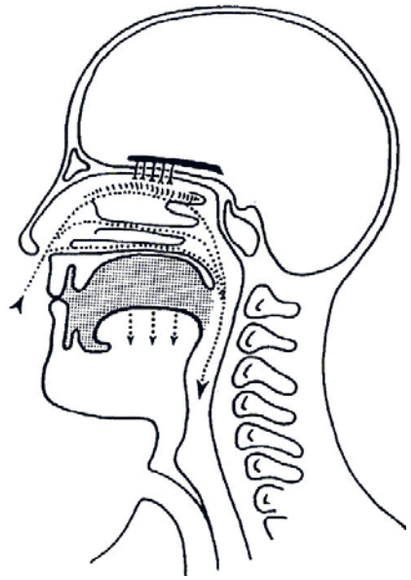
Olfactory function after total laryngectomy in Swedish patients after rehabilitation with the Nasal Airflow-Inducing Maneuver



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Birgit Risberg-Berlin Olfactory function after total laryngectomy in Swedish patients after rehabilitation with theNasal Airflow-Inducing Maneuver

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Olfactory function after total laryngectomy in Swedish patients after rehabilitation with the Nasal Airflow-Inducing Maneuver

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Göteborg 2008

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ABSTRACT

After a total laryngectomy the upper and lower airways are disconnected resulting in a wide range of adverse effects, e.g. deterioration of nasal functions in breathing, loss or decrease of normal sense of smell and taste, as well as loss of normal voice. Recently, a new method that can restore the sense of smell in laryngectomized patients has been developed, the Nasal Airflow-Inducing Maneuver (NAIM). The overall aims of this thesis were: 1) to describe the olfactory function in laryngectomized patients and to assess the results of repeated interventions with the NAIM; 2) to evaluate the long-term results 6 and 12 months after intervention; 3) to assess olfaction, health-related quality of life (HRQL) and communication 36 months after NAIM intervention; and 4) to use a clinical protocol to follow changes in the NAIM technique over time.

The study population consisted of 24 laryngectomized patients. Olfaction acuity was examined with the Scandinavian Odor Identification Test (SOIT). The patients were categorized as smellers (normosmia or hyposmia) or non-smellers (anosmia) based on the SOIT results. Their self-estimation of smell, taste, health-related quality of life and communication were measured with validated questionnaires. According to SOIT, 18 of 24 patients (75%) had impaired sense of smell before NAIM rehabilitation and 72% improved their sense of smell after 3 NAIM rehabilitation sessions. Further improvement was also seen at the 6 and 12 month follow-up, i.e. 83% and 88% respectively, were categorized as smellers according to SOIT results. Three years after NAIM rehabilitation all patients still alive (n=18) were re-examined and as many as 78% were still smellers. In addition, the patients reported an overall good HRQL and no mental distress. According to a structured protocol it was possible to identify improvements in NAIM key variables associated with improvements of the sense of smell over time.

It was concluded that olfactory impairment is common in laryngectomized patients, that NAIM is an effective method for restoring the sense of smell, and that the improvements endure in long-term. Consequently, olfactory rehabilitation according to the NAIM should be incorporated into routine rehabilitation programs for all laryngectomized patients. Furthermore, a protocol is a useful and reliable tool for evaluating use of the NAIM. Moreover, HRQL questionnaires should be complemented with more diagnose specific questionnaires when evaluating olfaction and communication in laryngectomized patients.

Key words: olfaction, total laryngectomy, Nasal Airflow-Inducing Maneuver, health-related quality of life.

LIST OF PUBLICATIONS

This thesis is based on the following papers, referred to in the text by their Roman numerals:

I. Screening and rehabilitation of olfaction after total laryngectomy in Swedish patients
Results from an intervention study using the Nasal Airflow-Inducing Maneuver

Risberg-Berlin B, Ylitalo R, Finizia C
Arch Otolaryngol Head Neck Surg 2006;132;301-306.

