enn Chang C, Yoon-Seok C, Chang-Hoon K, Kyubo K, Kyung-Su K, Jeung-Gweon L, et al. Surgical outcome of radical maxillectomy in advanced maxillary sinus cancers. *Yousei Med J* 2004;45:621–628.
5. Hong TS, Ritter MA, Tome WA, Harari PM. Intensity-modulated radiation therapy: emerging cancer treatment technology. *Br J Cancer* 2005;92: 1819–1824.
6. Looser KG, Shah JP, Strong EW. The significance of "positive" margins in surgically resected epidermoid carcinomas. *Head Neck Surg* 1978;1:107–111.
7. Konno A, Togawa K, Inoue S. Analysis of the results of our combined therapy for maxillary cancer. *Acta Otolaryngol Suppl* 1980;372:1–16.
8. Bhattacharyya N. Factors affecting survival in maxillary sinus cancer. *J Oral Maxillofac Surg* 2003;61:1016–1021.
9. Cianchetti M, Sandow PS, Scarborough LD, et al. Radiation therapy for minor salivary gland carcinoma. *Laryngoscope* 2009;119:1334–1338.
10. Ogawa K, Toita T, Kakinohana Y, et al. Postoperative radiotherapy for squamous cell carcinoma of the maxillary sinus: analysis of local control and late complications. *Oncol Rep* 2001;8:315–319.
11. Sadeghi A, Tran LM, Mark R, Sidrys J, Parker RG. Minor salivary gland tumors of the head and neck: treatment strategies and prognosis. *Am J Clin Oncol* 1993;16:3–8.
12. Van der Wal JE, Snow GB, Karim AB, Van der Waal I. Intraoral adenoid cystic carcinoma: the role of postoperative radiotherapy in local control. *Head Neck* 1989;11:497–499.
13. Garden AS, Weber RS, Morrison WH, Ang KK, Peters LJ. The influence of positive margins and nerve invasion in adenoid cystic carcinoma of the head and neck treated with surgery and radiation. *Int J Radiation Oncology Biol Phys* 1995;32:619–626.
14. Duncan GG, Epstein JB, Tu D, et al. Quality of life, mucositis, and xerostomia from radiotherapy for head and neck cancers: a report from the NCIC CTG HN2 randomized trial of an antimicrobial lozenge to prevent mucositis. *Head Neck* 2005;27:421–428.

15. Sciubba JJ, Goldenberg D. Oral complications of radiotherapy. *Lancet Oncol* 2006;7:175–183.
16. Pagare SS, Khosa SK. Osteoradionecrosis. *Int J Head Neck Surg* 2011;2: 27–32.
17. Connor NP, Cohen SB, Kammer RE, et al. Impact of conventional radiotherapy on health-related quality of life and critical functions of the head and neck. *Int J Radiat Oncol Biol Phys* 2006;65: 1051–1062.
18. Fang FM, Tsai WL, Chien CY, et al. Changing quality of life in patients with advanced head and neck cancer after primary radiotherapy or chemoradiation. *Oncology* 2005;68:405–413.
19. Logemann JA, Smith CH, Pauloski BR, et al. Effects of xerostomia on perception and performance of swallow function. *Head Neck* 2001;23:317–321.
20. Ashamalla H, Rafla S, Zaki B, Ikoro NC, Ross P. Radioactive gold grain implants in recurrent and locally advanced head-and-neck cancers. *Brachytherapy* 2002;1:161–166.
21. Jiang YL, Meng N, Wang JJ, et al. CT-guided iodine-125 seed permanent implantation for recurrent head and neck cancers. *Radiat Oncol* 2010;5:68.
22. Glaser MG, Leslie MD, Coles I, Cheesman AD. Iodine seeds in the treatment of slowly proliferating tumours in the head and neck region. *Clin Oncol* 1995;7:106–109.
23. Vikram B, Hilaris BS, Anderson L, Strong EW. Permanent iodine-125 implants in head and neck cancer. *Cancer* 1983;51:1310–1314.
24. Jen-Lee D, Liberman FZ, Park RI, Zinreich ES. Intraoperative I-125 seed implantation for extensive recurrent head and neck carcinomas. *Radiology* 1991;178:879–882.
25. Stannard CE, Hering E, Hough J, Knowles R, Munro R, Hille J. Post-operative treatment of malignant salivary gland tumors of the palate with iodine-125 brachytherapy. *Radiother Oncol* 2004;73:307–311.
26. Zhang J, Zhang JG, Song TL, et al. ^{125}I seed implant brachytherapy-assisted surgery with preservation of facial nerve for treatment of malignant parotid gland tumors. *Int J Oral Maxillofac Surg* 2008;37: 515–520.
27. List MA, Ritter-Sterr C, Lansky SB. A performance status scale for head and neck cancer patients. *Cancer* 1990;66:564–569.
28. Cox JD, Stetz J, Pajak TF. The toxicity criteria of the Radiation Therapy Oncology for Research and Treatment of Cancer (EORTC). *Int J Radiat Oncol Biol Phys* 1995;31:1341–1346.
