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LARYNGOLOGY

Evaluation of lasersurgery and radiotherapy as treatment modalities in early stage laryngeal carcinoma: tumour outcome and quality of voice

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Abstract For treatment of early stage (Tis-T2) laryngeal cancer the main choice is between microlaryngoscopy with carbon dioxide laser resection (laser surgery) and radiotherapy. Because both treatments provide excellent tumour control, secondary outcome variables such, as quality of voice may be of importance in treatment preference. In this study tumour outcomes and quality of voice were analysed for a cohort of patients with early stage (Tis-T2) laryngeal (glottic) carcinoma. The "physical subscale" of the voice handicap index questionnaire (VHI) and a validated five-item screening questionnaire were used. Analysis of 89 patients treated with laser surgery and 159 patients treated with radiotherapy revealed a 5-year local control of 75 and 86 % ($p = 0.07$). Larynx preservation (5-year) was, however, superior in patients treated with laser surgery, 93 vs 83 % ($p < 0.05$). Tumour outcomes were also analysed per tumour stage and none were of significant difference. Quality of voice was analysed in 142 patients. VHI scores were 12.4 ± 8.9 for laser surgery and 8.3 ± 7.7 for radiotherapy ($p < 0.05$), with a higher score reflecting a worse outcome. VHI scores per tumour stage for laser surgery and radiotherapy were, respectively, 12.0 ± 9.9 and 7.9 ± 7.5 in T1a ($p = 0.06$), 16.7 ± 9.0 and 4.9 ± 6.6 in T1b ($p < 0.05$). Outcomes of the five-item questionnaire showed voice deficiency in 33 % for laser surgery and 23 % for radiotherapy in T1a ($p = 0.330$) and 75 and 5 % for T1b ($p = 0.001$). Oncologic outcomes of laser surgery and radiotherapy were comparable. Larynx preservation is, however, preferable in patients initially treated with laser surgery. According to subjective voice analysis, outcomes were comparable in T1a lesions. Depth of laser resection is of influence on voice deficiency displayed by a significantly higher percentage of voice deficiency in patients treated with laser surgery for T1b lesions.

Keywords Larynx · Radiotherapy · Carbon dioxide laser surgery · Quality of voice · Voice handicap index · Tumour outcomes

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Introduction

Within the group of head and neck squamous cell carcinoma, the larynx is the most frequently affected site in Western Europe accounting for approximately 30 % of the cases. In 56–75 % the disease is diagnosed in an early stage (T1 and T2), most frequently arising from the glottis [1–3].

Treatment of early stage laryngeal carcinoma consists of carbon dioxide endoscopic laser surgery (henceforth laser surgery) radiotherapy or open partial laryngectomy with the intent to preserve laryngeal function. These treatment modalities have advantages and disadvantages. Laser surgery has the advantage that it can be repeated or succeeded by radiotherapy for recurrent disease: furthermore laser surgery is a 1-day treatment and costs of treatment are low in comparison to the other treatment modalities [4–7]. However, its dependency on patient anatomy and surgical expertise are disadvantages. For radiotherapy, there is no need for treatment under general anaesthesia, though treatment time is significantly longer and more surrounding healthy tissues can be damaged, sometimes leading to laryngeal edema, fibrosis or long-term damage of neck vessels [8]. Open partial laryngectomies have as main limitation the enlarged risk of deteriorated functional outcomes, combined with the necessity for postoperative tracheotomy. This operative approach, however, is less dependent on patient's anatomy in comparison to laser surgery [7, 9, 10]. All treatment modalities provide excellent effectiveness in tumour outcomes. Local control rates range 71–100 % for laser surgery and 73–95 % for radiotherapy in T1 tumours without involvement of the anterior commissure [11–15]. The average local control rate of open partial laryngectomies is 89.9 % following from the review of Thomas et al. [9]. Ultimately preservation of the larynx is often reported to be higher with use of laser surgery, 93–100 % [3, 16–19]. So far no randomized trials comparing treatment options for early glottic cancer have been reported. All data are derived from retrospective series.

