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Curative radiotherapy for early cancers of the lip, buccal mucosa, and nose—a simple interstitial brachytherapy technique employing angiocatheters as carriers for Iridium-192 wire implants

針對早期唇癌、口腔黏膜癌和鼻癌的放射治療——以血管導管為載體，植入放射性銥-192金屬線的簡單穿刺近接放射治療技術

Objectives. To evaluate treatment outcomes following interstitial brachytherapy for cancers of the lip, buccal mucosa, or nose.
Design. Retrospective study.
Setting. Regional hospital, Hong Kong.
Patients. A cohort of 13 patients treated uniformly by a simple interstitial brachytherapy technique employing plastic angiocatheters as carriers for Iridium-192 wires: all but one patient had T1 or T2 tumours and all but one had N0 disease.
Main outcome measures. Local and loco-regional control rates.
Results. Six of the 13 patients received external radiotherapy prior to interstitial brachytherapy. A median brachytherapy dose of 70 Gy was delivered to those treated with brachytherapy alone, while 35 Gy was delivered after a median external radiotherapy dose of 50 Gy to those receiving combined treatment. The 3-year actuarial local control rate was 75%. No significant late complications were observed.
Conclusions. Employing a simple brachytherapy technique using angiocatheters and Iridium-192 wires, in conjunction with external radiotherapy when appropriate, produces good outcomes for patients with early lip, nasal vestibule, and buccal mucosa cancers.

目的：評估穿刺近接放射治療技術對唇癌、口腔黏膜癌或鼻癌的治療結果。
設計：回顧研究。
安排：地區醫院，香港。
患者：13名接受了相同的簡單穿刺近接放射治療的病人，採用塑膠血管導管作載體，植入放射性銥-192金屬線。除了1名病人外，所有病人出現T1期或T2期原發腫瘤，和沒有出現淋巴結轉移（N0期）。
主要結果測量：局部控制率。
結果：13名病人中有6人在穿刺近接放射治療前接受了體外放射治療。對於只接受穿刺近接放射治療的病人，近接放射治療的劑量中位數是70戈瑞，而接受兩種治療的病人，體外放射治療的劑量中位數

Key words:
Brachytherapy;
Carcinoma, squamous cell;
Head and neck neoplasms;
Iridium radioisotopes;
Treatment outcome

關鍵詞：
近接治療；
癌症，鱗狀細胞；
頭部及頸部腫瘤；
銥放射性同位素；
治療結果

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為 50 戈瑞，而近接放射治療的劑量中位數是 35 戈瑞。3 年內精算本地控制率為 75% ，亦沒有出現明顯併發症。

結論：應用塑膠血管導管作載體，植入放射性銥 -192 金屬線的簡單穿刺近接放射治療技術，在適當時配合體外放射治療，對早期唇癌、鼻前庭癌和口腔黏膜癌有良好治療效果。

Introduction

Interstitial brachytherapy—implanting radioactive material into tumour tissue—achieves a high radiation dose to the target tumour volume while sparing neighbouring normal tissue. This is especially relevant for specific types of head and neck cancers, such as cancers of the lip, nasal vestibule, and buccal mucosa, because successful eradication of local tumour will obviate the need for mutilating surgery and confer both functional and cosmetic benefit. Local tumour control is crucial for a cure, as neck recurrence alone is infrequent (5-26%), and when present is often successfully salvaged by neck dissection.[1-4] High rates of local control and low rates of late complications have been reported with interstitial brachytherapy treatment for early cancers of the lip, nose, and buccal mucosa, with or without prior external radiotherapy.[3-9] In this report, we describe the methodology and outcome for a cohort of patients treated with a simple interstitial brachytherapy technique using angiocatheters.

