# Modular prosthesis of the Larynx: Current Stage

## Analysing the Information from the Recurrent Laryngeal Nerve

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***Abstract*- In previous publications we outlined the feasibility of a modular prosthesis of the larynx for patients suffering from laryngeal carcinoma. The larynx is located between the trachea and the pharynx with its main functions being phonation, protection and regulation of the air ways. Patients suffer severely from the diagnosis of a laryngeal carcinoma of the stages pT3 and pT4. In most cases this diagnosis will lead to a total laryngectomy, which usually leads to a dissatisfying postoperative rehabilitation. The postoperative consequences include the loss of the voice, the regular air ways via mouth and nose, the sense of smell, and the inability to build up an abdominal pressure.**

**This paper deals with the basic research on the nervus laryngeus recurrens for the development of a modular prosthesis of the larynx which eventually will enable the laryngectomee to talk with his native voice, to breathe via the regular air ways, and to build up abdominal pressure. The voice reproduction will be performed by a vocoder. Vocoders are electronic devices which emulate the human vocal tract by using adequate filter settings on discrete filter units thus consisting of both variable and permanent filter settings. The signal pattern in the nervus laryngeus recurrens will affect the variable filter settings of the vocoder according to the current voice intonation whereas the vocal range of the patient's voice gives the limit of the permanent filter settings.**

**In this work we put emphasis on the recording and analysis of the signal pattern in the nervus laryngeus recurrens. Therefore we tried to record the nerve potentials of this nerve first in a non-invasive approach by using skin electrodes along the anatomic course of the nerve. A sophisticated amplifier (Intan® Technologies RHA2000-Series Amplifier and RHA2116 Amplifier Board) was used to amplify the weak nerve potentials, but we had to cope with a poor SNR and strong signal distortions mostly due to muscle potentials from large muscles like the sternocleidomastoid muscle eventually delivering us only microphone potentials of the voiced parts of the speech generated by the muscle potentials of the laryngeal and pharyngeal muscles and not representing action potentials on the nerve thus rendering them useless for our needs. Further basic research in this field therefore is necessary, even taking an invasive approach into account.**

***Keywords*- *Prosthesis; Larynx; Vocoder; Nervus Laryngeus Recurrens; Action/Nerve Potential; Laryngectomy; Nervus Vagus***

## I. INTRODUCTION

The laryngeal carcinoma is a malignant tumor of the head-neck region. The incidence of the laryngeal carcinoma worldwide is approx. 160.000 [1]. The worldwide mortality is approx. 90.000 individuals per year. Although the incidence and mortality are slightly decreasing since the 1990s for male individuals, incidence and mortality in women are still increasing [2]. The main risk factor for laryngeal carcinoma is smoking, alcohol ingestion, and work-related exposure to dust and chemicals like halogenated hydrocarbons [3].

According to the cancer stage different ways of therapy are induced such as laser treatments, partial resection of the larynx in early stages or total resection of the larynx in advanced stages as well as radiation therapy. At the cancer stages pT3 and pT4 a total laryngectomy and implantation of a tracheostoma is performed thus leading to a permanent loss of the voice and the regular air ways [4, 5].

Current rehabilitation methods after total laryngectomy include an implantation of a vocal fistula using valve vocals, the use of electrolaryngeal speech aids or the acquisition of the esophageal voice using the gullet for phonation. These kinds of voice production are unsatisfying for the patient as such a voice sounds either rattling or like a monotonous robot voice [6, 7, 8].

In general the state of rehabilitation is dissatisfying to the patient, representing a significant loss of quality of life. Still today there is neither an existing therapy nor prosthesis to overcome this. In our previous work we introduced a prosthesis to preserve the own voice, restore the ability to smell by restoring the regular airways, and the ability to build up abdominal pressure [9].

In this publication we will focus on different methods to extract and analyse the signal patterns in the recurrent laryngeal nerve.



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## II. MODULAR PROSTHESIS OF THE LARYNX

The larynx (voice box) is located between the pharynx (fauces) and the upper end of the trachea (windpipe) with its main function being phonation (Fig. 1). It consists of a skeleton of cartilages which are connected to multiple muscles. The rima glotti, located in the middle of the larynx, is formed by two opposing vocal folds. This complete organ of phonation is called glottis. According to the length of the vocal cords the voice pitch is high or low. The resilience of the vocal folds, which is influenced by specific groups of muscles, is used to vary the pitch of tones produced by air which streams through the narrowed glottis. While multiple muscles are involved in closing the glottis, mainly one pair of muscles can significantly open it. This pair of muscles, M. crycoarytenoideus (the clinical abbreviation is “Posticus”), has a major influence on the pitch. Thus, according to the degree of contraction, the muscles are able to open the glottis maximally for forced inspiration or slightly for minor changes of the pitch. The Posticus muscle is innervated by the N. laryngeus recurrens, a nerve which arises from the 10th cranial nerve, N. vagus [10]. While the N. vagus is running caudally, the N. laryngeus recurrens clasps the subclavian artery on the right side and the aortal arch on the left side respectively to go back cranially to the larynx (hence the name “recurrens”). Further cranially the nerve can be found between the trachea and the esophagus, right behind the thyroid where it finally reaches the larynx (Fig. 2). The location of the nerve makes it difficult to non-invasively receive action potentials of the nerve.

