



## Original Contributions

# A case-cohort study of recurrent salivary adenoid cystic carcinoma after iodine 125 brachytherapy and resection treatment <sup>☆, ☆, ☆</sup>



Bin-bin Li, PhD <sup>a,\*</sup>, Xiao-Yan Xie, MD <sup>b</sup>, Sheng-Nan Jia, MD <sup>a</sup>

<sup>a</sup> Department of Oral Pathology, Peking University School and Hospital of Stomatology, Beijing, PR China

<sup>b</sup> Department of Oral Radiology, Peking University School and Hospital of Stomatology, Beijing, PR China

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## ABSTRACT

Recurrent adenoid cystic carcinoma (rAdCC) can be challenging to be treated with brachytherapy, although brachytherapy is safe and effective in treating head and neck cancers. Patients of adenoid cystic carcinoma (AdCC), who underwent resection and iodine 125 (<sup>125</sup>I) radioactive seed implantation, were recruited for this study. Clinical data, surgical details of resection and seed implantation, histologic characteristics, and prognosis were studied. There were 16 rAdCC cases among 140 cases of AdCC treated with brachytherapy and resection. The mean follow-up duration for the recurrent cases was 61 months. The 3-year local control rate of rAdCC was 51.6%, and the overall disease-specific survival rate was 49.4%. Eight patients showed distant metastasis (50%, 8/16). The histologic grades of 10 rAdCCs were upgraded (62.5%, 10/16). Two cases displayed sarcomatous transformation after brachytherapy (1.4%, 2/140). Although the overall local control rate and survival rate were relatively favorable, some rAdCCs with an aggressive phenotype appeared to respond poorly to <sup>125</sup>I seed implantation. Preventive adjuvant chemotherapy should be prescribed for these rAdCCs.

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## 1. Introduction

Adenoid cystic carcinomas (AdCCs) originating from the salivary gland are aggressive tumors characterized by multiple late local recurrence and distant metastases [1]. The most appropriate treatment for AdCC appears to be radical resection combined with radiotherapy [2]. A new technique of permanent radioactive seed implantation has made it possible to deliver radiotherapy more precisely and safely than conventional radiotherapy and has been implemented extensively in the field of radiotherapy worldwide [3]. This technique has the potential to improve local tumor control because of highly conformal delivery of radiotherapy [4].

For head and neck cancer, permanent interstitial implantation of iodine 125 (<sup>125</sup>I) seeds can be used to treat salivary gland tumors to obtain a high tumor control rate. Clinical data have shown that seed implantation is effective in treating malignant tumors with positive excision margins in the maxilla [5] and in inhibiting the growth of metastasized lymph nodes [6].

For patients with recurrent parotid gland cancers, <sup>125</sup>I brachytherapy delivered the excellent local control and good survival rate [7]. However, all these reports assessed the clinical outcome of various salivary cancers together. There are no specific reports of the clinicopathologic

characteristics of AdCC after brachytherapy. Herein, we report a series of recurrent AdCC (rAdCC) cases after seed implantation. It is very critical for clinicians to consider the oncologic outcomes of these types of cancers.

## 2. Materials and methods

## 2.1. Patients

A retrospective chart review of 140 patients who underwent brachytherapy in Peking University School and Hospital of Stomatology from 2001 to 2012 was performed. These patients comprised the full analytic cohort of this study based on the following criteria: (i) AdCCs originating from the salivary glands, (ii) gross tumor resection performed before seed implantation, and (iii) primary and recurrent tumor mass diagnosed by 2 professional pathologists. Follow-up information was obtained by clinical interviews or by reviewing patients' medical records. The investigated parameters included the sex and age distributions, anatomic location, TNM stage, histologic type, tumor characteristics, treatment before seed implantation, surgical findings, and postoperative outcomes.

## 2.2. Surgical treatment and seed implantation

All patients underwent primary surgery followed by <sup>125</sup>I radioactive seed implantation. The aim of primary surgery was to get a maximal tumor excision with tumor-negative margins, which was aided by frozen section examination when appropriate. In addition, 2 patients (no. 3 and 9, Table) underwent traditional radiotherapy after surgery. According to the American Joint Committee on Cancer staging manual,

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\* Corresponding author. Department of Oral Pathology, Peking University School and Hospital of Stomatology, 22 South Ave Zhongguancun, Haidian District, Beijing 100081, PR China. Tel.: +86 10 82195221; fax: +86 10 82193402.

E-mail address: [kqlibinbin@aliyun.com](mailto:kqlibinbin@aliyun.com) (B. Li).

**Table**  
Patient and tumor characteristics (n = 16)

No.	Sex/age	Location	Primary tumor		Treatment before implant	Recurrent tumor after seed implant	
			Stage	Solid component (%/G)		Stage	Pathology/G
1	F/61	Palate	III	>30%/G1	Surgery	II	AdCC/G2
2	M/54	Palate	I	>30%/G1	Surgery	II	AdCC/G1
3	F/60	Parotid	I	<30%/G1	Surgery/RT	I	AdCC/G2
4	M/38	Tongue	I	>30%/G1	Surgery	IVC	AdCC/G2
5	F/50	Parotid	I	>30%/G1	Surgery	I	S/G2
6	F/60	Parotid	I	<30%/G1	Surgery	I	AdCC/G1
7	M/42	Parotid	II	>30%/G1	Surgery	IVB	AdCC/G2
8	F/60	Parotid	I	<30%/G1	Surgery	IVA	AdCC/G2
9	F/40	Palate	I	>30%/G1	Surgery/RT	IVC	S/G2
10	M/61	Palate	I	<30%/G1	Surgery	IVA	AdCC/G1
11	F/35	Palate	I	<30%/G1	Surgery	IVA	AdCC/G2
12	F/35	Palate	I	>30%/G1	Surgery	IVC	AdCC/G2
13	M/62	Submandibular	I	<30%/G1	Surgery	IVC	AdCC/G1
14	M/72	Sublingual	I	<30%/G1	Surgery	I	AdCC/G1
15	M/46	Sublingual	I	>30%/G1	Surgery	IVC	AdCC/G2
16	F/34	Buccal	I	<30%/G1	Surgery	IVC	AdCC/G1