Because there appears to be little or no difference in oncologic outcomes between laser surgery and radiotherapy, treatment costs, side effects, patient preferences and functional outcome in terms of quality of voice may have an important role in the choice between laser surgery and radiotherapy. Several studies have addressed these issues, but results are not equivocal. One meta-analysis [20], one study [4] and a review of 15 studies [21], of which 12, did not find a (significant) difference in voice outcome between both treatment modalities, whereas others claim that either radiotherapy [22, 23] or laser surgery [24, 25] has a better outcome in terms of voice quality.

The aim of this retrospective study was to evaluate treatment outcomes for early stage (T1 and T2) glottic laryngeal carcinoma in an 8-year period within The Netherlands Cancer Institute. Tumour outcomes and subjective quality of voice following radiotherapy or laser surgery were analysed.

Patients and methods

Patient characteristics

The study population consists of 260 patients with early stage (≤T2) glottic laryngeal carcinoma treated at The Netherlands Cancer Institute between January 2000 and July 2008. In this retrospectively collected database, 12 patients were excluded from further analyses because of previous/synchronous malignancy of the head and neck ($n = 8$), laryngeal cancer of unusual (neuro-endocrine) histology ($n = 2$) or regional involvement at presentation ($n = 2$). Of the 248 eligible patients, 159 were treated with radiation and 89 with laser surgery.

Tumour staging

Classification was performed according to the 2002 UICC TNM staging system. Tumour stage ranged from carcinoma in situ (henceforth discussed as Tis), T1a, T1b and T2 for glottic carcinomas (Table 1). Staging modalities were direct laryngoscopy, (stroboscopy), ultrasound of the neck (combined with FNAC in case of suspicion of regional involvement) and chest x-ray. CT-imaging was performed in all T1b or T2 tumour stages.

Treatment

In 89 patients treatment consisted of direct microlaryngoscopy with complete resection of the lesion with CO_2 laser surgery. A Sharplan CO_2-laser 30C with Acuspot 712 micromanipulator and super-pulse, continuous, mode was used. Power setting varied from 2–9 W. The technique as

Table 1 Patient characteristics

Characteristics	Laser-surgery ($n = 89$)	Radiotherapy ($n = 159$)	p
Mean age (years) (range)	67 (41–87)	64 (39–89)	0.026
Sex ratio (male:female)	88:12 %	87:13 %	0.578
Primary tumour stage (glottic, N0) Tis/T1a/T1b/T2	23/49/15/2	3/54/27/75	<0.001
Mean follow-up (months), (range)	44 (3–89)	48 (2–108)	0.108
Loss to follow-up	3	8	0.398

described by Steiner [13], resecting the tumour after transection, was used. In small lesions the tumour was resected in one piece.

Radiotherapy was delivered to a total of 159 patients with a 4-MV ($n = 212$) or 6-MV ($n = 4$) photon linear accelerator. Patients were treated in a supine position, using a thermoplastic immobilization mask. Target areas included the larynx, using a standard parallel opposing technique with a field size of 6 cm × 6 cm for Tis and T1a/b glottic carcinomas without nodal disease (N0). For patients with T2 glottic carcinoma, target areas included the larynx and bilateral neck nodes, using either a parallel opposing beam technique with or without an adjacent anterior field covering the supraclavicular (level 4) area or a technique using intensity modulated radiotherapy (IMRT). Radiotherapy schedules were based upon Dutch national guidelines and radiotherapy was applied according to two schedules: schedule 1:25 × 2.4 Gy, total dose 60 Gy in 5 weeks (*n*: 104, for node-negative glottic carcinoma, ≤T1b, treated with 6 cm × 6 cm field), median overall treatment time 32 days, (fractions were delivered during 5 days a week) and schedule 2: 35 × 2.0 Gy, total dose 70 Gy in 6–7 weeks (*n*: 50, for T2 glottic carcinoma treated to larynx and nodal areas) overall treatment time 41 days. The total delivered dose ranged from 52.8 to 70 Gy. Five patients did not receive the hospital standard practice dose scheme because of change of schedule (*n*: 1), death during treatment (*n*: 1) or irradiation outside our centre (*n*: 3).