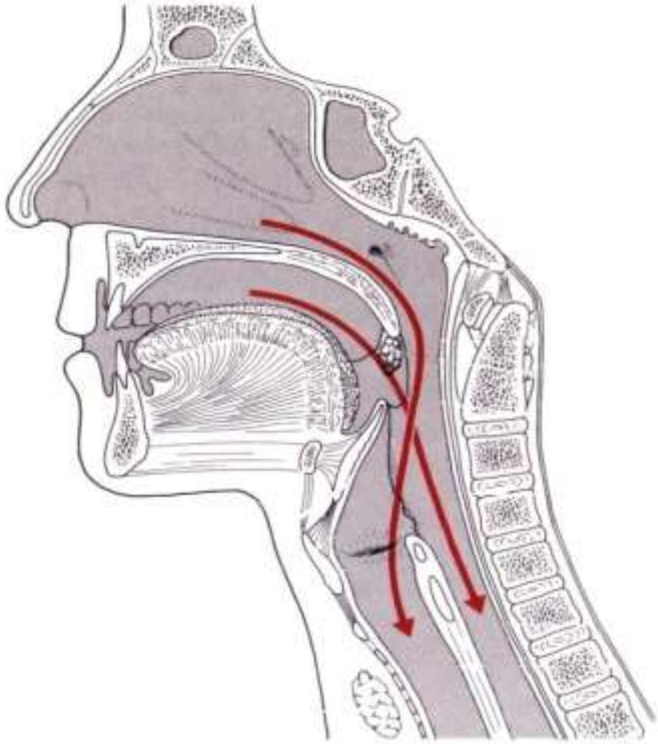

Fig. 1 Anatomy (courtesy of Schiebler, Anatomie, 9th Edition)

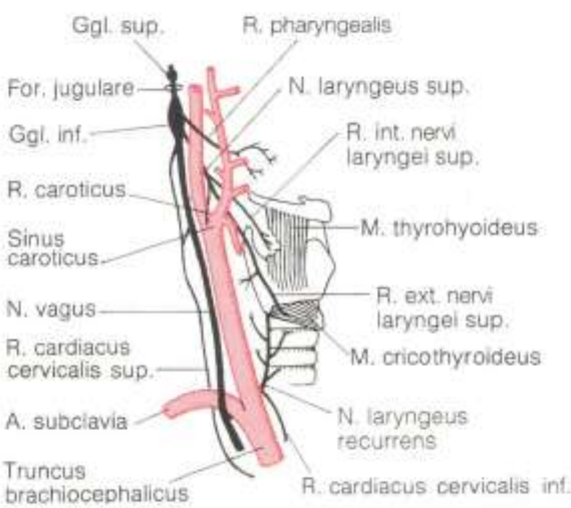


Fig. 2 Course of the N. laryngeus recurrens (courtesy of Schiebler, Anatomie, 9th Edition)



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The larynx is located ventrally whereas the gullet is located between the larynx and the vertebral column. The red arrows symbolize the ways of air and chyme, illustrating the difficulties resulting from the crossing of both ways (choking), which mainly is prevented by the tongue and the epiglottis.

The nervus laryngeus recurrens of each side or the Posticus muscle, if still existent after tumor surgery, are planned to be used for the neural or myogenic interface of our modular prosthesis.

A radiation therapy is often necessary to destroy remaining tumor cells after the laryngectomy. An implantation of the laryngeal prosthesis would not be possible after radiation therapy as the tissue is harmed by ionizing radiation (radiation fibrosis, ulcerations) which will impede the engraftment of the laryngeal prosthesis [11, 12]. Implantation of the laryngeal prosthesis before radiation therapy is not feasible, either, due to the radiation doses. Doses vary from 30 to 70 Gray and severely harm electronic components made out of semiconductors where radiation can generate high currents in the circuitry leading to a permanent destruction [13, 14]. Furthermore, a permanently implanted electronic device can become useless by aging, especially the batteries, or component failure. In the case of component failure or the necessity of a hardware update, or in the case of a mechanical failure the whole prosthesis would have to be explanted meaning further straining surgery to the patient.

