The Results of Radiotherapy for T1 Glottic Cancers; Influence of Radiation Beam Energy

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We analyzed the influence of various parameters on the results of radiotherapy for T1 glottic cancer by assessing the outcomes of 60 patients with this cancer who received definitive radiotherapy between 1985 and 1994. Seven patients were treated with a cobalt-60 unit, and the other 53 with a linear accelerator (26 patients at 3-MV, 10 at 6-MV, and 17 at 10-MV). Of the 17 patients treated at 10-MV, 4 also received part of their treatment with a cobalt-60 unit. The total radiation dose ranged from 56 Gy to 70 Gy (mean, 61 Gy). The total radiation dose of 51 patients (85%) was 60 Gy. The factors found to influence local control were the strength of the radiation beam energy and whether or not there was gross tumor invasion of the anterior commissure. The local control rate was 71% in the patients treated with a 10-MV linear accelerator, 56% in those treated with a 6-MV linear accelerator and, 97% in those treated with a cobalt-60 unit or a 3-MV linear accelerator ($P = 0.0173$). The local control rate was 43% in the patients with gross anterior commissure invasion and 88% in those without ($P = 0.0075$). We conclude that low energy photon beams are more suitable for the treatment of early glottic cancers, especially if the lesion grossly invades the anterior commissure.

Key words: T1 glottic cancers, radiotherapy, radiation beam energy

Radiotherapy is an established method for treatment of T1 glottic cancers, with local control rates typically over 80% (1). For the preservation of good voice quality, radiotherapy has advantages over surgery. However, when radiotherapy fails, as occurs in some cases, surgery is performed as a salvage treatment. To identify factors contributing to the local control of radiotherapy for T1 glottic cancer, we reviewed the records of our patients with this cancer.

We found that the difference of radiation beam energy was one factor influencing local control. In this paper, we present the results of radiotherapy for patients with T1 glottic cancer and our analysis of the influence of the radiation beam energy on local control.

Materials and Methods

Sixty patients with T1 glottic cancers received definitive radiotherapy between January 1985 and July 1994 at Okayama University Hospital and Okayama Saiseikai Hospital in Okayama, Japan. Radiotherapy for T1 glottic cancer was performed in the same manner at these two institutions. The 59 men and 1 woman ranged in age from 46 to 79 years (mean, 64 years). All patients were undergone direct laryngoscopy, with staging performed according to the fifth edition of the TNM classification of malignant tumors published by the International Union Against Cancer (UICC) (2). T1 tumors were classified as follows: T1a, involvement of one true vocal cord with or without involvement of the anterior commissure ($n = 43$); and T1b, involvement of both true vocal cords ($n = 17$). The patients were also subdivided into the following groups: those with gross invasion of the tumor into the anterior commissure ($n = 7$) and those without such spread ($n = 53$). All lesions were demonstrated by biopsy to be squamous cell carcinoma. Of the 60 carcinoma lesions, 42 were well differentiated, 12 moderately, and 1 poorly, and in 5 the grade was unknown. No patient had lymph node metastasis at the initial diagnosis.

All 26 patients treated at Okayama Saiseikai Hospital

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were treated with a 3-MV linear accelerator; those treated at Okayama University Hospital before April 1992 were treated with a 10-MV linear accelerator (n = 13), a cobalt-60 unit (n = 7), or a combination of these (n = 4). The patients were treated in the supine position without immobilization devices. The target site was directly marked on the skin as a preliminary. Wedge filters to provide a more homogeneous dose distribution were not used. Ten patients treated at Okayama University Hospital after July 1992 were treated with a 6-MV linear accelerator. These patients were treated in the supine position with immobilization devices, and wedge filters were used.

Right and left lateral parallel opposed fields were used in all patients. The average field size was 30 cm^2, and typically ranged from 5 × 5 cm to 6 × 6 cm (Fig. 1). The doses reported in this study refer to the central absorbed dose calculated at the central axis. The total radiation dose ranged from 56 Gy to 70 Gy (mean, 61 Gy). The total radiation dose of the 51 patients (85 %) was 60 Gy. The daily dose fraction was 2 Gy for all patients. All courses of radiotherapy were delivered using once-daily fractionation, 5 days per week. The mean treatment time was 46 days (range, 40–75 days).