Voice evaluation

Patients with glottic cancer alive at last follow up without recurrent disease ($n = 179$) were contacted by telephone to participate in an analysis regarding voice quality. A total of 142 patients (response rate 79 %) consented to this. Excluded from this evaluation were patients with current laryngeal cancer (*n*: 1), linguistic barrier (*n*: 5) or patients treated with both modalities discussed in this article or laryngectomy (*n*: 15). Evaluation of voice impairment experienced by patients was performed using two validated questionnaires; the "physical subscale" of the "voice handicap index" (henceforth VHI) and a five-item screening questionnaire (henceforth five-item questionnaire), designed by van Gogh et al. [24]. VHI is a widely used self-administered questionnaire with a Likert-type scale indicating how frequently each situation is experienced. The 'physical' subscale consists of ten questions, with responses grading from 0 to 4, with higher scores representing severe voice handicap. The maximal score on this domain is 40 points [26]. The five-item questionnaire is composed of five questions on a ten-point scale covering vocal abilities and related social situations [24]. An overview of both questionnaires is given in Appendix 1. Due to the retrospective design of the study, no data for baseline voice quality evaluation were available.

Follow-up

The minimal duration of follow-up was 12 months from diagnosis, with the exception of patients who were lost to follow-up or died during this period. Regular follow-up ended 60 months after start of initial treatment. Follow-up included physical examination, laryngoscopy with the flexible endoscope and an annual chest x-ray. Details regarding follow-up are described in Table 1.

End points and statistical analysis

All patients were followed at the Netherlands Cancer Institute. Patient characteristics were compared by Fisher's exact test, Chi-square test and Kruskal–Wallis test. Recurrences were categorized as local recurrence, regional recurrence and/or distant metastases. A local recurrence was defined as a recurrence involving the initial tumour site, with a maximal recurrence interval of 5 years between initial presentation and date of recurrence. Recurrence-free interval was calculated from the date of therapy to the date of local recurrence, regional recurrence or distant metastases. Patients without any of these events were censored at the time of death from any cause or at last follow-up. Larynx preservation and disease specific survival were also used as end-points. The probabilities of local control (with initial treatment modality), larynx preservation, disease-specific survival and overall survival were calculated using Kaplan–Meier with the log-rank test assessing equality of distributions. Students' *t* test was used to compare averages and the Chi squared test for comparing proportions. *p* values <0.05 were considered significant. All analyses was performed by SPSS for windows, version 18.0.

Results

Patient and tumour characteristics

Patient and tumour characteristics of the group treated with laser surgery ($n = 89$) and the group treated with radiotherapy ($n = 159$) were compared (Table 1). There were no statistically significant differences in sex or duration of follow-up. However, primary and regional tumour stages were not distributed equally between the two groups. Tumour stage was higher in the radiotherapy group, which contained the vast majority of patients with stage T2 carcinomas as well as the majority of T1b carcinomas.

Table 2 Tumour outcome for laser surgery and radiotherapy in all patients

	Laser surgery ($n = 89$)	Radiotherapy ($n = 159$)	p
Local recurrence	17	18	0.091
Mean time to recurrence ± SD (months)	13 ± 15	16 ± 15	
Regional recurrence	2	2	0.620
Mean time to recurrence ± SD (months)	4 ± 2	7 ± 1	
Distant metastases	–	1	0.641
Mean time to recurrence ± SD (months)	–	7	
Local control (with initial treatment modality)	77	142	
5-year local control	75 %	86 %	0.070
Larynx preservation	87	142	–
5-year larynx preservation	93 %	83 %	0.049
Disease specific survival (DSS)	95	196	
5-year disease specific survival	99 %	94 %	0.054
Overall survival (OS)	80	125	
5-year overall survival	90 %	72 %	0.106