To overcome these limitations the laryngeal *prosthesis* has to be divided into a stationary and an exchangeable module (Fig. 3). Stationary and exchangeable modules are made up of a biocompatible, fungicidal and bactericidal material. The stationary module has interfaces to connect the laryngeal recurrent nerve to the *prosthesis* and another interface to connect the exchangeable module's electronic devices. The exchangeable module is inserted into the stationary module by a simple plug-and-turn connector. The exchangeable module contains the valve appliances, the electronic devices plus power supply, the interface to the stationary module, and the epiglottis *prosthesis*. After the surgical removal of the *larynx* the stationary module is implanted permanently.

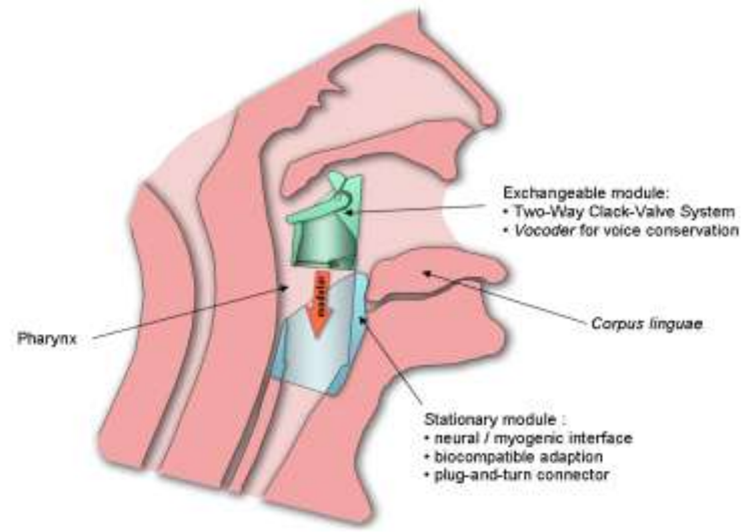


Fig. 3 Modular prosthesis of the *larynx*

In our studies we focus on two main parts of the *prosthesis*: A *prosthesis* for the epiglottis acting as a valve system and a *vocoder*, which is responsible for voice reproduction. In the figure a simple epiglottis *prosthesis* is shown.

## III. VOICE CONSERVATION AND ELECTRONICS

One of the most valuable characteristics of the laryngeal *prosthesis* is the reproduction of the patient's native voice. An electronic device inside the *prosthesis* (Fig. 3) receives input from the *N. laryngeus recurrens* and N. phrenicus to generate the voiced parts of phonation using the native voice of the patient as a template.

Voice in general consists of voiced and unvoiced parts. Voiced parts are generated by pressured airflow from the lung leading to vibrating vocal folds inside the *larynx*. Unvoiced parts are sounds that are not generated by the vocal folds. Unvoiced parts can be generated by air flow passing tongue and teeth. The individual voice gets its uniqueness from the shape of the *larynx*, neck, mouth, tongue and teeth – and mostly from the shape, thickness and length of the vocal cords [15]. This is referred to as the vocal tract which is removed in a total *laryngectomy*.

Nowadays, telecommunication systems, e.g. cellular handsets, commonly use algorithms to emulate vocal tracts. *Vocoders* are electronic devices that are utilizing mathematical models to reproduce the vocal tract [16]. The original reason for using *vocoders* in telecommunication is to save bandwidth for data transmission. A v*ocoder* can also be used to emulate the vocal tract in a laryngeal *prosthesis*, thus generating speech with the patient's native voice.



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Most *vocoders* have implemented Adaptive Multi-Rate Codecs (AMR) or other speech encoding methods that are based on Code-Excited Linear Prediction codec (CELP), which is an extension of Linear Prediction based codecs (LP) [17]. LP based algorithms are using aligned tubes of different lengths and radiuses as a model of the vocal tract (Fig. 4). Input to the decoder consists of a variable part and a fixed part. The variable part describes the change in loudness and pitch of the voice during speech. The fixed part describes unique parameters to program the *vocoder* which represent the basic characteristics of the patient's native voice. The laryngeal *prosthesis* takes input from the *N. laryngeus recurrens* and the *N. phrenicus* and calculates the necessary variable parameters for the *vocoder* (Fig. 5) whereas the fixed parameters are set by firmware programming.

