ORIGINAL ARTICLE

Taylor&Francis healthsciences

# Voice Quality after Treatment for T1a Glottic Carcinoma

## *Radiotherapy Versus Laser Cordectomy*

Marco Krengli, Mario Policarpo, Irene Manfredda, Paolo Aluffi, Giuseppina Gambaro, Massimiliano Panella and Francesco Pia

From the Division of Radiotherapy (M. Krengli, I. Manfredda, G. Gambaro), Division of ENT (M. Policarpo, P. Aluffi, F. Pia), and Section of Public Health (M. Panella), University of Piemonte Orientale 'Amedeo Avogadro' and Azienda Ospedaliera 'Maggiore della Carità', Novara, Italy

Correspondence to: Prof. Marco Krengli, Divisione di Radioterapia, Università degli Studi del Piemonte Orientale 'Amedeo Avogadro', Azienda Ospedaliera 'Maggiore della Carità', Corso Mazzini 18, 28100 Novara, Italy. Tel: +39-0321-3733424. Fax: +39-0321-3733698. E-mail: krengli@tera.it

Acta Oncologica Vol. 43, No. 3, pp. 284–289, 2004

The purpose of this study was to assess the anatomic and functional outcomes and compare the voice quality in patients affected by T1a glottic carcinoma treated with curative intent with radiotherapy or laser cordectomy. Fifty-seven cases were analysed: 27 after curative radiotherapy and 30 after laser cordectomy. All patients were studied with videolaryngostroboscopy, voice analysis by narrow spectrogram, and vocal parameters (Jitter, Shimmer, noise/harmonic ratio, and diplophonia). Videolaryngostroboscopy showed severe glottic inadequacy in 25% of cases treated with radiation and insufficient compensation 'ventricular band' or 'with arytenoid hyperadduction' in 65% of cases after surgery. Severe dysphonia on the electro-acoustic analysis of voice was observed in 25% of cases after radiation and 70% after laser ($p < 0.001$). Fundamental frequency and vocal parameters showed more favourable results in the radiation group ($p < 0.001$). Voice assessment showed better results after radiotherapy compared with laser cordectomy. Voice outcome should be carefully considered in the treatment decision for T1 glottic carcinoma.

*Received 2 June 2003*
*Accepted 9 January 2004*

Radiotherapy and surgical cordectomy are considered the two standard options in the treatment of T1a glottic carcinoma. The results in terms of local control and survival are very similar, especially taking into consideration salvage therapy (1, 2). During recent decades, both techniques have changed substantially: radiotherapy has considerably improved due to implementation of 3D treatment plans based on detailed imaging study and surgery has become more conservative thanks to a laser $CO_2$ technique that allows the use of an endoscopic approach and avoids large resections, with a lower incidence of intra- and postoperative complications. The costs of the two treatment modalities have been compared with non-univocal results probably related to the different reimbursement systems in the various countries (3). Therefore, the treatment decision should be taken after comprehensive informed consent by the patient considering carefully all the aspects including the functional long-term results of the two different approaches. This study aims to assess the anatomic and functional outcomes and compare the voice quality in patients affected by T1a glottic carcinoma treated with curative intent with 3D radiotherapy or laser cordectomy.

## MATERIAL AND METHODS

From 1990 to 2001, 202 patients were treated for T1 glottic carcinoma in our institution: 80 with radiotherapy and 122 with laser cordectomy. This study included a group of 57 patients, 55 male and 2 female, aged from 55 to 81 (median 62.5) affected by histologically proven T1a glottic carcinoma with no tumour recurrence who agreed to undergo examinations for voice evaluation (Table 1). No patient was a professional voice user. All cases were discussed by a multidisciplinary team including an ENT surgeon and a radiation oncologist and the patients received complete information about the two treatment options in terms of potential results and possible side effects. The treatment was curative radiotherapy in 27 patients and $CO_2$ laser cordectomy in 30.

