

Intra-operative margin diagnosis during transoral laser microsurgery for glottic cancer prevents mucosal recurrence



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Abstract

Background: Transoral laser microsurgery (TLM) for early glottic cancer is an important treatment option for laryngeal preservation. To preserve postoperative voice quality, the bare minimum and sufficient resection is performed according to the extent and deep invasion of the tumor. Due to the narrow and small surgical field, resection with a sufficient safety margin is difficult.

We usually perform intra-operative frozen margin diagnosis at the lateral margin and a deep margin (Total 5-6 samples). When the margin is supposed to be positive, additional resection is performed. However, the accurate intra-operative margin evaluation is hard because the tissue is damaged by the laser. Therefore many surgeons judge the margin by their experiences. In this study, we investigated the value of the intra-operative margin diagnosis during TLM to improve the prognosis of glottic cancer.

Patients and methods: A retrospective study was performed on patients with glottic cancer who underwent TLM as an initial treatment in our hospital between 2010 and 2016. Intra-operative margin diagnosis (frozen section), permanent pathological diagnosis (permanent section), European Laryngological Society (ELS) classification, local recurrence, and the prognosis was assessed. In the margin evaluation, the pathological diagnosis was classified as follows, positive (+): Carcinoma, carcinoma in situ and severe dysplasia, unclear (±): dysplasia and difficult to diagnose, negative (-): others. The recurrence was classified into ‘mucosal’ (horizontal) and ‘deep’ (vertical).

Results: Sixty-six patients with squamous cell carcinoma were enrolled. (T classifications, Tis: 7, T1a: 34, T1b: 9, T2: 15, and T3: 1, ELS classifications, Type I: 4, Type II: 21, Type III: 23, Type IV: 5, Type V: 10, and Type VI: 3) Survival rates after five years were as follows, overall: 90.7%, disease-specific: 98.3%, recurrence-free: 88.4%, laryngeal preservation: 95.5%.

Margin diagnosis of the frozen section was (+): 10 cases, (±): 18 cases, and (-): 38 cases. All (+) and (±) were found in samples with a lateral margin, not with a deep margin. Margin diagnosis of the permanent section was (+): 26 cases, (±): 21 cases, and (-): 19 cases.

Seven cases had recurrences with 4 deep and 3 mucosal. Frozen section was (+): 1 case, (±): 3 cases, (-): 3 cases and permanent section was (+): 5 cases, (±): 1 case, and (-): 1 case. All 3 cases with frozen (-) were permanent (+) and mucosal recurrence rescued with TLM or radiation. In 4 cases with frozen (+) and (±), only 1 case had very small mucosal recurrence rescued with TLM. The other 3 cases had deep recurrences after ELS Type III or higher. Total laryngectomies were performed to rescue. Additional resection was performed in all 28 cases with frozen (+) and (±). Only 1 case had a mucosal recurrence and 3 cases had deep recurrences.

Conclusions: These results indicated that additional resection based on the frozen section prevents a mucosal recurrence. On the other hand, it might be insufficient in the evaluation of a deep margin. In cases with deep resection, even if the frozen section was negative, careful postoperative follow-up is necessary.

Introduction

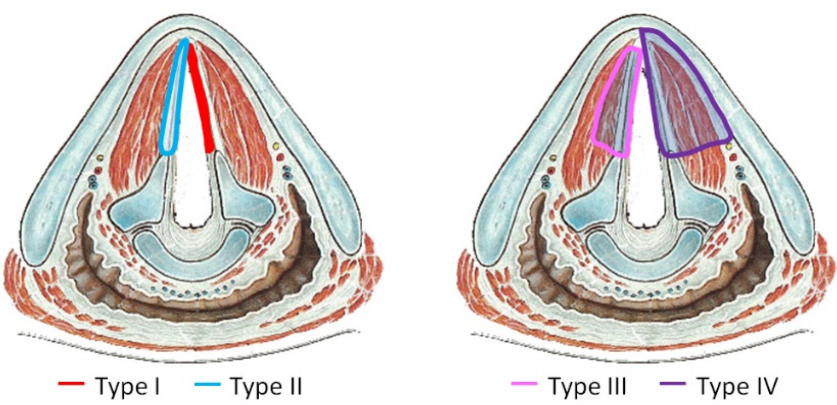
Transoral laser microsurgery: TLM

- Surgical option for laryngeal preservation
- For early-stage glottic cancer (Tis-T3)
- Local control rate: 86-95% (T1) and 76-89% (T2)

Disadvantages:

- To maintain voice quality and limited glottic cavity
→ Difficult to resect with **sufficient safety margin**
- Pathological diagnosis of **surgical margin**
→ Difficult to **accurate diagnosis** due to cauterization
- Positive rate of permanent pathological margin : 45-81%
Recurrence rate with positive margin: 14 to 50%