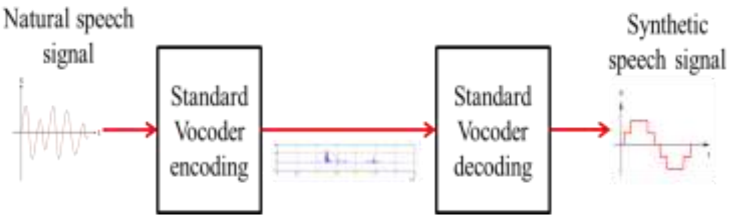


Fig. 4 *Vocoder* in telecommunication applications

The natural speech is encoded and transmitted to a standard *vocoder* (mobile phone). Here a synthetic voice is produced.

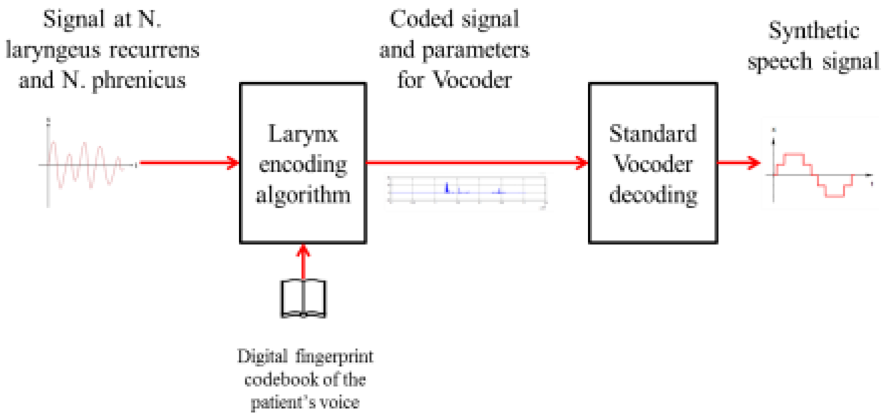


Fig. 5 *Vocoder* in laryngeal *prosthesis*

Transferred to our feasibility study, the natural speech can be encoded and conserved before a total *laryngectomy*. Based on this data the *vocoder* is able to reproduce the synthetic speech in the modular *prosthesis*. The voice signal is recoded by *nerve potentials* from the recurrent laryngeal nerve.

Due to the uniqueness of an individual's vocal tract, i.e. in shape and size and other characteristics, the voice of a human being is like a distinct fingerprint. From the digital signalling point of view, the uniqueness of a voice fingerprint lies in the shape, pitch and location of formants of each voiced sound. The calculation is based on the patient's individual voice characteristics which were conserved earlier. In order to speak with the original patient's voice, it is necessary to capture and conserve the patient's voice characteristics as accurately as possible.

Therefore the approach includes the method to capture individual voice characteristics before resection. This includes recording of the voice while the patient is performing a set of voiced sounds and hereby trains the system. The training set is chosen in a way that covers most parts of the patient's voice spectrum. The algorithm in the laryngeal prosthesis recalculates the neural signals to input parameters for the vocoder so that formants are placed and shaped to reproduce the patient's native voice.

The *action potential*s of the recurrent laryngeal nerve have to be analysed and correlations between the pitch of the voice and the *action potential*s have to be found to finally implement a real-time interface between the nerve and the *vocoder*, which will allow dynamic filter settings in the *vocoder* according to the pitch. There are two possible approaches to collect *action potential*s of the recurrent laryngeal nerve: invasive and non-invasive. Advantage of the invasive approach lies in the higher quality of the gained signal while perturbations (e.g. muscle potentials) are widely reduced. The disadvantage of the invasive method is in the risks of each invasive procedure (e.g. infection, bleeding, severing the nerve). The non-invasive method will yield a poorer signal quality due to perturbations by muscle potentials, skin resistance, etc.

At the current stage of our research we are pursuing the non-invasive way. To capture the weak potentials of the recurrent laryngeal nerve via electrodes placed on the skin extremely sophisticated amplifiers with excellent gain and signal-to-noise ratio (SNR) are necessary. In this research project we used a system from Intan® Technologies (www.intantech.com), LLC, named the RHA2000-Series Amplifier USB Evaluation Board (RHA2000-EVAL) together with the Amplifier Board RHA2116.



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A Windows based software is included to observe and record all 16 amplifier channels in real-time. Each channel is characterized by a 16-bit accuracy at a sampling rate of 25 kHz. Software notch filters suppress line noise at both 50 Hz and 60 Hz. The upper bandwidth of the amplifier can be programmed to any value between 10 Hz and 20 kHz while the lower bandwidth can range between 0.02 Hz and 1.0 kHz, thus allowing the acquisition of different types of signals, e.g. EEG or EKG (0.1 to 100 Hz) and neural action potentials (250 Hz to 7.5 kHz).

Data are transferred to a hard disk drive in binary format and can be exported to applications like MATLAB® as well.