Methods

Patients

Between June 1996 and March 2004, 13 patients with cancers of the lip, nasal vestibule, or buccal mucosa were treated by radiotherapy. The diagnosis was confirmed by histology in all cases. All patients had been reviewed by clinical oncologists and head and neck surgeons in combined meetings before individual treatment plans were formulated. Radiotherapy was considered the treatment of choice in all cases as opposed to initial surgery or follow-up surgery for those with initial resections prior to referral. Surgery was not selected as a treatment modality due to the possibility of unacceptable functional or cosmetic loss, poor medical status or extreme old age, as well as patient preference. Clinical characteristics of the 13 patients are summarised in Table 1. The mean age of the patients was 59 years. There were four patients with cancer of the lip, two with cancer of the nasal vestibule, and seven with cancer in the buccal mucosa. The majority had squamous cell carcinoma (SCC), one patient had mucoepidermoid carcinoma, and another an alveolar soft-part sarcoma of the buccal mucosa. Twelve of the 13 tumours were staged as T1 or T2 tumours; mean tumour size was 2.4 cm. Only one of the 13 patients had palpable neck lymphadenopathy at presentation.

Table 1. Patient characteristics and treatment summary (n=13)

Characteristic/treatment	Data*
Age (years)	
Mean	59
Range	18-87
Male:female	9:4
Tumour site	
Lip	4
Buccal mucosa	7
Nasal vestibule	2
Tumour-node-metastasis (TNM) staging	
T1N0M0	7
T2N0M0	4
T2N2M0	1
T3N0M0	1
Primary tumour size (cm)	
Mean	2.4
Median	2
Range	1-5
Histology	
Squamous cell carcinoma	11
Mucoepidermoid carcinoma	1
Alveolar soft-part sarcoma	1
Prior surgical resection	4
Brachytherapy	13
External RT† prior to brachytherapy	6
Prior external RT and chemotherapy	2
Prior external RT alone	4
Median external RT dose (Gy)	50
Treatment to neck nodes	5

* Data are expressed as the number of patients, unless otherwise specified

† RT radiotherapy

Overall treatment

A summary of patient treatment is included in Table 1. Four patients had surgical resection before definitive radiotherapy. One patient with a verrucous squamous carcinoma of the lower lip involving the commissure, had had a debulking biopsy to obtain adequate tissue for histological diagnosis after three previous failed attempts at small biopsy. The other three patients (including one with mucoepidermoid carcinoma and one with alveolar soft-part sarcoma) had prior limited local excision of their buccal mucosa cancer. Resection margins were reported as close or involved in the final surgical excision specimens, warranting further radiotherapy treatment. Altogether, 10 of 13 patients had gross macroscopic residual tumour before definitive radiotherapy.

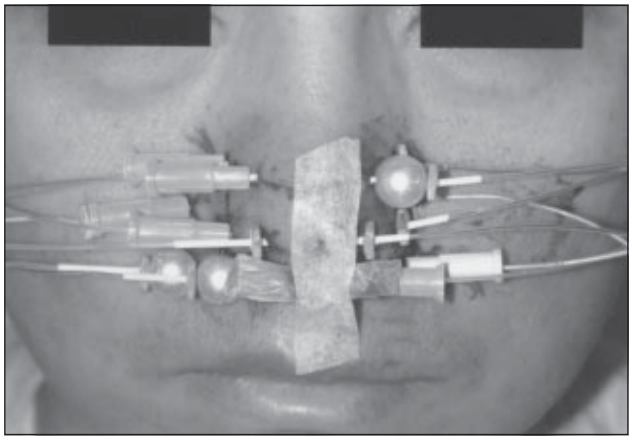

Fig 1. Volume implant of nasal vestibule cancer using 18-gauge angiocatheters

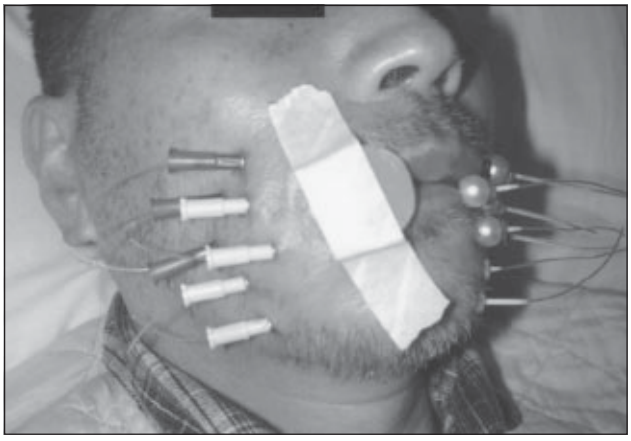

Fig 2. Double-plane implant of lip cancer using 16-gauge angiocatheters. A wax bolus was placed over ulcerated tumour for optimal tumour dosing