Radiotherapy was performed by using 6 MV or $^{60}Co$ photons. All patients were immobilized with a headrest and customized thermoplastic masks. The treatment plan was studied on a single CT slice with 2D dose calculation until 1998 and with contiguous CT slices of 5 mm thickness with a 3D convolution algorithm since 1999. For 3D study, the

 ISSN 0284-186X
DOI: 10.1080/02841860410026233

**Table 1**

*Characteristics of patients with voice assessment*

| | Radiotherapy | Laser cordectomy |
|---|---|---|
| No. of patients | 27 | 30 |
| M/F | 26/1 | 29/1 |
| Age | 55–81 (median 69) | 56–80 (median 67.5) |
| Follow-up | 24–120 months (median 60) | 24–120 months (median 62) |

clinical target volume (CTV) was defined as the ipsilateral cord from the anterior commissural to the arytenoid; the spinal cord was drawn in all the slices included in the treatment volume plus a 2 cm margin. Two oblique wedged beams were used; the size varied from $5 \times 5$ cm to $6 \times 6$ cm and the angle was chosen based on the size and location of the CTV. Attention was paid to avoid the spinal cord at the exit of the beams whenever possible. The dose was prescribed to the ICRU point and ranged from 66 to 70 Gy. Conventional fractionation of 1.8–2.0 Gy was used. DVHs for CTV and spinal cord were obtained for the 3D treatment plans. Surgery consisted in $CO_2$ laser cordectomy. Following the 'Nomenclature Committee of the European Laryngological Society' (4), the surgical procedures were classified as type III in 10 cases and type IV in 20 (Table 2).

No patient had speech re-education. All patients received assessment of voice 24–120 months (median 62) after radiation or surgical treatment. The anatomic and functional results including phonatory compensation were studied by videolaryngostroboscopy using the video software Mediastrobo. The voice and the vocal parameters were recorded and analysed by using MDVP4003 and CSL50 (Kay). The Narrow spectrogram was performed based on the Yanagihara classification (5). The fundamental frequency (F0) reflecting the vocal cord vibration during phonation was calculated in Hz. The following vocal parameters were obtained and analysed: microperturbation of frequency (Jitter: normal value 1.06%) and intensity (Shimmer: normal value 3.18%) during the vibration of the vocal cord, noise/harmonic ratio reflecting the amount of noise in the voice (NHR: normal value 0.19), and degree of sub-harmonics (diplophonia). The Narrow spectrogram was based on the pronunciation of the Italian word 'AIUOLE' and the vocal analysis was performed by pronunciation of 'A' for at least 3 seconds.

**Table 2**

*Classification of endoscopic cordectomies proposed by the European Laryngological Society Working Committee (4)*

| Type of cordectomy | Extension of cordectomy |
|---|---|
| Subepithelial cordectomy (type I) | Superficial layer of lamina propria |
| Subligamental cordectomy (type II) | Superficial portion of vocal muscle |
| Transmuscolar cordectomy (type III) | Medial portion of vocal muscle |
| Total cordectomy (type IV) | Inner perichondrium of thyroid lamina |
| Extended cordectomy (type V) | Surrounding laryngeal areas |

Discrete variables were expressed as percentage (95% confidence levels [$CL_{95\%}$]), continuous variables as means ($CL_{95\%}$). The normality of the distribution for quantitative variables was verified with the Shapiro–Wilks test. The comparison between the two groups of patients was performed by statistic analysis using the Student's $t$-test or the Mann–Whitney U-test for quantitative variables, and the $\chi^2$ test or Fisher's exact test for qualitative variables. We used two-sided tests. We considered p-values of $< 0.05$ significant, and p-values of $< 0.01$ strongly significant. Statistical analysis was performed with Statistica software (STASOFT).

## RESULTS

Local control was obtained in 91.2% of the patients treated with radiotherapy and 95.9% of those who underwent laser cordectomy. Recurrent disease was observed in 7/80 (8.8%) cases after radiotherapy and 5/122 (4.1%) after surgery. Salvage therapy consisting in total laryngectomy obtained local control in 4/7 patients primarily treated with radiation and in 5/5 treated with laser cordectomy.