We chose five healthy individuals, three male, two female, as subjects to run different tests on each subject delivering altogether 25 samples. These tests were speech of predefined words (counting down in German from 10 to 0 and the recitation of an old German folk song), voiceless repetition of the last two tests, and a simple humming. We placed skin electrodes (3M™ Red Dot™) on the ventral parts of a subject's neck closest to the course of the recurrent laryngeal nerve (Fig. 6) while placing an electrode on the right ankle as a remote ground. The Intan® amplifier operated at 250 Hz to 7.5 kHz for neural action potential recording.

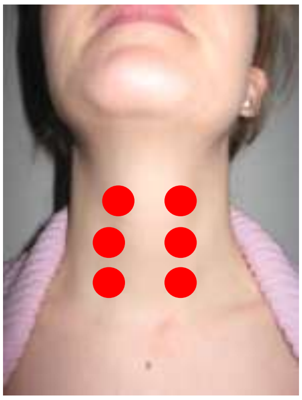

Fig. 6 Areas closest to the recurrent laryngeal nerve for electrode placement.

Due to the very high amplification we had to cope with a lot of background noises. To minimize them subjects had to enter an RF cabin (Faraday cage) so that we could eliminate radio irradiance. Furthermore we used double-shielded cables between electrodes and amplifier. Then we made a record while the subject was slowly breathing and another record while the subject stopped breathing to check the level of background noises (Fig. 7 and 8), then followed by a record while the subject was asked to say predefined words both voiced and voiceless. Fig. 9 and 10 are examples illustrating the scope of such a session. Fig. 11 is an example of a recording of the subject who hums for about 10 seconds. Fig. 12 is an example of a recording of the subject voicelessly counting down from 10 to 0 in German. This was repeated five times with each subject. Then, we replaced the electrodes, trying different positions and filter settings, always leading to the same results.

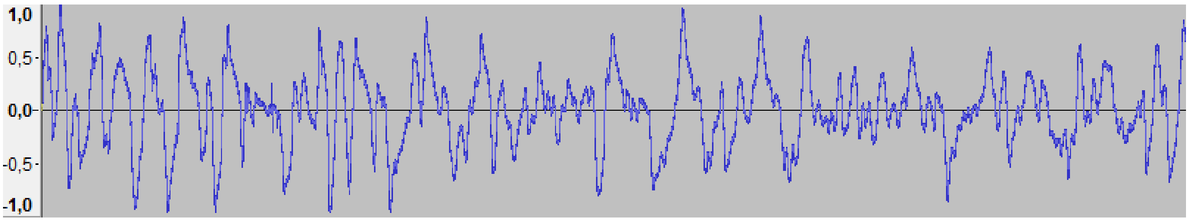


Fig. 7 Scope of a subject holding breath

The signal is very much distorted by ECG, muscle potentials and noise resulting from poor skin resistance although high quality electrodes (3M™ Red Dot™) have been used.

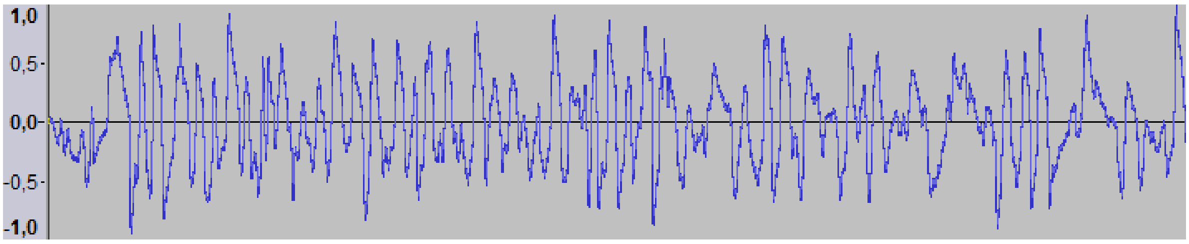


Fig. 8 Scope of a subject slowly breathing

More spikes are noticed due to the activity of the diaphragm and intercostal muscles.



