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ORIGINAL ARTICLE

The predictive value of videostroboscopy in the assessment of premalignant lesions and early glottis cancers

A. Rzepakowska[1], E. Sielska-Badurek[1], E. Osuch-Wójcikiewicz[1], M. Sobol[2], K. Niemczyk[1]

[1] Department of Otolaryngology, Medical University of Warsaw
[2] Department of Biophysics and Human Physiology, Medical University of Warsaw

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ABSTRACT:

Objective: To assess the sensitivity and specificity of larngovideostroboscopy (LVS) in the diagnosis of precancerous and malignant lesions of the vocal folds.

Material and methods: In 175 patients (128 men and 47 women), aged 19-88 years, mean age 61.5, who were admitted to the clinic with diagnosed premalignant conditions of vocal fold mucosa (leukoplakia, chronic hypertrophic inflammatory lesions) and thickening or tumor on the vocal fold, there was performed LVS before the laryngeal microsurgery. The LVS study included: localization of the leasion, movement of the vocal folds, mucosal wave, shape of glottis clousure, amplitude and symmetry of vocal fold vibration. In the evaluation, a point scale was applied for the individual functional parameters. The scale ranged from 0 to 14. Patients with impaired vocal fold motion or absent mucosal wave were positive on LVS for malignant lesions. Those with limitted mucosal wave were positive on LVS for dysplastic lesions. The results were compared with the final histopathological examination and the sensitivity, specificity, accuracy, positive (PPV) and negative (NPV) predictive value were calculated.

Results: On the basis of histopathological examination, benign lesions (normal or inflammatory mucosa) accounted for 20% of diagnoses, hypertrophy and parakeratosis for 28%, low and middle grade dysplasia accounted for 10% and malignant lesions (high-grade dysplasia, pre-invasive cancer, Invasive cancer) were diagnosed in 42% of patients. The overall mean score for LVS was 4.5 and 8.0, respectively for benign and malignant lesions. Sensitivity, specificity, accuracy, PPV and NPV of LVS in detecting malignant lesions were respectively - 95.6%, 23.8%, 61.1%, 57.6% and 83.3% and in detecting both premalignant and malignant lesions were respectively – 90.7%, 31.4%, 78.9%, 84.1% and 45.8%.

Conclusions: Because of the high sensitivity of LVS in detecting precancerous and malignant lesions, this method is a very good tool for screening of pathology within the larynx.

KEYWORDS: laryngovideostroboscopy, precancerous lesions, larynx, glottis, early glottic cancer

INTRODUCTION

Most benign and precancerous lesions of the larynx are located on the vocal folds, and almost half of the malignant laryngeal tumors involve the glottis. Symptoms reported by patients and risk factors are very similar for benign, precancerous and malignant lesions, which makes clinical differentiation impossible [1]. Progression of benign to precancerous or malignant lesions is often observed. Diagnosis and distinguishing between benign, precancerous and malignant lesions at an early stage would make it possible to plan radical treatment during the first laryngeal microsurgery .

Currently, endoscopy of the larynx is routinely performed in patients with laryngeal pathology. Figure 1. Due to the anatomy of the vocal folds and a unique mechanism of phonatory vibrations, it is necessary to assess the vibration on stroboscopy in the case of pathology involving glottis. The first stroboscopic examination was conducted in 1878 by Oertel [2]. The image obtained during stroboscopy is, however, a virtual image of the vocal cord vibration adjusted to the image registration rate of the human retina (5 movements per second). The real frequency of vocal fold vibration is about 256 Hz in females and 120 Hz in males.

MATERIALS AND METHODS

The study included 175 patients (47F, 128M) aged 19 to 88, with the mean age of 61.5, who were referred to our department for directoscopy or laryngeal micsrosurgery due to the initial diagnosis of precancerous or malignant lesions of the glottis. The exclusion criteria included: diagnosis of benign lesions (Reinke's edema, polyps, nodules, cysts)and glottic tumors causing immobilization of the vocal fold on laryngoscopy examination with a mirror. In the studied population, 76 patients were diagnosed with vocal fold tumor, 45 – with leukoplakia, 34 – vocal fold hypertrophy, 10 – papilloma, and 5 patients were suspected of cancer recurrence following radiotherapy. Table 1

Tab. I. Demographical and clinical data of the studied patients.