Definitive radiotherapy treatment for seven patients consisted of interstitial brachytherapy alone, while the remaining six patients had external radiotherapy (median dose, 50 Gy) prior to interstitial brachytherapy. Both the mean and median total tumour dose (interstitial brachytherapy with or without external radiotherapy) were 75 Gy for the group as a whole. The median total tumour dose prescribed was 70 Gy and 82.5 Gy for those with interstitial brachytherapy alone and those with additional external radiotherapy, respectively. The two patients with nasal vestibule SCC received a course of external radiotherapy by direct electron beam of up to 30 and 40 Gy, followed by interstitial brachytherapy. Full-course interstitial brachytherapy was not used as it can predispose to radionecrosis of the nasal septal cartilage. All four patients with cancer of the lip had interstitial brachytherapy alone as definitive radiotherapy. Four of the seven patients with cancer of the buccal mucosa had external radiotherapy prior to interstitial brachytherapy. Of these four patients, three had more bulky tumours (two T2 and one T3). The remaining patient had recurrent mucoepidermoid carcinoma after two previous excisions for a T1 tumour, with the final resection margins showing microscopic tumour involvement. External radiotherapy was employed to minimise the chance of a geographical miss in those with more extensive disease or recurrent disease. One of the patients with a T2 tumour had a single cycle of carboplatin plus 5-fluorouracil neoadjuvant chemotherapy before external radiotherapy due to rapid tumour progression. Another patient with a T2N2 (stage IVA) tumour received two cycles of cisplatin plus 5-fluorouracil neoadjuvant chemotherapy before external radiotherapy, and then 4 weekly cycles of moderate dose of cisplatin concurrent with external radiotherapy. This combined treatment was planned in line with current recommendations for chemoradiotherapy in advanced stage III and IV head and neck cancers.[10,11] Age (69 years) and poor performance status of the other patient with advanced stage disease (T3N0, stage III) precluded chemotherapy as part of definitive treatment.

Five patients received treatment to the neck, including the patient with a T2N2 tumour who had therapeutic high-dose radiation to bilateral cervical regions—68 Gy to the involved nodes in the ipsilateral submandibular region and 60 Gy to the other cervical lymphatic regions. Two patients with T2N0 and T3N0 SCC of the buccal mucosa had prophylactic ipsilateral neck irradiation of up to 50 Gy. Another patient with T2N0 SCC of the buccal mucosa and a patient with T2N0 verrucous squamous carcinoma of the lip underwent ipsilateral levels I to III selective neck dissection.

Interstitial brachytherapy technique

A customised mandibular spacer, consisting of a thin layer of lead shield (2 mm) embedded in wax, was fabricated to fit snuggly in the buccal-alveolar sulcus, between the buccal mucosa and the lateral surface of the mandible, to shield the mandible from the Iridium-192 wires during brachytherapy. Wax nostril plugs or tissue-equivalent boluses were also custom-made to optimise mucosal surface dosage and as solid support within the nostrils for the angiocatheters required for a volume implant (Figs 1, 2). Dental surgeons were routinely consulted before implant to assess the need for dental extraction.

Angiocatheters (Angiocath; Becton Dickinson Infusion Therapy Systems Inc, Sandy [UT], US) used were 16 gauge, with a plastic sheath of 1.1-mm inner

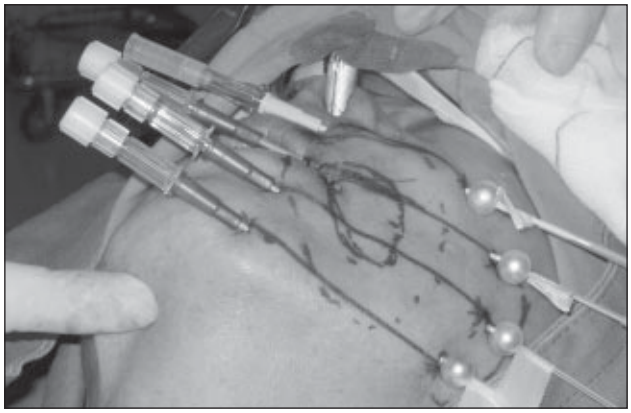

Fig 3. Single-plane implant of a T2 squamous cell carcinoma of the left buccal mucosa involving the commissure