II. Effectiveness of olfactory rehabilitation with the Nasal Airflow-Inducing Maneuver after total laryngectomy
One-year follow-up study

Risberg-Berlin B, Ylitalo Möller R, Finizia C.
Arch Otolaryngol Head Neck Surg, 2007;133;650-654.

III. Effects of total laryngectomy on olfactory function, health-related quality of life, and communication: A 3-year follow-up study

Risberg-Berlin B, Rydén A, Ylitalo Möller R, Finizia C
Submitted Arch Otolaryngol Head Neck Surg

IV. Development of a clinical instrument improving rehabilitation of olfaction with the Nasal Airflow-Inducing Maneuver in Swedish laryngectomized patients

Risberg-Berlin B, Rydén A, Ylitalo Möller R, Finizia C
In print Acta Oto-Laryngologica

CONTENTS

ABBREVIATIONS

CCCRC	Connecticut Chemosensory Clinical Research Center
CN	Cranial Nerve
EORTC	The European Organization for Research and Treatment of Cancer
EORTC QLQ-C30	The EORTC Quality of Life Questionnaire Core 30
EORTC QLQ-H&N35	The EORTC Quality of Life Questionnaire Head and Neck Module
HADS	The Hospital Anxiety and Depression Scale
H&N	Head & Neck
HEOG	Human Electro-Olfactogram
HME	Heat and Moisture Exchange
HRQL	Health Related Quality of Life
NAIM	Nasal Airflow-Inducing Maneuver
OERP	Olfactory Event-Related Potential
POPS	Present Odor Perception Scale
QoL	Quality of Life
QOTA	Questions on Odor, Taste and Appetite (later called AHSP; The Appetite, Hunger feelings and Sensory Perception questionnaire)
SEMA	Swedish Emergency Management Agency
SLP	Speech Language Pathologist
SOIT	Scandinavian Odor Identification Test
S-SECEL	The Swedish Self-Evaluation of Communication Experiences after Laryngeal Cancer
TNM	Classification system for malignant tumors; Tumor, Node, Metastases
UICC	Union International Contre le Cancer

INTRODUCTION

In Sweden the incidence of head and neck (H&N) cancer is around 1500 cases annually. Cancer in the larynx is the most common H&N site, with approximately 200 new cases per year [1]. During the last 10 years the incidence of laryngeal cancer in the Western world has increased among women by 4.9% but decreased with 0.8% among men [2]. Tobacco and alcohol use, particularly in combination, are considered the main predisposing factors [3, 4]. The dominating histopathological type of laryngeal cancer worldwide is squamous cell carcinoma. The laryngeal tumors are classified according to a global standard, the TNM-staging system and developed by the International Union against Cancer [5]. This classification describes tumor stage (T1-4), regional metastases (N0-3) and distant metastases (M0-1). For description of the localization of the tumor the larynx is divided into three anatomical regions 1) the supraglottic 2) the glottic and 3) the subglottic (Figure 1 and Table 1).

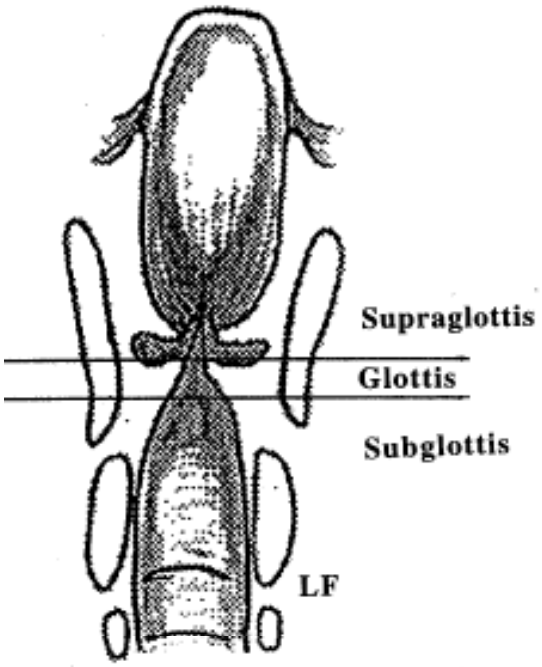

Figure 1. *The three anatomical regions of the larynx.*

Table 1. *TNM-classification and staging of laryngeal cancer (UICC, TNM, Classification of Malignant Tumors 6th ed, 2002)*