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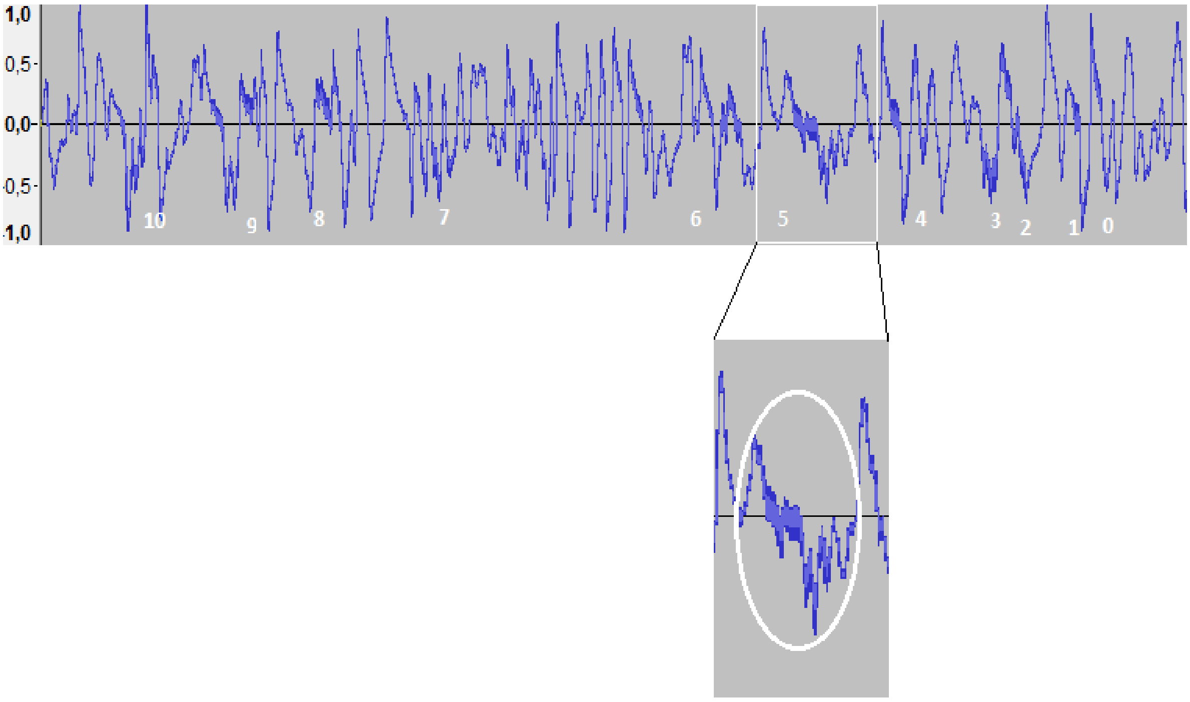


Fig. 9 Scope of a subject counting down from 10 to 0

The signal is very much distorted by muscle potentials and noise resulting from poor skin resistance although high quality electrodes have been used. Nevertheless, the sections of phonation can be recognized as harmonic waves over the noise.

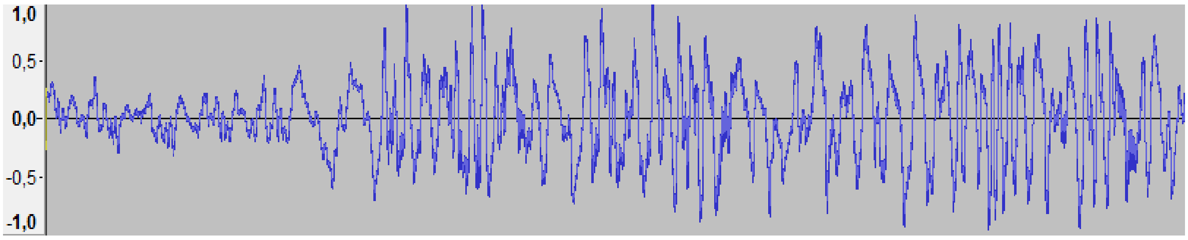


Fig. 10 Scope of a subject reciting "Von den blauen Bergen kommen wir"

Here too, the sections of phonation can be recognized as harmonic waves over the noise.

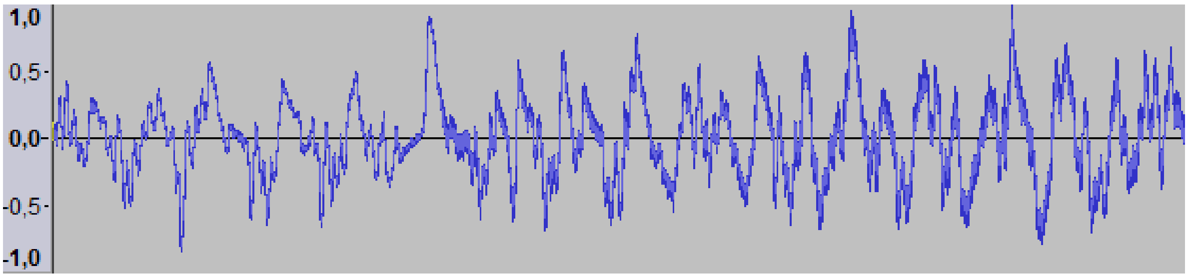


Fig. 11 Scope of a subject humming

The section where the humming begins can be identified as the part in the scope where the harmonic waves are noticed.