Table 3 Outcomes for glottic Tis

	Laser surgery ($n = 24$)	Radiotherapy ($n = 3$)	p
Local recurrence	6	0	0.277
Mean time to recurrence ± SD (months)	18 ± 18	–	–
Local control (with initial treatment modality)	20	3	
5-year local control	86 %	100 %	0.566
Larynx preservation	23	3	
5-year larynx preservation	95 %	100 %	0.808
Disease specific survival (DSS)	22	3	
5-year disease specific survival	100 %	100 %	–
Overall survival (OS)	21	3	
5-year overall survival	96 %	66 %	0.084

Tumour outcomes

Recurrent disease was observed in 19 patients (21 %) in the laser surgery group: 17 local and 2 regional recurrences. For the radiotherapy group recurrent disease was observed in 21 patients (13 %); 18 local, 2 regional- and 1 distant recurrences. There was no significant difference between CO_2 laser and RT in local control. Larynx preservation ($p < 0.05$), disease-specific survival and overall survival were less favourable in the radiotherapy group (Table 2). Local recurrences and control, larynx preservation, disease-specific survival and overall survival were analysed separately for different T categories.

Table 4 Outcomes for glottic T1a

	Laser surgery ($n = 50$)	Radiotherapy ($n = 54$)	p
Local recurrence	7	3	0.307
Mean time to recurrence ± SD (mth)	20 ± 28	20 ± 11	
Local control (with initial treatment modality)	45	51	
5-year local control	81 %	93 %	0.382
Larynx preservation	50	52	
5-year larynx preservation	100 %	93 %	0.267
Disease specific survival (DSS)	50	53	
5-year disease specific survival	100 %	96 %	0.519
Overall survival (OS)	45	44	
5-year overall survival	86 %	89 %	0.561

Patients with glottic Tis carcinoma ($n = 27$) developed local recurrence in the laser surgery group in 6 out of 24 (25 %) and in the radiotherapy group in 0 out of 3. In 3 of 6 patients recurrence was diagnosed within 3 months after initial treatment. Salvage therapy of the recurrences consisted of endoscopic re-treatment ($n = 3$) or radiotherapy ($n = 3$) with total control of disease. In one patient eventually a total laryngectomy with postoperative radiotherapy ($n = 1$) was necessary. None of the outcomes differed statistically significant between both treatment modalities (Table 3).

Patients with glottic T1a carcinoma ($n = 104$) developed local recurrence in the laser surgery group in 7 out of 50 (14 %) and in the radiotherapy group in 3 out of 55 (6 %). Local recurrences in the laser surgery group were treated with endoscopic re-treatment ($n = 4$) or radiotherapy ($n = 3$). Local recurrence after radiotherapy was treated with total laryngectomy ($n = 2$) and laser surgery ($n = 1$). Eventually one patient died due to secondary recurrent disease in the radiotherapy group. There were no significant differences in outcome measures between both treatments (Table 4).

Patients with glottic T1b carcinoma ($n = 42$) developed local recurrence in the laser surgery group in 3 out of 15 (20 %) and in the radiotherapy group in 4 out of 27 (15 %). Local recurrences in the laser group were treated with laryngectomy ($n = 2$) or radiotherapy ($n = 1$). In the

radiotherapy group the local recurrences were treated with a laryngectomy ($n = 3$) or laser surgery ($n = 1$). There were no regional recurrences in the radiotherapy group and two regional recurrences (13 %) in the laser surgery group (p 0.052). One was treated with a neck dissection ($n = 1$) whereas the other patient died before treatment of an unrelated cause. Except for these regional recurrences there was no significant difference in oncologic outcome between both groups (outcomes combined with T2 are shown in Table 5).