Total number of patients; F/M	175; (47F, 128 M)
females; mean age; range	60,7±10,5; 62 (35–82)
males; mean age; range	61,8±11,0; 62,5 (19–88)
Clinical diagnosis	
Vocal fold tumor	76
leukoplakia	45
hypertrophy	39
papilloma	10
suspected recurrance, post-RTx	5

All patients were assessed preoperatively using laryngovideostroboscopy (LVS) (Xion Endo STROB E, Berlin, Germany) including assessment of mobility of the vocal folds, presence of mucosal wave, type of glottal closure during phonation, symmetry and amplitude of vibrations. The examination was conducted by two separate examiners with immense experience in stroboscopic evaluation. The lesion was classified as precancerous (expecting histopathological diagnosis of low- or middle-grade dysplasia), when the LVS examination revealed limited mucosal wave. As a criteria of malignancy in functional assessment of the glottis, we assumed impaired vocal mobility and/or the absence of mucousal wave. The evaluation of specific laryngeal functions was conducted using a clinical scale based on the proposition of the European Laryngological Society [3]. The point scale is presented in Table 2. The range was from 0 in patients with normal glottal function to 14 in patients with bilateral maximal impairment of the assessed parameters. The final diagnosis was made based on the pathology study results.

Tab. II. The laryngovideostroboscopy functional assessment with application of the score scale.

Vocal fold mobility	right	normal-0	limited -1	none -2
	left	normal-0	limited -1	none -2
Mucosal wave	right	present-0	limited -1	none -2
	left	present-0	limited -1	none -2
Glottic closure		longitudinal-0	posterior insufficiency -0	other insufficiency -1
Symmetry of vocal fold vibration		simultaneous-0	non-simultaneous-1	
Amplitude of vocal fold vibration	right	normal-0	decreased-1	none-2
	left	normal-0	decreased-1	none-2

Statistical analysis was conducted using Statistica12 package StatSoft, Dell Statistica Partner. The sensitivity, specificity, accuracy, positive and negative predictive values (PPV and NPV) of functional glottal assessment during LVS were assessed for differentiating malignant lesions. $P < 0.05$ was considered statistically significant. Continuous variables were compared using the non-parametric ANOVA test as well as the Wilcoxon matched pairs signed rank test with Bonferroni correction ($p = 0.017$). The Kruskal-Wallis H test was used to compare variables with non-normal distribution.

RESULTS

In the studied group, normal mucosa within the lesion was diagnosed in 13 patients (7.4%) based on the pathology study, inflammation of the mucosa – in 23 patients (13.1%), hyper- and parakeratosis – in 49 (28%), low-grade dysplasia – in 8 (4.5%), middle-grade dysplasia – 10 (6%), high-grade dysplasia – 12 (7%), carcinoma in situ – in 11 (6.3%) and invasive cancer – in 49 patients (28%). Despite normal vocal fold mobility on initial examination using a mirror, LVS revealed limited vocal cord mobility in 2 patients. Unfortunately, in 32 out of 175 patients (18%) the assessment of vocal fold function on LVS was impossible due to compensation mechanism such as vestibular fold phonation. In those patients, the evaluation of mucosal wave, symmetry and amplitude of vibration was impossible. The percentage of patients, in whom precise LVS evaluation was not possible, was higher in patients with dysplasia (20-25%), carcinoma in situ and invasive cancer (20-27%) compared to patients with benign lesions (4-18%). Table 3. For the rest of the patients, nor-

Tab. III. Percentage results of mucosal wave in LVS with respect to final histopathological diagnosis among all patients (n=175).