diameter, 1.5-mm outer diameter, and with a metallic stylet of 1-mm outer diameter. The angiocatheters served as carriers, into which Iridium-192 wires of 0.3-mm diameter impregnated into nylon catheters of 0.8-mm diameter were afterloaded once the catheters had been inserted subcutaneously across the tumour bed and secured (Fig 3). Angiocatheters come in different lengths, ranging from 8 to 16 cm, depending on the manufacturer. Selection of the most appropriate length involves a compromise between flexibility (longer catheters are better) and ease of use (shorter catheters are better). One can elect to use smaller 18-gauge catheters (outer diameter and inner diameter of the plastic sheath 1.3 mm and 0.9 mm, respectively) to achieve less traumatic implantation in sites such as the nasal vestibule (Fig 1).

General anaesthesia is essential to ensure optimal positioning of the implant. A margin of 1 cm in the anteroposterior and caudo-cephalic directions of the gross tumour is generally used to define the implanted tumour volume. The implanted tumour volume is then inked on the skin surface to facilitate optimal planning of the alignment of the angiocatheters and their entry and exit points on the skin. As the Paris system stipulates the radioactive sources to be parallel and equidistant from one another, the angiocatheters are inserted parallel to one another across the implanted tumour volume.[12] Spacing between the catheters is such to encompass the full thickness of the implanted tumour volume.[12] For tumours of less than 7 to 8 mm thick, a single-plane implant with spacing of 1.5 to 2 cm is desirable. A double-plane or volume implant with 1- to 1.2-cm intervals is usually required for adequate coverage of thicker lesions (Figs 1, 2). For single-plane implants, the catheters are inserted in a plane approximately half-way between the two lateral borders of the tumour, while the peripheral angiocatheters of a volume or double-plane implant are inserted just lateral to the implanted tumour volume (Fig 3).

Afterloading of Iridium-192 is usually performed at the bedside with aseptic technique behind 3-cm thick lead shields. Prior to this, the exact active lengths of the Iridium-192 wires have been determined from orthogonal films by physicists specialising in brachytherapy. The 3-dimensional positions of the catheters are entered into the computer and reconstructed. The Paris system is strictly followed during the computation algorithm of dosimetry, and the duration of the implant is calculated when the total dose and the prescribed dose rate (the reference dose rate in the Paris system, which is 85% of the basal dose rate) are specified. The total dose generally prescribed for T1 and T2/3 cancer is 65 Gy and 70 Gy, respectively, if brachytherapy is the only treatment. A 30 to 40 Gy brachytherapy boost is prescribed after 30 to 50 Gy external radiotherapy when the latter is deemed necessary. The dose rate for a typical implant is around 40 to 60 cGy/hour, necessitating a total duration of 5 to 6 days for full brachytherapy dose delivery.

Brachytherapy treatment

Brachytherapy treatment data for all patients are summarised in Table 2. A total of eight single-plane, three double-plane, and two volume implants were employed. All seven cases of buccal mucosa cancer were treated by single-plane implant, and both nasal vestibule cancers were treated by volume implant. Three of the four lip cancers were treated by double-plane implant and one was treated by single-plane implant. In configuring the implants, the median number of wires was 4 (range, 2-9), the mean length of the active wire was 24 cm (range, 8-41 cm), and the wires were implanted at a mean separation of 1.2 cm (range, 0.7-2.3 cm). For the eight single-plane implants, the median number of wires used was 4 and the mean separation between the wires was 1.4 cm. A total of 4, 4, and 7 wires were used for the three double-plane implants, while 7 and 9 wires were used for the two volume implants.