Patients with glottic T2 ($n = 77$) carcinoma were mainly treated with radiotherapy (75/77), whereas only two were treated with laser surgery. Therefore in Table 5 this group is taken together with T1b tumours. A total of 11 patients (14 %) developed local recurrence, one in the laser surgery group. This patient was repeatedly treated with CO_2 laser. In the radiotherapy group, of the ten patients with a local recurrence, all were treated with a laryngectomy. Two of the 78 patients developed regional recurrences and one distant metastases as first recurrence. One laryngectomy was performed for recurrent pneumonia's due to chronic aspiration resulting in a total of 11 laryngectomies.

Quality of voice

Table 6 shows the outcomes obtained from the voice handicap index 'VHI' "physical subscale" questionnaire and the five-item questionnaire designed by van Gogh [24]. Both questionnaires show an overall superior outcome of voice subjective quality of voice in patients treated with radiotherapy. For the VHI median scores were 8.3 and 12.4 respectively for the patients treated with radiotherapy or laser surgery, with a higher score reflecting a worse outcome (p value < 0.05). If split between T1a and T1b, only for the T1b subgroup these results were of significance. For the five-item questionnaire the percentage of patients with voice deficiency was 37 % in the group treated with laser surgery, versus 23 % in the group treated with radiotherapy. Only in the T1b group this difference was statistically significant (p value 0.001). Two patients in the T2 subgroup (n 40) were treated with laser surgery, therefore we did not perform a comparative statistical analysis on this group.

Table 5 Outcomes for glottic T1b and T2

	Laser surgery ($n = 17$)	Radiotherapy ($n = 102$)	p
Local recurrence	4	14	0.288
Mean time to recurrence ± SD (months)	20 ± 16	18 ± 16	
Local control (with initial treatment modality)	14	89	
5-years local control	78 %	80 %	0.310
Larynx preservation	15	88	
5-year larynx preservation	67 %	75 %	0.097
Disease specific survival	16	96	
5-year disease specific survival	100 %	91 %	0.980
Overall survival	14	77	
5-year overall survival	85 %	81 %	0.885

Discussion

Several treatment options are currently available for early laryngeal cancer and the optimal treatment is still under debate [27]. In this retrospective study, we compared tumour outcomes and voice quality in patients with Tis-T2 glottic larynx carcinoma treated with radiotherapy or CO_2-laser surgery to analyse the results of these treatment modalities.

For the whole study population it appears that larynx preservation, disease-specific survival and overall survival are less favourable in the radiotherapy group than the CO_2 laser surgery group. Larynx preservation is significantly better in patients treated with laser surgery, 93 versus 83 % ($p < 0.05$). Although literature points out that larynx preservation is higher in patients treated with laser surgery, we also think that this is influenced by the selection bias in our study; more advanced tumours were treated with radiotherapy [15, 19]. The recurrence and mortality rates found in our study are in accordance with those reported in other studies, with the exception of the recurrence rates regarding carcinoma in situ treated with laser surgery. Our finding that in 6 of the 24 patients local disease recurred within 5 years after treatment is high compared to reported recurrence rates [1, 2, 4, 19, 28]. Additional analysis reveals that in three out of six patients local disease recurred within 3 months after initial treatment. Due to this brief interval between treatment and relapse we suspect that resection margins influence our outcome. In all of these cases pathological assessment regarding surgical margins was inconclusive due to cauterization effects. We chose to monitor these patients by means of close follow-up instead of re-resection or treatment with radiotherapy. Examination of specimens resected with laser surgery is considered difficult [29]. Remacle et al. [30] investigated the reliability of frozen section and conclude that this is a reliable method to evaluate margin status. Although this assessment has drawbacks, in particular its time consuming nature, it can be considered in case of suspected irradical resection. The oncologic outcome in this study confirms that laser surgery is a safe technique in T1a and a selection of T1b glottic tumours. In this study, no modality was superior oncologically. Ample evidence is available about the similar effectiveness of laser surgery and radiotherapy