[%]	NORMAL MUCOSA N=13	INFLAMMATION N=23	HYPERTROPHY N=49	LOW-GRADE DYSPLASIA N=8	MIDDLE-GRADE DYSPLASIA N=10	HIGH-GRADE DYSPLASIA N=12	CARCINOMA IN SITU N=11	INVASIVE CANCER N=49
Mucosal wave								
present (%)	61,5	47	36,7	45	30	33,4	18,2	13,5
limited (%)	19,2	33,5	26,5	20	18,8	12,5	36,4	18,4
absent (%)	15,4	13	18,4	10	31,3	29,2	18,2	47,8
Impossible to assess (%)	3,9	6,5	18,4	25	19,9	24,9	27,2	20,3

Tab. IV. The results of LVS scores for respective histopathological diagnoses in 143 patients

	normal	Inflammation	hypertrophy	low-grade dysplasia	middle-grade dysplasia	high-grade dysplasia	carcinoma in situ	invasive cancer
LVS Mean ± SD	4,5 ±2,9	4,7 ±3,0	5,2 ±2,7	6,3 ±3,6	6,8 ±3,2	8,3 ±3,0	7,3 ±1,9	8,0 ±2,3
LVS median	4	5	5	6,5	6,5	7,5	7	8
LVS range	0–9	0–10	0–10	0–11	2–12	3–12	4–10	1–12

mal mucosal wave was more common in case of benign lesions (37-61%) compared to those with dysplasia (30-45%) and cancer (18-23%). However, the percentage of patients, in whom the mucosal wave was absent, was the highest in case of invasive cancer (48%) and in patients with middle- and high-degree dysplasia (29-31%).

The sensitivity of LVS in detecting dysplasia or invasive cancer was 90.7%, and the specificity was 31.4%. The accuracy of this method reached 78.9%, and the positive and negative predictive values were 84.1% and 45.8% respectively.

The sensitivity of LVS in detecting malignant lesions was 95.6%, and the specificity was 23.8%. The accuracy of this method reached 61.1%, and the positive and negative predictive values were 57.6% and 83.3% respectively.

Based on the clinical scale for LVS assessment, in 143 patients, in whom the evaluation of vocal fold vibration was possible, much higher cumulative scores were observed in case of dysplastic lesions and cancer (6.3-8.3) compared to benign lesions (4.5-5.2). Table 4. We applied Receiver Operatig Characteristics (ROC) curves to decide on the cut-off level of LVS scoring for optimal sensitivity and specificity, and we obtained the value of 3 for differentiation of benign and precancerous lesions, and the value of 6 for differentiation of hypertrophic and malignant lesions. Fig. 2 and 3.

DISCUSSION

Arens et al. proved that the thickness of vocal fold mucosa increases depending on its condition as follows: normal epithelium - 147μm, low-grade dysplasia – 258 μm, middle-grade dysplasia - 301 μm, carcinoma in situ 445 μm, invasive cancer – 974 μm [4]. The increased vocal fold thickness causes an increase in its size and affects vibration of the vocal folds. In our study, we observed a significantly higher rate of absent mucosal wave in patients with invasive glottal cancer (48%), middle- (31%) and high-grade dysplasia (29%) compared to benign lesions (13-15%). Djukic et al. presented similar results as to the absence of mucosal wave in precancerous and malignant lesions of the larynx: 15% in patients with hypertrophy, 38.5% in middle-grade dysplasia and 54.5% in high-degree dysplasia [5]. The high sensitivity of LVS confirms that this methods allows to correctly confirm early cancer in 95.6 % patients, however, the low specificity indicates that only in 23.8% of patients with glottic lesions it can be correctly excluded. In the literature, there are studies showing high sensitivity of LVS in identifying malignant lesions ranging from 86% to 100% [6-10]. Data concerning its specificity varies in the cited studies from 7% to 93% [6-10].