The anatomic and functional results are strictly related to the treatment modality and consequently the parameters are different after radiotherapy and surgery. In this case, no direct comparison can be made between the two treatments. The functional assessment by videolaryngostroboscopy in the group of 27 patients treated with radiotherapy showed reduction of the mucosal cord wave in 80.5% ($CL_{95\%}$: 72.2–90.1%) of cases and severe glottic inadequacy during phonation in 25.9% ($CL_{95\%}$: 15.5–36.3%). This finding was observed not only at the level of the vocal cord affected by the tumour but also in the contralateral cord. The phonatory compensation was normal in all cases. After surgery, videolaryngostroboscopy allowed documentation of both anatomic and functional outcomes. As far as the anatomic results are concerned, a satisfactory 'well shaped' fibrotic neocord was observed in all 10 patients who underwent type III cordectomy, while an insufficient neocord was evident in the 20 cases treated with type IV with fixity of the ipsilateral arytenoid in 3 patients. The phonatory compensation was related to the surgical outcome: 'cord-neocordal' in the cases treated with type III cordectomy, and 'ventricular band' or 'with arytenoid hyperadduction' after type IV cordectomy. The electroacoustic analysis of voice detected moderate–severe dysphonia (type II–III of Yanagihara) in 74.1% ($CL_{95\%}$: 63.7–84.5%) of patients after radiotherapy and 30.0%

($CL_{95\%}$: 19.1–40.9%) after laser cordectomy; severe dysphonia (type IV of Yanagihara) was observed in 70.0% ($CL_{95\%}$: 59.1–80.9%) of cases after surgery and only in 25.9% ($CL_{95\%}$: 15.5–36.3%) after radiation (Fig. 1). This difference between the two treatment groups was statistically significant ($p < 0.001$). The mean value of the fundamental frequency (F0) was 167.8 Hz ($CL_{95\%}$: 147.8–187.8 Hz) after radiotherapy and 134.5 Hz ($CL_{95\%}$: 122.6–146.5 Hz) after laser cordectomy ($p < 0.01$). The mean values of the vocal parameters for the two groups of patients were as follow: Jitter 5.9% ($CL_{95\%}$: 3.8–7.9%), Shimmer 12.2% ($CL_{95\%}$: 10.2–12.3%), NHR 0.34 ($CL_{95\%}$: 0.3–0.4) after cordectomy and Jitter 2.3% ($CL_{95\%}$: 1.8–2.8%), Shimmer 8.0% ($CL_{95\%}$: 6.5–9.6%), NHR 0.2 ($CL_{95\%}$: 0.2–0.2) after radiotherapy (Figs. 2,3,4). This difference of results between the two groups was statistically significant ($p < 0.001$) for all 3 parameters with more favourable values for the radiation group. No significant difference was observed for diplophonia that occurred in 18.5% ($CL_{95\%}$: 9.3–27.7%) of patients treated with radiotherapy and in 23.3% ($CL_{95\%}$: 13.3–33.4%) of patients treated with laser cordectomy.

## DISCUSSION

Radiotherapy has a recognized role in cancer therapy as conservative treatment that can preserve anatomy and organ function in various areas of the body. As a matter of fact, literature data document the superiority of radiation therapy in the preservation of vocal function in laryngeal cancer at an early stage when compared with surgical cordectomy with external approach (1). During recent decades, the anatomic and functional outcomes of surgery have substantially improved due to the implementation of laser cordectomy, which replaced the conventional surgical approach in the treatment of T1 glottic carcinoma (2, 3, 6–8).