29. Nath R, Bice WS, Butler WM, et al. AAPM recommendations on dose prescription and reporting methods for permanent interstitial brachytherapy for prostate cancer: report of Task Group 137. *Med Phys* 2009;36: 5310–5322.
30. Pernot M, Aletti P, Carolus JM, et al. Indications, techniques and results of postoperative brachytherapy in cancer of the oral cavity. *Radiother Oncol* 1995;35:186–192.
31. Beitler JJ, Smith RV, Silver CE, et al. Close or positive margins after surgical resection for the head and neck cancer patient: the addition of brachytherapy improves local control. *Int J Radiat Oncol Biol Phys* 1998;40:313–317.
32. Katz TS, Mendenhall WM, Morris CG, Amdur RJ, Hinerman RW, Villaret DB. Malignant tumors of the nasal cavity and paranasal sinuses. *Head Neck* 2002;24:821–829.
33. Harrison LB. Applications of brachytherapy in head and neck cancer. *Semin Surg Oncol* 1997;13:177–184.
34. Grimard L, Esche B, Lamothe A, Cygler J, Spaans J. Interstitial low-dose-rate brachytherapy in the treatment of recurrent head and neck malignancies. *Head Neck* 2006;28:888–895.
35. Reuther T, Schuster T, Mende U, Kubler A. Osteoradionecrosis of the jaws as a side effect of radiotherapy of head and neck tumour. *Int J Oral Maxillofac Surg* 2003;32:289–295.
36. Vikram B, Mishra S. Permanent iodine-125 implants in postoperative radiotherapy for head and neck cancer with positive surgical margins. *Head Neck* 1994;16:155–157.
37. Park RI, Liberman FZ, Lee DJ, Goldsmith MM, Price JC. Iodine-125 seed implantation as an adjunct to surgery in advanced recurrent squamous cell cancer of the head and neck. *Laryngoscope* 1991;101:405–410.
38. Goffinet DR, Martinez A, Fee WE Jr. ^{125}I vicryl suture implants as a surgical adjuvant in cancer of head and neck. *Int J Radiat Oncol Biol Phys* 1985;11:399–402.
39. Jolly DE, Nag S. Technique for construction of dental molds for high-dose-rate remote brachytherapy. *Spec Care Dentist* 1992;12:219–224.
40. Lyzak WA, Fleming TJ. Fabrication and use of an intracavitary radiotherapeutic applicator for the posterior sinus wall: a case report. *J Prosthodont* 1995;4:133–136.
41. Myers LL, Nussenbaum B, Bradford CR, Teknos TN, Esclamado RM, Wolf GT. Paranasal sinus malignancies: an 18-year single institution experience. *Laryngoscope* 2002;112:1964–1969.
42. da Cruz Perez DE, Pires FR, Lopes MA, de Almeida OP, Kowalski LP. Adenoid cystic carcinoma and mucoepidermoid carcinoma of the maxillary sinus: report of a 44-year experience of 25 cases from a single institution. *J Oral Maxillofac Surg* 2006;64:1592–1597.
43. Lupinetti AD, Roberts DB, Williams MD, et al. Sinonasal adenoid cystic carcinoma: the M.D. Anderson Cancer Center Experience. *Cancer* 2007; 110:2726–2731.
44. Mucke T, Tannapfel A, Kesting MR, et al. Adenoid cystic carcinoma of minor salivary glands. *Auris Nasus Larynx* 2010;37:615–620.
45. Bianchi B, Copelli C, Cocchi R, Ferrari S, Pederneschi N, Sesenna E. Adenoid cystic carcinoma of intraoral minor salivary glands. *Oral Oncol* 2008;44:1026–1031.
46. Kokemueller H, Eckardt A, Brachvogel P, Hausamen JE. Adenoid cystic carcinoma of the head and neck—a 20 years experience. *Int J Oral Maxillofac Surg* 2004;33:25–31.
47. Huang MX, Ma DQ, Sun KH, Yu GY, Guo CB, Gao F. Factors influencing survival rate in adenoid cystic carcinoma of the salivary glands. *Int J Oral Maxillofac Surg* 1997;26:435–439.
48. Balamucki CJ, Amdur RJ, Werning JW, et al. Adenoid cystic carcinoma of the head and neck. *Am J Otolaryngol*. http://dx.doi.org/10.1016/j.amjoto.2011.11.006.
49. Bhattacharyya N. Survival and staging characteristics for non-squamous cell malignancies of the maxillary sinus. *Arch Otolaryngol Head Neck Surg* 2003;129:334–337.
50. Chen AM, Bucci MK, Weinberg V, et al. Adenoid cystic carcinoma of the head and neck treated by surgery with or without postoperative radiation therapy: prognostic features of recurrence. *Int J Radiat Oncol Biol Phys* 2006;66:152–159.
51. Hsu HC, Huang EY, Wang CJ. Postoperative adjuvant radiotherapy for adenoid cystic carcinoma of the head and neck: treatment results and prognostic factors. *Chang Gung Med J* 2003;26:646–653.