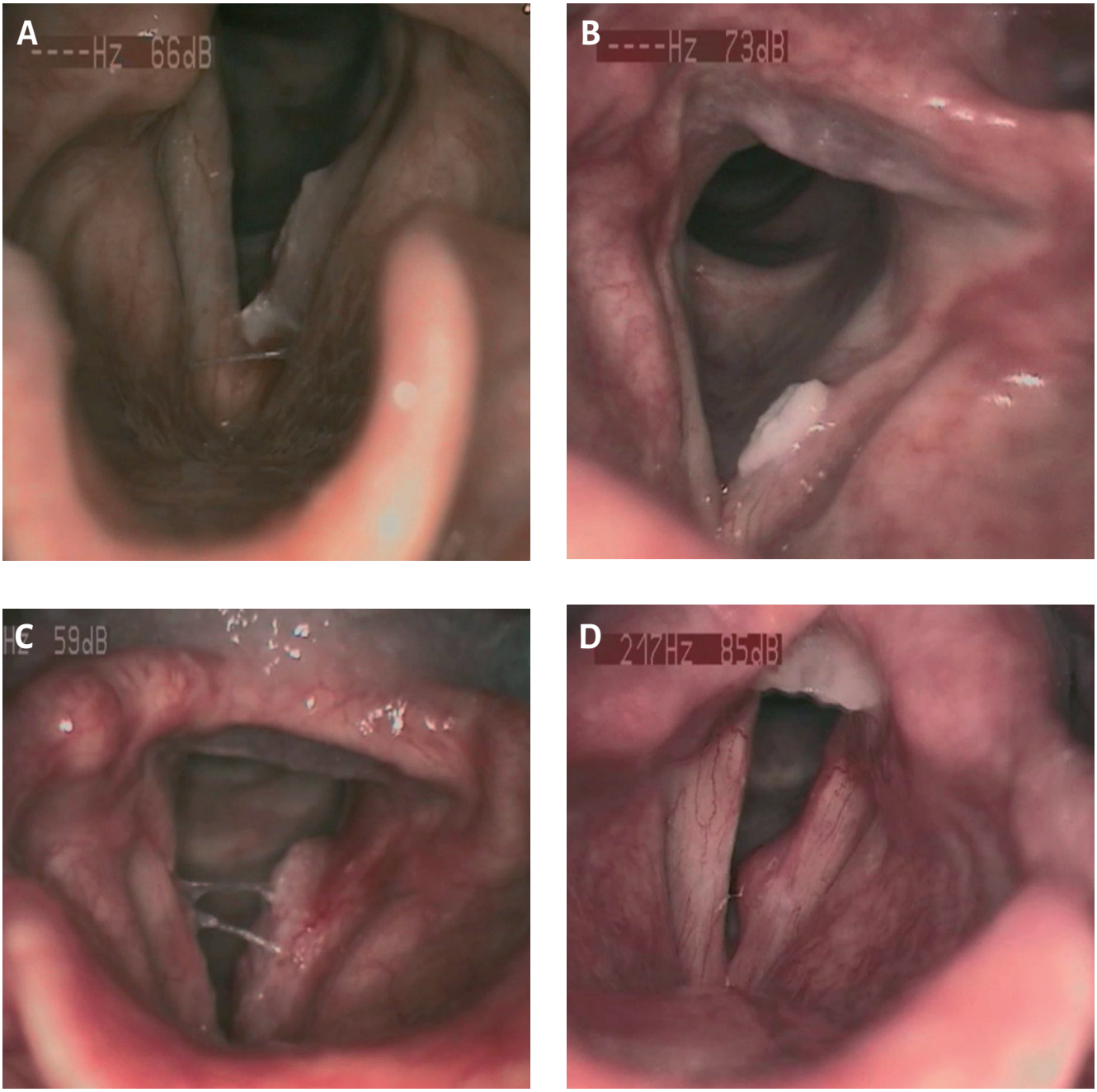

Fig. 1. Laryngovideostroboscopy images of different glottic lesions (histopathology results): 1a - parakeratosis, 1b – middle-grade dysplasia, 1c – invasive cancer, 1d – hyperplasia, interstitial edema.