The median brachytherapy dose prescribed for the group was 52.5 Gy (range, 30-76.5 Gy), which was delivered over a median duration of 99.1 hours (range, 59.0-214.4 hours) at a median dose rate of 50 cGy/hour (range, 27-105 cGy/hour). Of those treated by brachytherapy alone, the median dose was 70 Gy (range, 61.4-76.5 Gy), while a median of 35 Gy

Table 2. Brachytherapy treatment data

	Single-plane implant, n=8	Double-plane implant, n=3	Volume implant, n=2	Total, n=13
Cancer type	7 buccal, 1 lip	3 lip	2 nose	7 buccal, 4 lip, 2 nose
Tumour-node-metastasis (TNM) stage	4 T1N0 2 T2N0 1 T2N2 1 T3N0	1 T1N0 2 T2N0	2 T1N0	7 T1N0 4 T2N0 1 T2N2 1 T3N0
Brachytherapy alone	4 (50%)	3 (100%)	0 (0%)	7 (54%)
Mean brachytherapy dose (Gy)	50.49	72.17	37.50	52.83
Mean total tumour dose (Gy)	75.49	72.17	77.50	75.03
Mean wire length (cm)	22.5	28.5	23.1	24.0
Mean separation distance between wires (cm)	1.4	1.0	0.9	1.2

(range, 30-40 Gy) was given as a brachytherapy boost after a median dose of 50 Gy (range, 30-50 Gy) as external radiotherapy. As stated previously, the median total tumour dose prescribed was 70 Gy and 82.5 Gy for those with interstitial brachytherapy alone and those treated by combined external radiotherapy and interstitial brachytherapy, respectively.

Statistical analysis

The Kaplan-Meier method was used to calculate the actuarial local control rate and overall survival. Follow-up and local control intervals were measured from the end of planned treatment to the last day of follow-up or date of death, and to the last day of follow-up or the date of diagnosis of local failure, respectively. The Statistical Package for the Social Sciences (Windows version 10.0; SPSS Inc, Chicago [IL], US) was used for analysis.

Results

Table 3 summarises the treatment for and outcomes of the 13 patients. Nine of the 10 patients with gross tumour before planned definitive therapy showed a complete response; one T2N0 cancer of the buccal mucosa persisted despite treatment. Overall, after a median follow-up period of 42.8 months (range, 11.4-88 months), three patients had local failure, while another patient had a recurrence in the ipsilateral neck. Two of the local failures and the neck recurrence were successfully salvaged surgically. Two patients had died, one with a local recurrence of buccal mucosa cancer beyond surgical salvage, and the other with a metachronous contralateral oral cavity cancer. The 3-year actuarial local control rate for the cohort after planned definitive radiotherapy was 75%. The actuarial local control rates after additional surgical salvage and the overall survival at 3 years were 92% and 89%, respectively.

The patient with the small lip cancer (1 cm) who had local recurrence at 14.2 months had been treated with brachytherapy alone, prescribed up to 70 Gy and delivered through a single-plane implant consisting of only two wires at a separation of 1 cm. His recurrence was salvaged surgically, with no functional or cosmetic loss. In contrast, despite receiving the highest total radiotherapy dose of 87.5 Gy—combined external radiotherapy (50 Gy) and single-plane interstitial brachytherapy (37.5 Gy)—the patient with T3 buccal mucosa cancer had local recurrence at 9.9 months. His recurrence was deemed inoperable and he subsequently died. The third local failure occurred in a patient with a 4-cm T2N0 buccal mucosa tumour who had persistent local disease after planned radiotherapy. He underwent successful surgical salvage at 4.3 months. The only neck recurrence occurred at 5.1 months in a patient with a T2N0 poorly differentiated SCC of the lower lip, measuring 2.5 x 1.5 x 0.8 cm. He was treated by double-plane interstitial brachytherapy delivering 76.5 Gy. The ipsilateral submandibular lymph node recurrence was successfully salvaged by radical neck dissection.

All patients experienced brisk skin (WHO grade 2-3) and severe mucositis (WHO grade 3) around the implanted volume. The mucositis required meticulous antiseptic oral rinses and soothing dental gel for a few weeks, with the majority of acute reactions subsiding within 4 to 6 weeks. There were no significant functional or cosmetic deficits observed during follow-up evaluation. The catheter entry and exit marks over the skin had faded with time and there were no unsightly scars. Complaints of spontaneous facial twitching were made by two patients with buccal mucosa cancer at 15 and 27 months post-treatment, respectively. These patients were later diagnosed with spontaneous twitching of ipsilateral facial muscles, possibly due to radiotherapy-related