Our series comparing radiotherapy with $CO_2$ laser cordectomy includes 57 cases and represents one of the largest series in the literature. The two groups were comparable for patient and tumour characteristics in respect of gender, age, and stage. All patients completed the planned treatment with excellent compliance. The results in terms of local control observed in the present

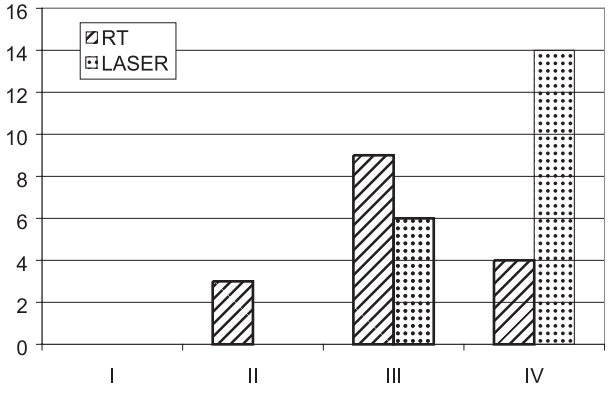


*Fig. 1.* Electroacoustic analysis of voice based on Yanagihara classification after radiotherapy and laser cordectomy; the advantage for the irradiated group was statistically significant ($p < 0.001$).

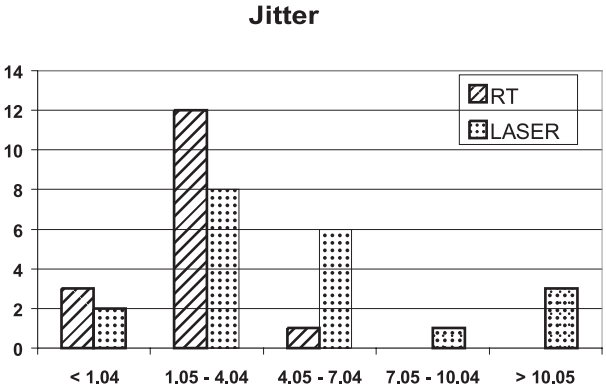


*Fig. 2.* Values of Jitter for the two treatment groups. The difference was statistically significant ($p < 0.001$) with more favourable results for the irradiated patients.

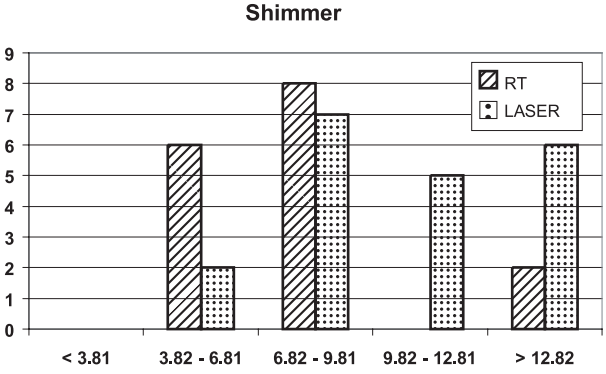


*Fig. 3.* Values of Shimmer for the two treatment groups. The difference was statistically significant ($p < 0.001$) with more favourable results for the irradiated patients.

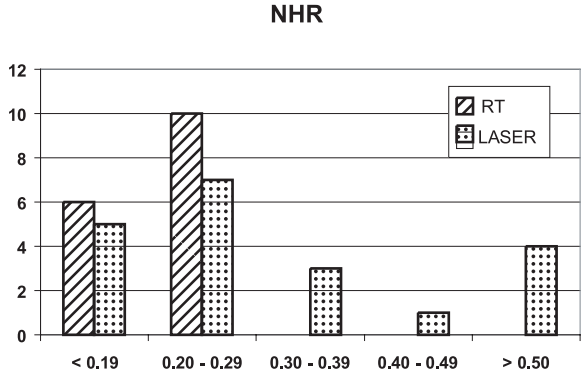


*Fig. 4.* Values of NHR (noise/harmonic ratio) for the two treatment groups. The difference was statistically significant ($p < 0.001$) with more favourable results for the irradiated patients.

series did not substantially differ from those reported in the literature (1–3, 8–10) and also in our experience the results of salvage laryngectomy after local recurrence were less effective when the first-line treatment consisted in radiotherapy as reported by Markou et al. (11). Anatomic and functional outcome and voice quality were studied after follow-up $>2$ years to be sure that the post-treatment changes were stabilized. In fact, literature data suggest that 6–12 months after radiotherapy and 6–24 months after surgery no changes in voice quality are expected (6, 7, 12).