Table 6 Quality of voice in patients with glottic localisation

Tumour stage	Questionnaire	Laser surgery	Radiotherapy	*p*
Tis ($n = 13$)		($n = 13$)		
	VHI, mean ± SD (range)	10.6 ± 6.1 (0–20)	–	–
	five-item	31 %	–	–
T1a ($n = 67$)		($n = 36$)	($n = 31$)	
	VHI, mean ± SD (range)	12.0 ± 9.9 (0–28)	7.9 ± 7.5 (0–24)	0.06
	five-item	33 %	23 %	0.330
T1b ($n = 22$)		($n = 8$)	($n = 14$)	
	VHI, mean ± SD (range)	16.7 ± 9.0 (0–26)	4.9 ± 6.6 (0–21)	0.003
	five-item	75 %	7 %	0.001
T2 ($n = 40$)		($n = 2$)	($n = 38$)	
	VHI, mean ± SD (range)	10.0 ± 4.2 (7–13)	9.9 ± 8.0 (0–30)	–
	five-item	0 %	29 %	–
Total ($n = 142$)		($n = 59$)	($n = 83$)	
	VHI, mean ± SD (range)	12.4 ± 8.9 (0–28)	8.3 ± 7.7 (0–30)	0.005
	five-item	37 %	23 %	0.0 62

* Median time to voice evaluation; laser surgery 51 months, radiotherapy 66 months (p 0.02)

as treatment for T1a larynx carcinomas [3, 11–13, 15–18, 28, 31]. Also for T1b and T2 carcinomas similar results can be obtained using either radiotherapy or laser surgery [32–35]. Peretti et al. [36] evaluated clinical outcomes of laser surgery in 595 patients with glottic tumours stage T1–3, revealing a local control of respectively 86 and 72 % in the T2 and T3 group. Laryngeal preservation was 95 and 73 % in the T2 and T3 group. In general it can be stated that local control of laser surgery is comparable to radiotherapy [34, 37, 38], although some studies report higher local control with laser surgery [19]. As laser surgery can be repeated and radiotherapy can be kept in reserve, in most reports the organ preservation rate is better when using CO_2 laser [39]. Laser surgery as treatment for T1b and T2 carcinoma is incidental in our institute; therefore no conclusions can be extracted from the data comparing these treatment modalities. However, we can conclude that radiotherapy is an effective method in these patients and CO_2 laser can be used in selected cases.

In this study, quality of voice after treatment was analysed by means of the "physical subscale" of the voice handicap index (VHI) [26] and a five-item questionnaire designed by van Gogh et al. [24]. Because patients were contacted by telephone, we chose to restrict the interview to the two questionnaires. This enabled us to restrain the duration of the interview and thereby reduce the threshold for patients to participate. Secondly we decided to refrain ourselves from an observer assessment of quality of voice by a research tool as GRBAS as we feared that the distortion of the sound produced by the telephone transmission could influence this assessment. The analysis resulted in a significantly higher score on the "physical subscale" of the VHI in the group treated with laser surgery, reflecting a worse outcome for voice quality. This group also had a poorer outcome in the five-item questionnaire with borderline significance. Analysis per tumour stage showed that this was mainly caused by the T1b patients, as the scores in the T1a group did not differ significantly. However, one should consider that in deeply infiltrative T1a lesions, we generally opted for radiotherapy. Several studies addressed the issue of voice quality in patients treated with laser surgery or radiotherapy. Our search revealed one meta-analysis and a large number of retrospective studies. In the article of Peeters et al., also discussed in the meta-analysis of Cohen et al., a significantly better VHI score was found in patients with glottic T1a tumours treated with laser surgery as compared to radiotherapy [20, 25]. However, in this study, mainly very superficial T1a glottic carcinomas were treated. The majority of articles addressing this issue conclude that voice outcomes do not differ (significantly) between both treatment modalities. The most recent one of Sjögren et al. found no difference in voice outcome after laser surgery and radiotherapy when using perceptual (VHI), acoustic (GRBAS), aerodynamic and subjective examinations such as videostroboscopy in patients with glottic T1a laryngeal carcinoma [40]. Cohen et al. conclude in their meta-analysis of six retrospective studies that both treatment modalities offer comparable VHI scores for patients with T1 glottic carcinoma [20]. Five other studies also conclude that outcomes are comparable or not significantly different [4, 24, 41–43]. Tamura et al. found an increased fundamental frequency and air flow rate in patients with glottic T1a carcinoma treated with laser surgery, however this difference was not significant [42]. Van Gogh et al. found higher voice impairment after radiotherapy when using a self-designed five-item questionnaire; however this difference was not significant either [24]. Three other studies conclude that quality of voice, when analysing acoustic (GRBAS) and/or perceptual