Poor evidence and consensus on the treatment of pathological margin positive cases



Objective

Investigate the value of the intra-operative margin diagnosis during TLM to improve the prognosis of glottic cancer

Patients & Methods

Study Design: Single-center retrospective study

Patients: 66 TLM cases (Fresh cases) between 2010-2016

Assessment:

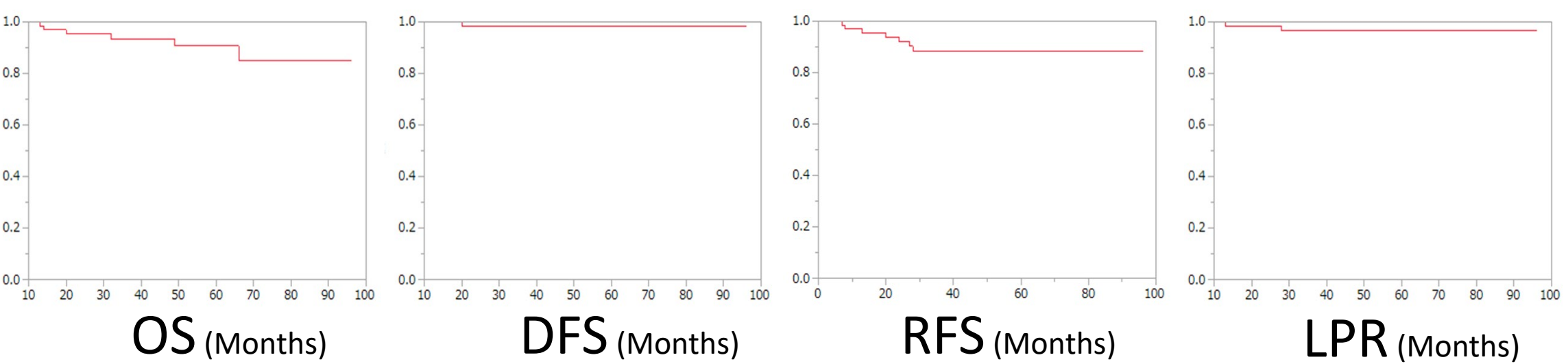
- Surgical resection classified by ELS classification
- Pathological diagnosis of margin
Intra-operative frozen section & Permanent section
- Local recurrence and its site (horizontal or deep direction)
- 5-year rate of overall survival (OS), disease-specific survival (DFS), recurrence-free survival (RFS), laryngeal preservation (LPR) (Kaplan-Meier method)

Pathological classification of margin diagnosis	
Positive (+)	Carcinoma / CIS / Severe dysplasia
Unclear (±)	Dysplasia / Undetermined
Negative (-)	Negative / Others

Patients		ELS classification	
Number	66	Type I	4(6%)
Age	69.9 ± 7.6	Type II	21(31.8%)
Male / Female	62/4	Type III	23(34.8%)
T classification		Type IV	5(7.5%)
Tis	7(10.1%)	Type Va	10(15.1%)
T1a	34(51.5%)	Type VI	3(4.5%)
T1b	9(13.6%)		
T2	15(22.7%)		
T3	1(1.5%)		