Many studies in the literature on subjective evaluation by patients themselves and voice experts showed non-univocal results (7, 13, 14). Delsupehe et al. (7) and McGuirt et al. (13) reported no difference after radiotherapy or laser surgery while Rydell et al. (14) found better results in the irradiated group. Various studies reporting patients' and doctors' subjective feelings refer to satisfactory or normal voice in 75–90% of irradiated patients with T1–T2 tumours (15–17).

In our study, the assessment of voice was performed by videostroboscopic analysis of anatomic and functional outcome and spectrographic evaluation including the classic narrow spectrogram and a number of digital parameters. Subjective evaluation by experienced voice listeners was not accomplished in the present analysis but could be included in a future study.

Videolaryngostroboscopy showed significant changes in the mucosal cord wave in the majority of irradiated patients (81%) and phonatory glottic inadequacy in one-quarter of cases. These findings are in accordance with other data in the literature (12, 18–20): stiff mucosa wave dynamics, hyperventricular fold activity, chronic inflammation, fold tissue inelasticity, and glottal incompetence were observed after radiotherapy (12) and irregularities in the vibration of the vocal fold in two-thirds of irradiated patients (18). The more pronounced glottic wave after radiotherapy was observed in our experience in both vocal cords, as reported by Wedman et al. (21). Large tumours, pre-radiation stripping and high dose as well as old age and smoking after treatment are reported as risk factors (15, 20, 22). After laser surgery, the best results at videolaryngostroboscopy with neocord compensation were observed in cases with a more conservative resection (type III) in comparison with cases with a more extended surgical approach (type IV) in which the compensation was clearly pathologic with a ventricular band and arytenoid hyperadduction. Similar data were reported by other authors and support the observation that the functional outcome is related to the extension of the local resection in depth. In particular the extension of resection to a part or all of the vocal muscle seems to be the crucial point: better results are obtained with type I or II, intermediate with type III, and less favourable with type IV resection of the European Laryngological Society classification (4, 6, 23).

In our experience, the comparison between the two groups treated with radiotherapy or laser surgery was based on the electroacoustic analysis of voice. Significantly more favourable results for dysphonia (Yanagihara), F0, Jitter, Shimmer, and NHR were observed in the irradiated patients. The data reported in the literature after radiotherapy are non-univocal: F0 and Jitter were the parameters that changed most for Verdonck-de Leeuw et al. (20); Rovirosa et al. (12) found F0, Jitter, Shimmer, and NHR higher in comparison with a non-irradiated control group; Lehman et al. (24) and Honocodeevar-Boltezar and Zargi (25) did not observe any change in F0 after radiation while Stoicheff et al. (16) described a decrease in F0 due to oedema of the mucosa, and Dagli et al. (26) an increase in F0 related to stiffness secondary to fibrosis of the vocal fold. Aref et al. (27) found alteration of F0, Jitter, Shimmer, and NHR after radiation. A possible reason for these apparently contradictory findings could be the inhomogeneity of the series, the different doses, and the time of follow-up. As far as laser surgery is concerned, Peretti et al. (23) found statistically significant difference in the distribution of values of Jitter, Shimmer, and NHR between the treated group and the control group of untreated patients only for types III, IV, and V and not for I–II cordectomy.