(VHI) outcomes in patients with T1 (a) glottic carcinoma, is significantly better when patients are treated with radiotherapy [22, 23, 44].

A crucial point when comparing outcomes after laser surgery and radiotherapy is that all studies are retrospective and treatment allocation is not random. Analysis of quality of voice is influenced by treatment selection biases. In general, as in our study, radiotherapy is used more frequently in more extensive tumours. Peretti et al. showed that mean VHI scores doubled when resection included more than the superficial vocalis muscle [45]. In this study, the major contributor to inferior voice quality in the laser group is the group with tumour stage T1b. This confirms that a more extensive resection influences quality of voice negatively.

Conclusion

Oncological outcomes of both laser surgery and radiotherapy are similar in T1a laryngeal cancer. Larynx preservation is preferable in patients initially treated with laser surgery. The numbers in this study are too small to allow any conclusions on oncological outcomes in stage T1b laryngeal cancer, although we believe laser surgery can be a safe procedure in selected cases. In treatment choice therefore other considerations play an important role. Apart from treatment duration, costs and toxicity, for glottic cancer, the estimated voice outcome is the most important issue. According to subjective voice analysis outcomes were comparable in T1a lesions. For T1b lesions patients treated with laser surgery had a significantly higher percentage of voice deficiency. Therefore patients with deeply infiltrative T1a lesions and T1b lesions should be made aware that their voice quality might be worse when a laser resection is carried out.

Conflict of interest The authors have no conflict of interest.

Appendix 1

See Tables 7 and 8.

Table 7 Overview of five-item questionnaire (designed by VUmc: Amsterdam, The Netherlands)

Question	Answer											
1. Does your voice sound deviant (e.g. breathy or rough)?	Very much	1	2	3	4	5	6	7	8	9	10	Not at all
2. Do you encounter problems holding conversation due to your voice?	Very much	1	2	3	4	5	6	7	8	9	10	Not at all
3. Do you encounter problems making a telephone call due to your voice?	Very much	1	2	3	4	5	6	7	8	9	10	Not at all
4. Do you encounter problems shouting?	Very much	1	2	3	4	5	6	7	8	9	10	Not at all
5. Do you have to strain to produce voice?	Very much	1	2	3	4	5	6	7	8	9	10	Not at all

Overall voice impairment: >1 question answered with or below 5

Table 8 Overview of voice handicap index (VHI) questionnaire, physical subscale

Question	Answer
1. I run out of air when I talk	Normal/mild/moderate/severe
2. The sound of my voice varies throughout the day	Normal/mild/moderate/severe
3. People ask, "what is wrong with your voice"?	Normal/mild/moderate/severe
4. My voice sounds creaky and dry	Normal/mild/moderate/severe
5. I feel as though I have to strain to produce voice	Normal/mild/moderate/severe
6. The clarity of my voice is unpredictable	Normal/mild/moderate/severe
7. I try to change my voice to sound different	Normal/mild/moderate/severe
8. I use a great deal of effort to speak	Normal/mild/moderate/severe
9. My voice is worse in the evening	Normal/mild/moderate/severe
10. My voice "gives out" in the middle of speaking	Normal/mild/moderate/severe

Normal: 1 point, mild: 2 points, moderate: 3 points, severe: 4 points (total: 40 points)

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