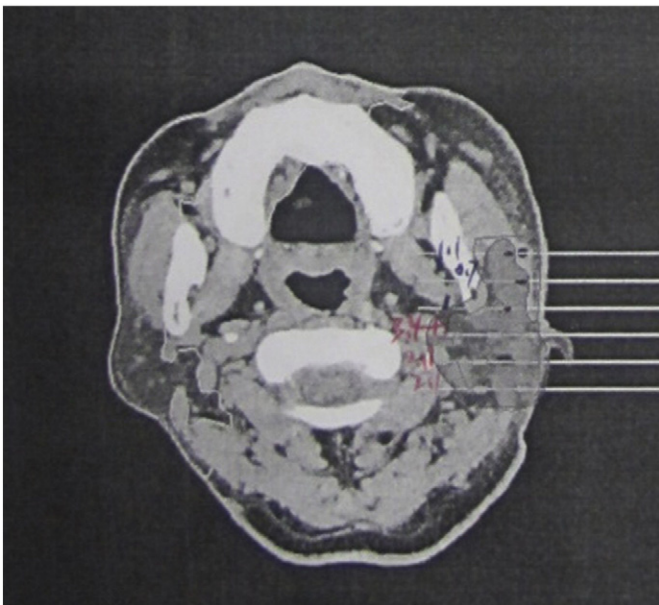
Abbreviations: F, female; M, male; G, histologic grade; RT, radiotherapy; S, sarcoma.

the definition of TNM and general rules of the TNM system, all tumors were classified into different clinical stages [8].

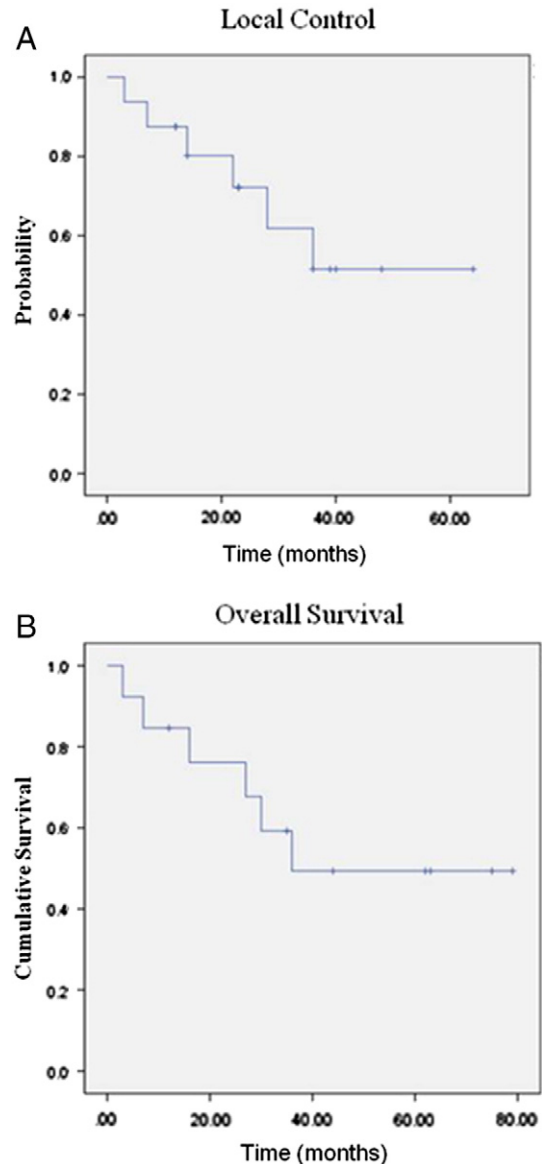
Radioactive seed implantation was performed by the seed implanting brachytherapy system (Beijing Astro Science and Technology Development Limited Company, China). The placement of seed implants was determined from computed tomographic scans and intraoperative photographs of the target area. The  $^{125}\text{I}$  radioactive seeds (22 keV) were purchased from Beijing Atom High Technology Limited Company (Beijing, China). The seed activity was 0.7 mCi with a half-life of 59.6 days. The matched peripheral dose was 60 Gy. Dosage in 90% of the target area (D90) was greater than 80 Gy. Less than 50% of the target region received 150% of the prescribed dose (V150). The reference point was located 0.5 cm outside the target area, where the dose was 90% of the isodose line. The implantation was performed through a 1-cm wide passage, and the seeds were implanted at a depth of 1 cm (Fig. 1).

### 2.3. Pathology

The immediate pathologic examination of specimens collected intraoperatively was conducted for testing surgical margins. Postoperatively,



**Fig. 1.** Computed tomographic scans and intraoperative photographs determined the placement of seed implants in the target area.



**Fig. 2.** The local control rate (A) and the actuarial overall survival rate (B) in 16 patients with rAdCC after the implantation of  $^{125}\text{I}$  seeds.

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