A number of studies comparing voice quality after radiotherapy and laser cordectomy are available in the literature, again with non-univocal results (Table 3). The first comparison was made by Hirano et al. (18) who found no objective differences between the two treatment modalities in intensity of phonation and maximum phonation time; however, results could be influenced by the fact that 50% of patients treated by laser received also radiotherapy. McGuirt et al. (13) failed to find significant differences for various parameters such as F0, Jitter, Yanagihara types, and mucosal wave irregularities comparing intermediate dose radiotherapy (63 Gy, 28 fractions) and laser surgery with conservation of at least half of the vocal fold in 24 patients. Rydell et al. (14) observed a better quality of voice after radiation (64 Gy, 32 fractions) in comparison with laser for breathiness, Jitter, and F0 but no difference for NHR and Shimmer. Similar results were reported by Elner and Fex (28) and Epstein et al. (9) using subjective parameters. Rosier et al. (10) observed no significant difference in a blinded study with a trend for better results in the radiotherapy group. Delsupehe et al. (7) found no difference in subjective analysis of voice and F0 6 months after radiotherapy with total dose of 64 Gy and 24 months after laser surgery. More recently, Wedman et al. (21) reported no difference in objective and subjective analysis of voice in 24 cases of T1a glottic cancer treated with radiotherapy or endoscopic laser surgery.

In conclusion, voice assessment with electroacoustic analysis by Narrow spectrogram and vocal parameters in our experience showed significant advantage in the group of

**Table 3**

*Studies of the literature on comparison between radiotherapy and laser cordectomy for T1a glottic carcinoma*

| Author | No. of patients | Advantage with RT | Advantage with laser | No difference |
|---|---|---|---|---|
| Hirano, 1985 | 31 | | | X |
| Elner, 1988 | 31 | X | | |
| Epstein, 1990 | 60 | X | | |
| McGuirt, 1994 | 34 | | | X |
| Rydell, 1995 | 36 | X | | |
| Rosier, 1998 | 18 | | | X |
| Delsupehe, 1999 | 42 | | | X |
| Wedman, 2002 | 24 | | | X |
| Present series | 57 | X | | |

patients treated by radiotherapy in comparison with those treated by laser cordectomy. In the surgical group, the more conservative approach (type III vs. type IV of the European Laryngological Society classification) (4) led to better anatomic and functional outcome.

Based on these results and the other data in the literature, the voice outcome should always be carefully considered in the decision on treatment modality for T1 glottic carcinoma.