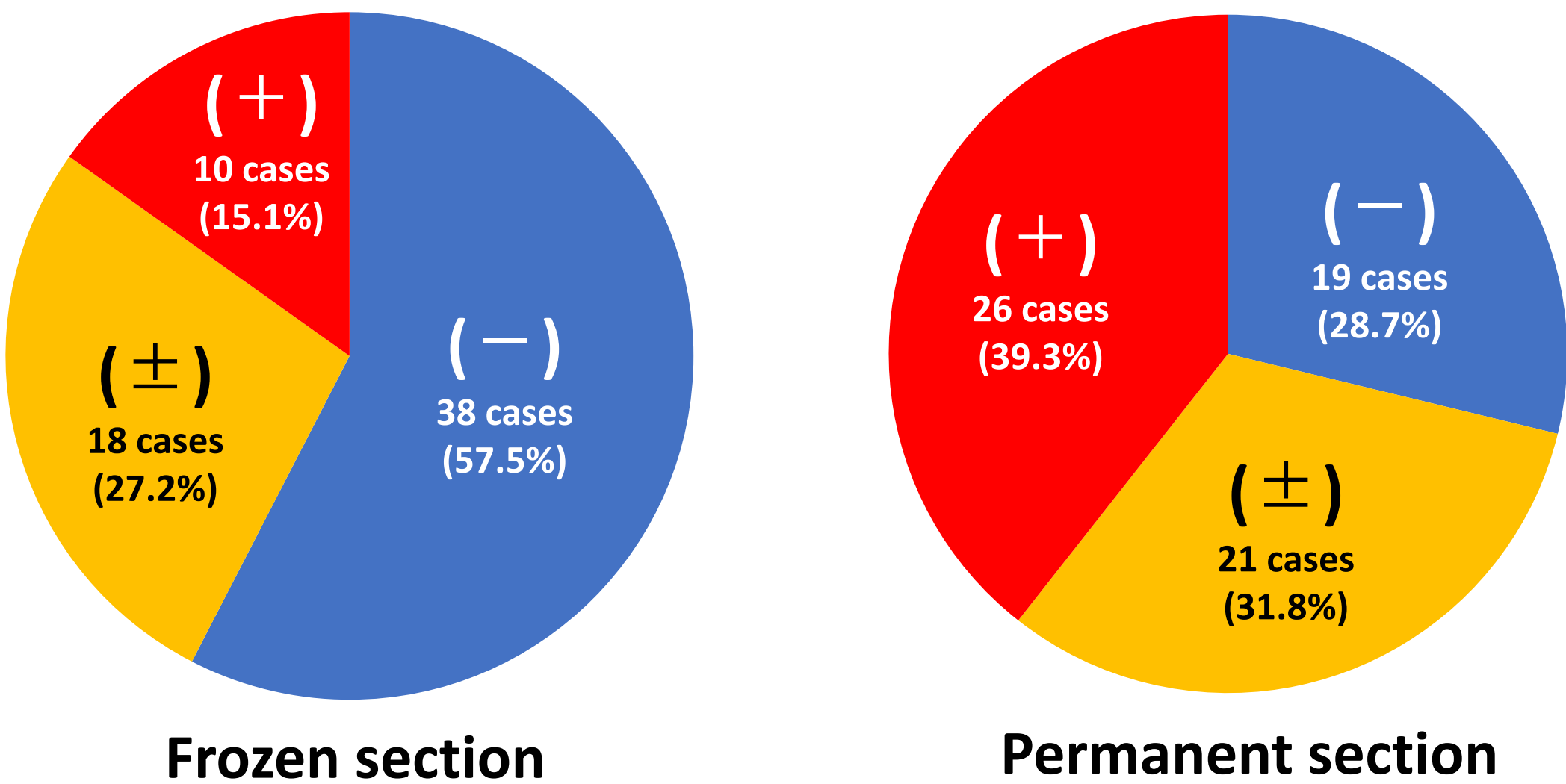
Results 1

Good oncological outcome with organ preservation
OS: 90.7%, DFS: 98.3%, RFS: 88.4%, LPR: 95.5%. (5 years)



Results 2

High rate of margin diagnosis with **(+) & (±)**
Frozen section: 28/66 (42.3%), Permanent section: 47/66 (71.2%)
* Most cases of (+) & (±) in frozen section were performed 2-3mm of additional resection without intra-operative frozen diagnosis.



Results 3

Recurrence: **7 cases (10.6%)** with 4 deep and 3 mucosal site
3 of permanent section (+) and 1 of frozen section (+) / (±):
- **Mucosal recurrence** rescued with **TLM or RT**
Other 3 cases: Deep resection of Type III or higher cases
- **Deep recurrence** rescued with **total laryngectomy**

	T	ESL	Time to rec. (Mon)	Pathological diagnosis			Recurrence site	Rescue
				Frozen section	Permanent section	additional resection		
1	1a	I	27	(-)	(+)		Mucosal	TLM
2	1a	II	8	(-)	(+)		Mucosal	TLM
3	2	IV	24	(-)	(+)		Mucosal	RT
4	1a	III	11	(±)	(±)	(-)	Deep	TL+Bil. ND
5	2	III	28	(±)	(±)	Laser vaporization	Deep	TL
6	1a	IV	20	(±)	(+)	(±)	Deep	RT & TL
7	1b	II	7	(+)	(-)	(-)	Mucosal	TLM

Frozen section	Recurrent cases	Permanent section	Recurrent cases
(+)	4/28(14.2%)	(+)	5/26(19.2%)
(±)		(±)	1/21(4.7%)
(-)	3/38(7.9%)	(-)	1/19(5.2%)
Total	7/66(10.4%)	Total	7/66(10.4%)

Results 4

Additional resection seems to be effective for **preventing mucosal recurrence**, while **insufficient for deep recurrence**.

	Additional resection			
	(+)	(±)	(-)	Total
Frozen section (+)(±)	2	9	17	28
Mucosal rec.	0	0	1	1
Deep rec.	0	2	1	3

Conclusion

- **Additional resection based on the frozen section prevents a mucosal recurrence.**
- **In cases with deep resection, even if the frozen section was negative, careful postoperative follow-up is necessary.**