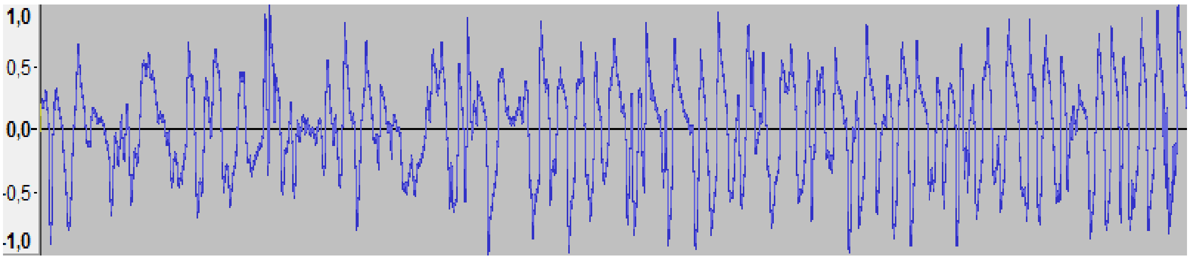


Fig. 12 Scope of a subject voicelessly counting down from 10 to 0

This scope shows no sections with harmonic waves.



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The voiced parts always sticked out of the noise as harmonic waves. When running the recorded scope data through a D / A converter, which was saved in a simple binary format, the phonated sections can acoustically be recognized if correct sampling rates are set in the D / A converter. The audio signal then resembles very much the voiced parts of the subject's sample although it is quite muffled.

## IV. CONCLUSIONS

The recorded potentials show strong distortions and a poor signal-to-noise ratio which is caused by several limiting factors. One limiting factor, if not the main limiting factor, is the size of the recurrent laryngeal nerve and its position. Located between the gullet and the windpipe, behind the thyroid, it lies deep in the neck and is surrounded by a number of muscles which strongly distort the signal of the nerve (especially big muscles like the sternocleidomastoid muscle). The signals recorded in the first experimental setting appear to be microphone potentials transmitted by the muscle potentials of the laryngeal and pharyngeal muscles and do not represent *action potentials* on a nerve thus rendering them useless for the implementation of the *prosthesis*' neural interface. One possible solution to overcome this limiting factor while still trying a non-invasive approach is a circular placement of the electrodes around the subject's neck eventually filtering the *action potentials* on the nerve by suitable mathematical methods, e.g. Gauss elimination, triangulation and curvilinear integrals (Fig. 13) as well as further noise minimization and optimized filtering of the amplifier inputs which will be subject to the next experiments. Depending on the results of the next experimental setup with a larger number of individuals an invasive approach will possibly have to be considered as the next step. Here, a good compromise between a reliable signal quality and a justifiable degree of invasiveness would be an endotracheal tube with surface electrodes which nowadays are routinely used in thyroid surgery to continuously monitor the recurrent laryngeal nerve (e.g. NIM® Intraoperative Nerve Monitoring System) [18]. In this setup the subject must not receive general anaesthesia but only local anaesthesia of the throat as she or he must remain alert and responsive to be able to say predefined words and sentences for recording. Further basic research on this field is necessary.

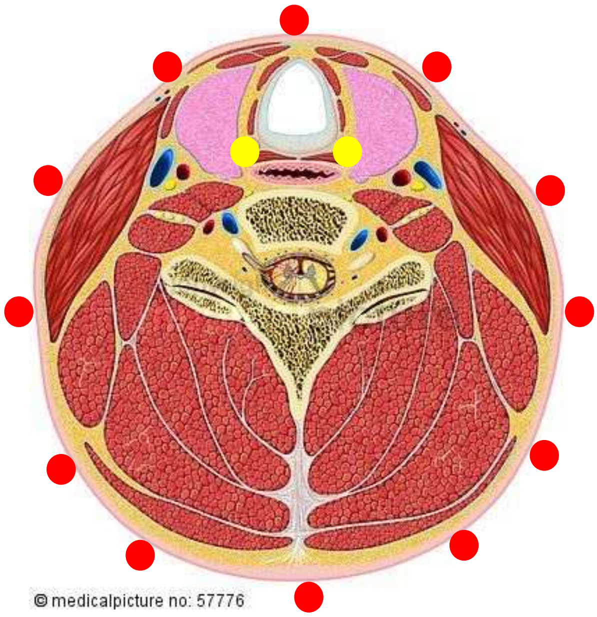


Fig. 13 An alternative non-invasive approach (courtesy of medical picture GmbH)

The red circles illustrate the position of the electrodes. The yellow circles illustrate the course of the recurrent laryngeal nerve.