Table 3. Treatment for and outcomes of 13 patients

Patient No.	Age (years), sex, cancer type	Site, histology, stage, size of tumour	Treatment	Outcome
1	81, F, lip	Well-differentiated SCC* of left lower lip, T1N0M0, 2 cm (prior verrucous squamous carcinoma of hard palate with 2 local recurrences salvaged by surgery and radiotherapy)	Brachytherapy 70 Gy	No evidence of disease but died at 53.2 months of 3rd local recurrence from hard palate verrucous squamous carcinoma
2	66, M, lip	SCC of lower lip mucosa, T1N0M0, 1 cm (prior history of radiotherapy for nasopharyngeal carcinoma)	Brachytherapy 70 Gy	Local recurrence at 14.2 months salvaged by wide local excision. No evidence of disease at 80.1 months
3	76, M, lip	Poorly differentiated SCC of lower lip, T2N0M0, 2.5 cm	Brachytherapy 76.5 Gy	Left submandibular lymph node recurrence at 5.1 months salvaged by left radical neck dissection. No evidence of disease at 60.9 months
4	61, M, lip	Verrucous squamous carcinoma of right lower lip, T2N0M0, 3 cm	Debulking resection for biopsy and then brachytherapy 70 Gy plus prophylactic ipsilateral selective neck dissection	No evidence of disease at 13.2 months
5	87, F, nasal vestibule	Well-differentiated SCC of nasal columella, T1N0M0, 1.5 cm	External radiotherapy (by electrons) 40 Gy and then brachytherapy 35 Gy	No evidence of disease at 91.4 months
6	44, M, nasal vestibule	Well-differentiated SCC of nasal columella, T1N0M0, 1.5 cm	External radiotherapy (by electrons) 30 Gy and then brachytherapy 40 Gy	No evidence of disease at 16.9 months
7	22, F, buccal mucosa	Alveolar soft-part sarcoma of left buccal mucosa, T1N0M0, 1.5 cm	Local excision with clear margins and then brachytherapy 65 Gy	No evidence of disease at 90.3 months
8	69, M, buccal mucosa	SCC of left buccal mucosa, T3N0M0, 5 cm	External radiotherapy (by photons) 50 Gy to primary tumour and left neck, then brachytherapy 37.5 Gy	Inoperable local recurrence at 9.9 months, died of disease at 20.2 months
9	85, F, buccal mucosa	Well-differentiated SCC of right buccal mucosa, T1N0M0, 1.5 cm	Local excision with close margins and then brachytherapy 61.4 Gy	No evidence of disease at 42.9 months
10	18, M, buccal mucosa	Mucoepidermoid carcinoma of right buccal mucosa, T1N0M0, 1 cm	Local excision twice with positive margins, external radiotherapy (by photons) 50 Gy and then brachytherapy 30 Gy	No evidence of disease at 64.9 months
11	36, M, buccal mucosa	Moderately differentiated SCC of right buccal mucosa, T2N2M0, 3.5 cm	2 cycles of cisplatin-based neoadjuvant chemotherapy, external radiotherapy (by photons) 50 Gy to primary tumour and 68 Gy to neck nodes concurrent with 4 courses of weekly cisplatin, and then brachytherapy 35 Gy	No evidence of disease at 46.2 months
12	56, M, buccal mucosa	Well-differentiated SCC of right buccal mucosa, T2N0M0, 4 cm	1 cycle of carboplatin-based neoadjuvant chemotherapy, external radiotherapy (by photons) 50 Gy to primary tumour and right neck, and then brachytherapy 35 Gy	Had persistent primary tumour, salvaged by surgical excision at 4.3 months. No evidence of disease at 16.2 months
13	70, M, buccal mucosa	SCC of left buccal mucosa, T2N0M0, 3.5 cm	Brachytherapy 70 Gy and then prophylactic ipsilateral selective neck dissection	No evidence of disease at 12.4 months

* SCC squamous cell carcinoma

hyperactivity. Both had external radiotherapy and interstitial brachytherapy. The patient with more frequent facial twitching had also had two prior local excisions for his mucoepidermoid carcinoma. There was no osteoradionecrosis, soft-tissue or skin necrosis observed. Cosmetically disfiguring and functionally debilitating scars over the former tumour bed were not seen in patients with long-term loco-regional control. Lens dose had been estimated for some patients when the implant was judged to be in close proximity to the eyes and was found to be well below cataractogenic dose levels. No clinical cataract was detected. No second cancer was found in the tumour bed.