One negative factor that limits the possibility of reliable use of functional assessment during LVS to distinguish malignant and precancerous lesions is the presence of laryngeal compensation mechanisms leading to phonatory vibration of structures located superiorly to the glottis. In those cases, the functional analysis of the vocal folds is impossible. Another problem of functional assessment of the larynx is observed in patients, who have undergone laryngeal microsurgery with resection of the epithelium and deeper layers of the vocal fold. The functional result will be different post type I and II cordectomy compared to more radical type III cordectomy, after which no vibra-

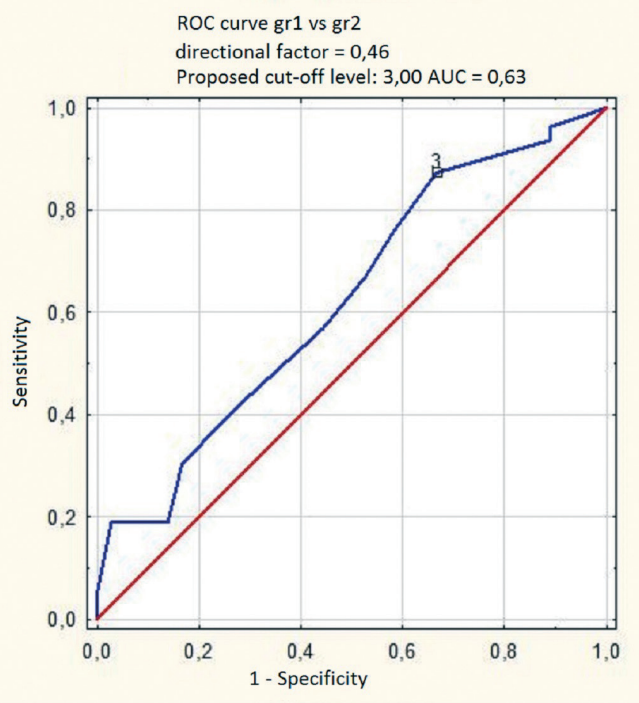

Fig. 2. The ROC curve (receiver operating characteristics) for LVS scores in differentiation benign from precancerous glottic lesions with the cut-off point equal to 3.

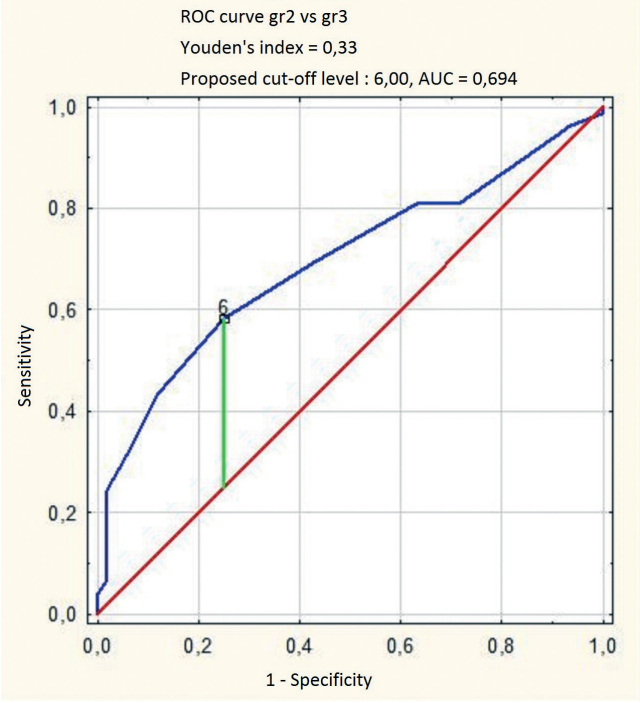

Fig. 3. The ROC curve (receiver operating characteristics) for LVS scores in differentiation precancerous lesions from malignant with the cut-off point equal to 6.

tion is expected within the scar. Also, previous radiotherapy of the larynx disturbs normal histological stratified structure of the vocal fold, which in turn results in impaired vibration. The presented results do not take into account the impact of morphological assessment of the lesion on final diagnosis, which certainly is an important factor. In our study, we were interested in the effect of functional assessment of vocal fold vibration on final diagnosis in suspicious lesions of the glottis. The preliminary results of such assessment, with additional use of the proposed scale, seem very interesting.