## REFERENCES


[1] J. Ferlay, F. Bray, P. Pisani, “Globocan 2002: Cancer Incidence, Mortality and Prevalence Worldwide,” IARC Cancer Base No. 5. version 2.0. IARCPress, Lyon, 2004

[2] K. Giersipen, C. Brünings-Kuppe and C. Lehmann, “The Bremen Mortality,” Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz, vol. 47, no.5, pp. 451 – 456, 2004.

[3] C.A. Righini, A. Karkas and N. Morel, “Risk factors for cancers of the oral cavity, pharynx (cavity excluded) and larynx,” Presse Med, vol. 37(9), pp. 1229 – 1240, 2008.

[4] L. Giordano, S. Toma, R. Teggi, F. Palonta, F. Ferrario, S. Bondi and M. Bussi, “Satistfaction and Quality of Life in Laryngectomees after Voice Prothesis Rehabilitation,” Folia Phoniatrica et Logopaedica, vol. 63, no.5, pp. 231-216, 2011.

[5] A.J. Balm, M.W. van den Brekel, I.B. Tan and F.J. Hilgers, “The indwelling voice prosthesis for speech rehabilitation after total laryngectomy: a safe approach,” Otolaryngol Pol. , vol. 65, no. 6 , pp. 402-9, 2011.

[6] L. D'Alatri., F. Bussu, E. Scarano, G. Paludetti and M.R. Marchese, “Objective and Subjective Assessment of Tracheoesophageal




DOI: 10.5963/LSMR0303003

Prosthesis Voice Outcome," J Voice, pp. 1-7, 2011.

[7] T. Haderlein, E. Nöth, A. Batliner, U. Eysholdt, F. Rosanowski: "Automatic intelligibility assessment of pathologic speech over the telephone," Logoped Phoniatr Vocol. , vol. 36, no. 4, pp. 175-81, 2011.

[8] M. Wierzchowska and P.K. Burduk, "Early and late complications after implantation of the Provox 2 voice prosthesis in patients after total laryngectomy," Otolaryngol Pol., vol. 65, no. 3, pp. 184-7, 2011.

[9] F. Nazaradeh, M.A. Dupré, T. Doerge, C. Eckermann, W. Kelterer, D. Nazaradeh, S. Steltenkamp, "Advantages of voice reproduction and the development of a biomimetic self-regulating double-clack valve for a prosthesis of the larynx - a feasibility study," Conf Proc IEEE Eng Med Biol Soc. 2012, pp 827 - 830, 2012.

[10] T. Schiebler, W. Schmidt, K. Zilles, "Anatomie: Zytologie, Histologie, Entwicklungsgeschichte, makroskopische und mikroskopische Anatomie des Menschen," vol. 9, pp 435 – 441, 2011.

[11] W. Budach, "Das chronische Larynxödem als Spätreaktion nach Radiochemotherapie," HNO, vol. 46, no. 8, pp. 708 – 711, 1998.

[12] D.J. Adelstein, "Squamous Cell Head and Neck Cancer Recent Clinical Progress and Prospects for the Future," Humana Press, pp 79 – 92, 2005.

[13] B. Di, X.M. Li, Y.D. Shang, Q. Song, Z.F. Tao, J.M. Cheng, "Outcomes of salvage laryngectomy after initial radiation failure in laryngeal squamous cell carcinoma," Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi, vol. 46, no. 6, pp. 495-500, 2011.

[14] G.C. Messenger and M.S. Ash, "The Effects of Radiation on Electronic Systems," Van Nostrand Reinhold, New York, 1992.

[15] N. Tayama, R.W. Chan and K. Kaga, "Geometric characterization of the laryngeal cartilage framework for the purpose of biomechanical modeling," Ann Otol Rhinol Laryngol, vol. 110, no. 12, pp. 1154 – 1161, 2001.

[16] P. Vary, U. Heute and W. Hess, "Digitale Sprachsignalverarbeitung," Teubner, Stuttgart, Germany, 1998.

[17] R. Hofe, S.R. Ell, M.J. Fagan, J.M. Gilbert, P.D. Green, R.K. Moore, S.I. Rybchenko, "Speech Synthesis Parameter Generation for the Assistive Silent Speech," Interface MVOCA, 2011.

[18] T.M. Hemmerling, J. Schmidt, C. Bosert, K.E. Jacobi, P. Klein, "Intraoperative Monitoring of the Recurrent Laryngeal Nerve in 151 Consecutive Patients Undergoing Thyroid Surgery," Anesthesia & Analgesia, vol. 93, no. 2, pp. 396 - 399, 2001.



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