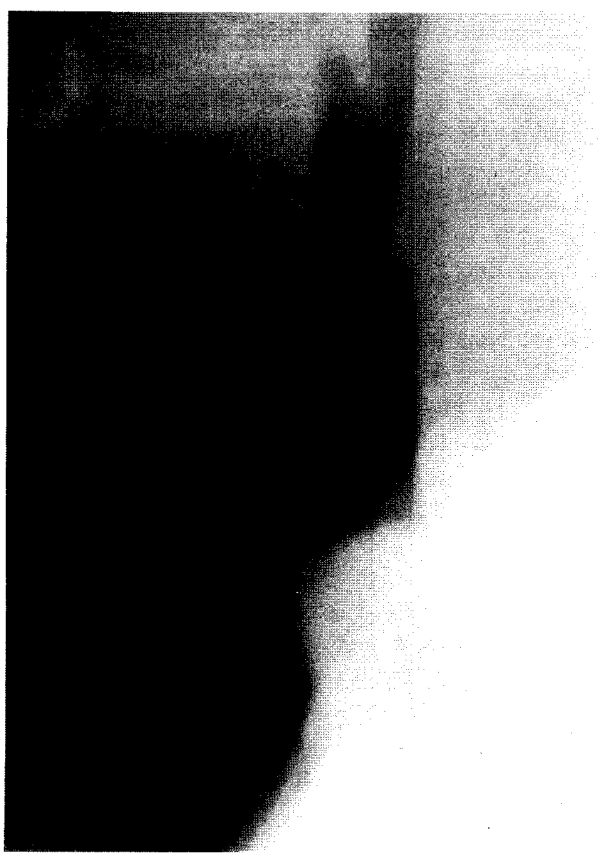

Fig. 1 Radiation treatment field (5 × 5 cm).

Local recurrence was diagnosed by direct laryngoscopy and biopsy. The local control rates were calculated for 57 patients, excluding 2 patients who died without local recurrence due to another malignancy within 2 years, and 1 patient who was lost to follow-up within 3 months. The mean follow-up period was 54 months (range, 3–111 months).

Various parameters were analyzed to assess their impact on local control rates using the log-rank test. The local control and survival curves were adjusted and expressed by the Kaplan-Meier method (3), and comparison of the curves was performed using the log-rank test (4). The local control and survival intervals were measured from the date of the beginning of radiotherapy, with a local control score of 0 assigned to patients in whom local control was never achieved.

Results

Of the 57 patients who were followed up, 13 (23 %) had local recurrence, 10 (77 %) of them within 2 years. The local control rate at two years was 83 % for all patients. Table 1 shows the actuarial local control rates at two years for subgroups classified by age, substage, presence or absence of gross invasion of the anterior commissure, histologic grade, radiation beam energy, field size, and treatment time. Factors identified as significantly influencing local control were the difference of radiation beam energy and the presence or absence of gross invasion of the anterior commissure by the tumor. The local control rate was 71 % for the patients treated with a 10-MV linear accelerator, 56 % for those treated with a 6-MV linear accelerator, and 97 % for those treated with a cobalt-60 unit or a 3-MV linear accelerator. The local control rate for the patients treated with a cobalt-60 unit or a 3-MV linear accelerator was significantly higher than that for the patients treated with a 6-MV or a 10-MV linear accelerator ($P = 0.0173$). No significant difference was recognized between the patients treated with a 6-MV and a 10-MV linear accelerator. The local control rate was 43 % for the patients with gross anterior commissure invasion and 88 % for those without

Table 1 Local control rates at 2 years in various subgroups

Parameters	Local control rates (%)	P*
Age (years)		
< 65 (n = 34)	83	NS
≧ 65 (n = 23)	83	
Substage		
T1a (n = 42)	86	NS
T1b (n = 15)	73	
Tumor grade (differentiation)		
Well differentiated (n = 39)	82	NS
Moderately or poorly differentiated (n = 13)	85	
Gross tumor invasion of the ant. commissure		
Present (n = 7)	43	0.0075
Absent (n = 50)	88	
Radiation beam energy		
Cobalt-60 or 3-MV (n = 31)	97	0.0173
6-MV (n = 9)	56	
10-MV (n = 17)	71	
Field size (cm^2)		
≦ 25 (n = 45)	80	NS
30 < (n = 12)	90	
Treatment time (days)		
≦ 42 (n = 16)	88	NS
43–49 (n = 28)	82	
≧ 50 (n = 13)	77	

*The log-rank test; NS: Not Significant; ant.: Anterior.

Table 2 Local control rates at 2 years

	10-MV	6-MV	Co-60 or 3-MV
Gross ant. commissure invasion	33% (n = 3)	0% (n = 2)	100% (n = 2)
No gross ant. commissure invasion	79% (n = 14)	71% (n = 7)	97% (n = 29)

ant.: See legend to Table 1.

($P = 0.0075$). However, no difference was recognized between these two subgroups among the patients treated with a cobalt-60 unit or a 3-MV linear accelerator (Table 2). No significant difference in local control rates was seen for the subgroups classified by age, substage, histologic grade, field size, or treatment time.