CONCLUSIONS

- Laryngovideostroboscopy is a very sensitive test in detecting vocal fold pathology and it can be used as a screening method.
- Unfortunately, functional assessment of vocal fold vibration is not specific and does not allow to precisely distinguish benign from malignant lesions.
- The proposed scale can be helpful in comparing laryngovideostroboscopy results in different laryngeal lesions.

REFERENCES

1. Paul B.C., Chen S., Sridharan S., Fang Y., Amin M.R., Branski R.C.: Diagnostic accuracy of history, laryngoscopy, and stroboscopy. Laryngoscope. 2013; 123: 215–219.
2. Colden D., Zeitels S.M., Hillman R.E., Jarboe J., Bunting G., Spanou K.: Stroboscopic assessment of vocal fold keratosis and glottic cancer. Ann. Otol. Rhinol. Laryngol. 2001; 110: 293–298.
3. Dejonckere P.H., Bradley P., Clemente P., Cornut G., Crevier-Buchman L., Friedrich G., Van De Heyning P., Remacle M., Woisard V.: A basic protocol for functional assessment of voice pathology, especially for investigating the efficacy of (phonosurgical) treatments and evaluating new assessment techniques. Guideline elaborated by the Committee on Phoniatrics of the European Laryngological Society (ELS). Eur. Arch. Otorhinolaryngol. 2001; 258 (2): 77–82.
4. Arens C., Glanz H., Wönckhaus J., Hersemeyer K., Kraft M.: Histologic assessment of epithelial thickness in early laryngeal cancer or precursor lesions and its impact on endoscopic imaging. Eur. Arch. Otorhinolaryngol. 2007; 264 (6): 645–649.
5. Djukic V., Milovanovic J., Jotic A.D., Vukasinovic M.: Stroboscopy in detection of laryngeal dysplasia effectiveness and limitations. J. Voice. 2014; 28: 262.e213–262.e221.

6. Mehlum C.S., Rosenberg T., Groentved A.M., Dyrvig A.K., Godballe C.: Can videostroboscopy predict early glottis cancer? A systematic review and meta-analysis. Laryngoscope. 2016; 126 (9): 2079–2084. doi: 10.1002/lary.25745. Epub 2015 Nov 3.
7. El-Demerdash A., Fawaz S.A., Sabri S.M., Sweed A., Rabie H.: Sensitivity and specificity of stroboscopy in preoperative differentiation of dysplasia from early invasive glottic carcinoma. Eur. Arch. Otorhinolaryngol. 2015; 272: 1189–1193.
8. Peretti G., Piazza C., Berlucchi M., Cappiello J., Giudice M., Nicolai P.: Pre- and intraoperative assessment of mid-cord erythroleukoplakias: A prospective study on 52 patients. Eur. Arch. Otorhinolaryngol. 2003; 260: 525–528.
9. Gugatschka M., Kiesler K., Beham A., Rechenmacher J., Friedrich G.: Hyperplastic epithelial lesions of the vocal folds: combined use of exfoliative cytology and laryngostroboscopy in differential diagnosis. Eur. Arch. Otorhinolaryngol. 2008; 265: 797–801.
10. Caffier P.P., Schmidt B., Gross M. et al.: A comparison of white light laryngostroboscopy versus autofluorescence endoscopy in the evaluation of vocal fold pathology. Laryngoscope. 2013; 123: 1729–1734.

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Corresponding author: Anna Rzepakowska; Klinika Otolaryngologii WUM; 02-097 Warszawa, ul. Banacha 1a; tel. 022 5992716; e-mail: arzepakowska@wum.edu.pl

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