Discussion

Cancers of the nose, lip, and buccal mucosa are uncommon in Hong Kong. This is possibly due to the absence of excessive sunlight exposure and pipe smoking (predisposing factors for lower lip cancer), and the absence of betel nut or tobacco leaf chewing (a predisposing factor for buccal mucosa cancer) among the predominantly urban Chinese population.[13-15] Only 10 cases of lip cancer and 16 cases of buccal mucosa cancer were diagnosed in Hong Kong in 2001 (personal communication).

Comparable results in terms of local control rate have been reported after surgery or radiotherapy for early cancers of the lip and buccal mucosa.[4,16-18] Interstitial brachytherapy, with radioactive material implanted within the tumour substance, provides an exceptionally high radiation dose to the tumour, but spares the surrounding normal tissue. The continuous low-dose-rate radiation delivery in brachytherapy helps reduce late radiation damage to normal tissues.[19] The short overall treatment time of 5 to 7 days also prevents tumour cell repopulation, frequently initiated a few weeks into the typical 6 to 7 weeks of an external radiotherapy treatment course.[19] Interstitial brachytherapy alone has been shown to achieve better local control in T2 cancer of the tongue than combined external and interstitial radiotherapy.[20]

The interstitial brachytherapy technique described in this report capitalises on the flexibility of the Paris system governing the physical rules and configuration of the implant of Iridium-192 wires.[12] Ready-to-use and readily available angiocatheters of varying lengths can be suitable carriers for the implant. The number, geometry, and length of catheters can be customised for individual implants to cater for differences in tumour size and thickness, as long as the Paris system is strictly followed. This is in contrast to the older Manchester system which necessitated rigid radioactive sources often of a fixed length, implanted at fixed separation from one another, and in rigid spatial distribution.[21,22] The possibility of afterloading radioactive Iridium-192 wires at the bedside some time after the implantation of the angiocatheters, instead of implanting preloaded radioactive needles, has several potential advantages. It avoids radiation exposure to staff in the operating theatre. It also allows a leisurely approach to implantation, with optimal geometric corrections if required, as well as some post-implant dose 'optimisation' by varying the length, activity, and implant duration of different Iridium-192 wires after careful computer-generated calculations. Notwithstanding its user-friendliness, the brachytherapy technique requires experience and frequent practice before it can be mastered.

Analysis of the brachytherapy treatment in the patient with a small T1 lip cancer of 1 cm noted that the observed local failure was perhaps not surprising. Although 70 Gy was prescribed, the cancer was treated by a single-plane implant, consisting of only two wires at a separation of 1 cm, indicating a very small implanted tumour volume and narrow safety margin of dose. Similarly, local failure after radiotherapy for a 5-cm buccal mucosa cancer was not completely unexpected, despite a high total radiotherapy dose of 87.5 Gy, as local control rate in T3 buccal mucosa cancers treated by radiotherapy is only about 50%.[8,18] In the current study, the actuarial local control rate of 75% at 3 years after brachytherapy with or without external radiotherapy and ultimate loco-regional control of 92% for this cohort of 13 patients was comparable with that of other reports. Indeed, the actuarial local control rate of 82% and ultimate local control rate of 100% for the 12 T1/T2 cancers only (excluding the patient with T3 buccal mucosa cancer) is not too different from the 81% to 96% local control rates reported for early lip and buccal cancers after radiotherapy.[3-5,9,16] Given the satisfactory local control rates of T1 and T2 cancers and the lack of serious complications, the brachytherapy dose of 65 to 70 Gy (for T1 and T2 cancers, respectively) when given alone may be optimal. When external radiotherapy is employed before interstitial brachytherapy for bulky T2 or T3 cancers, splitting the total tumour dose of 80 to 85 Gy to deliver 40 Gy through external radiotherapy and another 40 to 45 Gy through interstitial brachytherapy is preferred. This is in contrast to the dose allocation in four of the six patients with buccal mucosa cancer reported here, in whom external radiotherapy was preferentially weighted. This approach is

the current recommendation for combining external radiotherapy and interstitial brachytherapy when indicated for T2 cancer of the tongue.[23] Lastly, for advanced T3 cancers, concurrent chemotherapy during external radiotherapy may enhance the radiation-induced tumour cell-kill and provide opportunities for 'tumour-debulking' before interstitial brachytherapy, to achieve more optimal local control.[24]