## REFERENCES


1. Mendenhall WM, Parsons JT, Stringer ST, Cassisi NJ, Million RR. T1-T2 vocal cord carcinoma: a basis for comparing the results of radiotherapy and surgery. Head and Neck Surg 1988; 10: 373–7.
2. Spector JG, Session DG, Chao KS, et al. Stage I (t1 N0 M0) squamous cell carcinoma of the laryngeal glottis: therapeutic results and voice preservation. Head Neck 1999; 21: 707–17.
3. Luescher MS, Pedersen U, Johansen LV. Treatment outcome after laser excision of early glottic squamous cell carcinoma; a literature survey. Acta Oncol 2001; 40: 796–800.
4. Remacle M, Eckel HE, Antonelli A, et al. Endoscopic cordectomy. A proposal for a classification by the Working Committee, European Laryngological Society. Eur Arch Otorhinolaryngol 2000; 257: 227–31.
5. Yanagihara N. Significance of harmonic changes and noise components in hoarseness. J Speech Hear Res 1967; 10: 531–41.
6. Sittel C, Eckel HE, Eschenburg C. Phonatory results after laser surgery for glottic carcinoma. Otolaryngol Head Neck Surg 1988; 119: 418–24.
7. Delsupehe KG, Zink I, Lejaegere M, Bastian RW. Voice quality after narrow-margin laser cordectomy compared with laryngeal irradiation. Otolaryngol Head Neck Surg 1999; 121: 528–33.
8. Zeitels SM, Hillman RE, Franco RA, Bunting GW. Voice and treatment outcome from phonosurgical management of early glottic cancer. Ann Otol Rhinol Laryngol Suppl 2002; 190: 3–20.
9. Epstein BE, Lee DJ, Kashima H, Johns ME. Stage I glottic carcinoma: results of radiation therapy or laser excision. Radiology 1990; 175: 567–70.
10. Rosier JF, Gregoire V, Counoy H, et al. Comparison of external radiotherapy, laser microsurgery and partial laryngectomy for the treatment of T1N0M0 glottic carcinomas: a retrospective evaluation. Radiother Oncol 1998; 48: 175–83.
11. Markou K, Nikolaou A, Nalbadian M, Petridis D, Nicolaidis V, Daniilidis I. How often is total laryngectomy necessary for the treatment of T1 failures after radiotherapy or cordectomy? Eur Arch Otorhinolaryngol 2002; 259: 4–10.
12. Rovirosa A, Martinez-Celdran E, Ortega A, et al. Acoustic analysis after radiotherapy in T1 vocal cord carcinoma: a new approach to the analysis of voice quality. Int J Radiat Oncol Biol Phys 2000; 47: 73–9.
13. McGuirt WF, Blalock D, Koufman JA, et al. Comparative voice results after laser resection or irradiation of T1 vocal cord carcinoma. Arch Otolaryngol Head Neck Surg 1994; 120: 951–5.
14. Rydell R, Schalen L, Fex S, Elner A. Voice evaluation before and after laser excision vs. radiotherapy of T1A glottic carcinoma. Acta Otolaryngol 1995; 115: 560–5.
15. Karim AB, Snow GB, Siek HT, Njo KH. The quality of voice in patients irradiated for laryngeal carcinoma. Cancer 1983; 51: 47–9.
16. Stoicheff ML, Ciampi A, Passi JE, Fredrickson JM. The irradiated larynx and voice: a perceptual study. J Speech Hearing Res 1983; 26: 482–5.
17. Morgan DA, Robinson HF, Marsh L, Bradley PJ. Vocal quality 10 years after radiotherapy for early glottic cancer. Clin Radiol 1988; 39: 295–6.
18. Hirano M, Hirade Y, Kaawasaki H. Vocal function following carbon dioxide laser surgery for glottic carcinoma. Ann Otol Rhinol Laryngol 1985; 94: 232–5.
19. Harrison LB, Solomon B, Miller S, Fass DE, Armstrong J, Sessions RB. Prospective computer-assisted voice analysis for patients with early stage glottic cancer: a preliminary report of the functional result of laryngeal irradiation. Int J Radiat Oncol Biol Phys 1990; 19: 123–7.
20. Verdonck-de Leeuw IM, Hilgers FJ, Keus RB, et al. Multidimensional assessment of voice characteristics after radiotherapy for early glottic cancer. Laryngoscope 1999; 109: 241–8.
21. Wedman J, Heidmal JH, Elstad I, Olofsson J. Voice results in patients with T1a glottic cancer treated by radiotherapy or endoscopic measures. Eur Arch Otorhinolaryngol 2002; 259: 547–50.
22. Benninger MS, Gillen J, Thieme P, Jacobson B, Dragovich J. Factors associated with recurrence and voice quality following radiation therapy for T1 and T2 glottic carcinomas. Laryngoscope 1994; 104: 294–8.

23. Peretti G, Piazza C, Balzanelli C, Cantarella G, Nicolai P. Vocal outcome after endoscopic cordectomies for Tis and T1 glottic carcinomas. Ann Otol Rhinol Laryngol 2003; 112: 174–9.
24. Lehman J, Bless D, Brandeburg J. An objective assessment of voice production after radiation therapy for stage I squamous cell carcinoma of the glottis. Otolaryngol Head Neck Surg 1998; 98: 121–9.
25. Honocodeevar-Boltezar I, Zargi M. Voice quality after radiation therapy for early glottic cancer. Arch Otolaryngol Head Neck Surg 2000; 126: 1097–100.
26. Dagli AS, Mahieu HF, Festen JM. Quantitative analysis of voice quality in early glottic laryngeal carcinomas treated with radiotherapy. Eur Arch Otorhinolaryngol 1997; 254: 78–80.
27. Aref A, Dworkin J, Devi S, Denton L, Fontanesi J. Objective evaluation of the quality of voice following radiation therapy for T1 glottic cancer. Radiother Oncol 1997; 45: 149–53.
28. Elner A, Fex S. Carbon dioxide laser as primary treatment of glottic Tis and T1a tumours. Acta Otolaryngol Suppl 1988; 449: 135–9.