Of the 13 patients with local recurrence, 8 were undergone total laryngectomy, 3 partial laryngectomy, 1 cordectomy, and 1 received no salvage treatment. Three of the 57 patients had neck lymph node metastasis after radiotherapy of the primary lesion and underwent radical neck dissection. Of these 3 patients, 1 had local recurrence.

Five of the 57 patients died: 3 died of other malignancies (lung, esophageal and gastric cancer), and 2 died of neck lymph node metastasis. The actuarial survival rate at five years was 93%.

No patient had severe radiation-induced laryngeal complications requiring surgical intervention.

Discussion

In this study we found that local control for the patients treated with 6-MV or 10-MV linear accelerator was lower than local control for those treated with a 3-MV linear accelerator or cobalt-60 unit. Generally, in radiation therapy for glottic cancer, there is no problem if 4-MV or lower energy photon beams are used. However, there is no consensus with 6-MV photon.

As technology advances, different radiation therapy machines come into use. The number of cobalt-60 machines has decreased and the number of linear accelerators has increased. The mean energy of a cobalt-60 unit is 1.25 MV and that of a linear accelerator is higher than that of cobalt-60 unit. A higher energy photon is advantageous for deep-seated tumors, but disadvantageous for tumors near the surface. Given the anatomical characteristics of the larynx, a thin wedge-shaped structure in the anterior neck adjacent to the airway, there is a risk of underdosing the lesion if higher energy photon beams which have a build-up effect are used. Some dosimetry studies have confirmed this assertion (5–9). For example, Shimizu *et al.* measured the radiation dose by thermoluminescent dosimetry using neck phantoms with an air cavity similar to the human larynx and found that the dose was reduced with a 6-MV or 10-MV linear accelerator as compared to a cobalt-60 unit, especially at the anterior commissure (9). In clinical studies, there are some reports regarding the influence of radiation beam energy on treatment results for early glottic cancers. Foote *et al.* (10) reviewed these retrospective studies. He found that reports described one of the following: a) the local control rate was significantly lower in patients treated with 6-MV or higher energy photon beams than in patients treated with 4-MV or lower energy beams (11–13), as we have found, or b) the local control rate in patients treated with a 6-MV linear accelerator was comparable in patients with

Table 3 Published results regarding the influence of radiation beam energy on treatment results for T1 glottic cancers

Author (year), Num	Treatment machine	Local control (%)	T.D./Fr size (Gy)
Reserchers who reported that the difference of radiation beam energy was a factor influencing the local control.			
Sung *et al.*	Co-60 unit	87 (5-year)	Mean 61/2
(1979), n = 162	6-MV	60	Mean 63/2
	22-MV	74	Mean 61/2
Izuno *et al.*	Co-60 unit	88 (5-year)	Mean 63/1.8-2
(1990), n = 53	4-MV	91	Mean 64/1.8-2
	8/10-MV	60	Mean 66/1.8-2
Davineki *et al.*	Co-60 unit	85 (5-year)	Most patients 60/2
(1992), n = 281	4-MV	84	
	6-MV	70	
Yamamoto *et al.*	Co-60/3-MV	97 (2-year)	Mean 61/2
(1998), n = 57	6-MV	56	Mean 61/2
	10-MV	71	Mean 62/2
Reserchers who reported that the difference of radiation beam energy was not a factor influencing the local control.			
Akine *et al.* (1991), n = 154	6-MV	89 (5-year)	Median 67/1.9-3.1
Small *et al.*	Co-60 unit	85 (5-year)	Mean 64/mean 2.28
(1992), n = 103	4-MV	90	
	6-MV	92	
Rudoltz *et al.*	Co-60 unit	84 (5-year)	Median 64/1.8-2.2
(1993), n = 91	2-MV	100	
	4-MV	77	
	6-MV	86	
Foote *et al.* (1996), n = 73	6-MV	100 (2-year)	Median 65/median 2

T.D.: Total dose; Fr: Fraction; Num: Number.

a cobalt-60 unit, or a 2-MV or a 4-MV linear accelerator (10, 14-16). We cannot identify the source of the discrepancy between these results. However, we noted that the total radiation dose was higher in latter set of studies than in former (Table 3), and there is a possibility that the discrepancy is due to differences in the total dose. We think that underdosing of the lesion, when 6-MV photon beams were used, had little effect on the local control rate in the latter studies because the total dose was sufficient.

In conclusion, we think that 4-MV or lower energy photon beams are more suitable for the treatment of early glottic cancer, especially if the lesion involves a significant portion of the anterior commissure. If a 6-MV energy photon beam is used for the treatment of this cancer, a total radiation dose of 61 Gy is believed to be insufficient, and thus adjustments of the dose are necessary.

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