All 13 patients had a minimum follow-up period of about 1 year (range, 11.4-88 months). Among them, only one patient had a subsequent tumour in the neck although only three patients had been given neck radiotherapy treatment and two other patients had undergone prophylactic selective neck dissection. One patient received therapeutic radiotherapy for his N2 disease and remained disease-free in the neck. One of the two patients who received prophylactic neck irradiation had a T3 buccal mucosa cancer and he had local recurrence but no neck recurrence. The second patient had locally persistent T2 buccal mucosa cancer that was later surgically salvaged without neck failure. The two patients who underwent selective neck dissection remained disease-free in the neck. The only neck failure was seen in a patient with T2N0 lower lip cancer measuring 2.5 x 1.5 cm in length and width, respectively. The tumour thickness of 0.8 cm may have contributed to the failure in the ipsilateral submandibular region. There are reports suggesting that the thickness, along with the size of the lesion, is a significant prognostic factor for neck control in both buccal mucosa and lip cancers, echoing observations in tongue cancers.[2,25,26] We are currently performing routine imaging investigations such as ultrasonography or computed tomography scans of the neck, to look for radiologically evident cervical lymphadenopathy and then image-guided needle aspiration cytology for confirmation. Our policy is to perform selective dissection of level I, II, and III ipsilateral neck nodes for high-risk node-negative patients (T2 tumour or T1 tumour with >6 mm thick lip or buccal mucosa tumour), and radical neck dissection for node-positive patients, about 6 to 8 weeks after definitive brachytherapy. Two patients underwent ipsilateral selective neck dissection in line with our current policy, confirming their pN0 status. One patient who had hepatitis B cirrhosis with hypersplenism and thrombocytopenia contra-indicating any initial surgery received external radiotherapy to the ipsilateral node-negative neck for his T2N0 buccal mucosa cancer which unfortunately persisted locally and required subsequent salvage surgery.

With careful adherence to implantation rules and brachytherapy planning, use of mandibular shielding during brachytherapy, and avoidance of dental extraction after radiotherapy, there has not been any observation of osteoradionecrosis or soft-tissue necrosis. Among the 12 patients in clinical remission, including the two patients with local failure and the one patient with neck failure who subsequently underwent salvage surgery, the function of the nose, lip, and buccal mucosa was not compromised. Preservation of function after radiotherapy is considered a tremendous advantage over surgical resection, especially for patients with extensive cancer of the lip and buccal mucosa involving the lip commissure, when a comparable outcome is difficult to achieve by surgical reconstruction. Leaving at least a 5-mm margin between the ends of the active wires and the skin entry or exit points can avoid excessive skin dose and unsightly scars over the face. Acute radiation mucositis over the buccal mucosa and lip can be symptomatic for a few weeks after brachytherapy, requiring simple supportive treatment including antiseptic oral rinses, local dental ointment, and occasionally analgesics. Significant xerostomia and taste changes have not been reported as the parotid and submandibular salivary glands are not irradiated by the brachytherapy treatment.

Conclusions

Treatment results in this small cohort of patients with early nasal vestibule, lip, and buccal mucosa cancers suggest that satisfactory loco-regional cancer control can be achieved in the majority by definitive radiotherapy alone, of which interstitial brachytherapy is an integral, if not the most significant component. The brachytherapy technique described here is easy to learn and perform and has been proven to contribute significantly to the complication-free cure of these early cancers, without resorting to mutilating surgery. Our recommendation is to use primary interstitial brachytherapy alone, delivering 65 to 70 Gy for T1N0 or small T2N0 cancers in these regions, while external radiotherapy of up to 40 to 45 Gy can be prescribed before 40 to 45 Gy brachytherapy for bulky T2 or T3 cancers. Concurrent chemotherapy during external radiotherapy should be considered for T3 or node-positive disease when surgery is otherwise not indicated. After definitive radiotherapy to the primary tumour, ipsilateral selective neck dissection is indicated in thick T1N0 or T2N0 cancers, while radical neck dissection should be performed for the rare T1 or T2 node-positive cancers.

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