	Supraglottic	**Glottic**	**Subglottic**
T-stage	**Description**		
T1 Tumor	One subsite, normal vocal cord mobility	Limited to vocal cord (s), normal mobility T1a one vocal cord T1b both vocal cords	Limited to subglottis
T2 Tumor	Mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis; without fixation of the larynx	Supraglottis, subglottis, impaired vocal cord mobility	Extends to vocal cord (s) with normal/ impaired mobility
T3 Tumor	Vocal cord fixation or invades postcricoid area, pre-epiglottic tissues, paraglottic space, thyroid cartilage erosion	Vocal cord fixation, paraglottic space, thyroid cartilage erosion	Vocal cord fixation
T4a Tumor	Through thyroid cartilage; and/or invades tissues beyond the larynx	Through thyroid cartilage and/or invades tissues beyond the larynx	Through cricoid or thyroid cartilage and/or invades tissues beyond the larynx
T4b Tumor	Prevertebral space, mediastinal structures, carotid artery	Prevertebral space, mediastinal structures, carotid artery	Prevertebral space, mediastinal structures, carotid artery
Regional lymph nodes (N-stage) **N1** Ipsilateral single $\leq$ 3 cm **N2** **(a)** Ipsilateral single > 3 cm to 6 cm **(b)** Ipsilateral multiple $\leq$ 6 cm **(c)** Bilateral, contralateral $\leq$ 6 cm **N3** > 6 cm **Distant metastasis (M-stage)** **M1.** Distant metastasis present			

Staging of laryngeal cancer	**T**	**N**	**M**
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1, T2 T3	N1 N0, N1	M0 M0
Stage IVA	T1, T2, T3, T4a	N2 N0, N1, N2	M0 M0
Stage IVB	T4b Any T	Any N N3	M0 M0
Stage IVC	Any T	Any N	M1

The treatment for laryngeal cancer includes surgery, radiation and chemotherapy, or a combination of these, depending on type and size of the tumor. In most cases radiation is sufficient, but sometimes surgery is performed, i.e. in small tumors (laser surgery) or in larger tumors and cases of recurrence (laryngectomy). In Sweden approximately 50-60 patients are operated annually with a total laryngectomy due to laryngeal cancer. Total laryngectomy will lead to loss of natural voice, decreased lung function and sense of smell and taste with associated physical and psychological consequences [6]. The prevalence of hyposmia (reduced olfactory acuity) and anosmia (no olfactory acuity) in this patient population ranges from 68% [7] to 100% [8], depending on method of assessment. Despite these well-known side effects, there is a scarcity of studies on sense of smell and taste as well as their impact on quality of life in patients with laryngectomy [6, 7].

Olfactory system

Olfaction is a chemical sense which is important for detecting and identifying pleasant and unpleasant, as well as dangerous, odors in our environment and for triggering distinct memories or emotional moments. Our ability to recognize and remember 10000 different odors was not understood until 1991 when Axel and Buck (awarded the 2004 Nobel Prize in Medicine) published their description about one thousand different genes for odorant reception [9]. A schematic description is given in Figure 2.

The olfactory system comprises the olfactory epithelium and olfactory nerves, the olfactory bulb and tract, and several areas of olfactory cortex [10]. The olfactory epithelium is located at the top of the nasal cavities and consists of olfactory neurons with olfactory hairs, cilia. The cilia contain receptors for capturing the odorant molecules and the odorant information is passed on to the brain via nerve processes. As soon as olfactory information reach the brain, the odor can be detected, consciously or unconsciously, and thereby an action or reaction may be initiated.

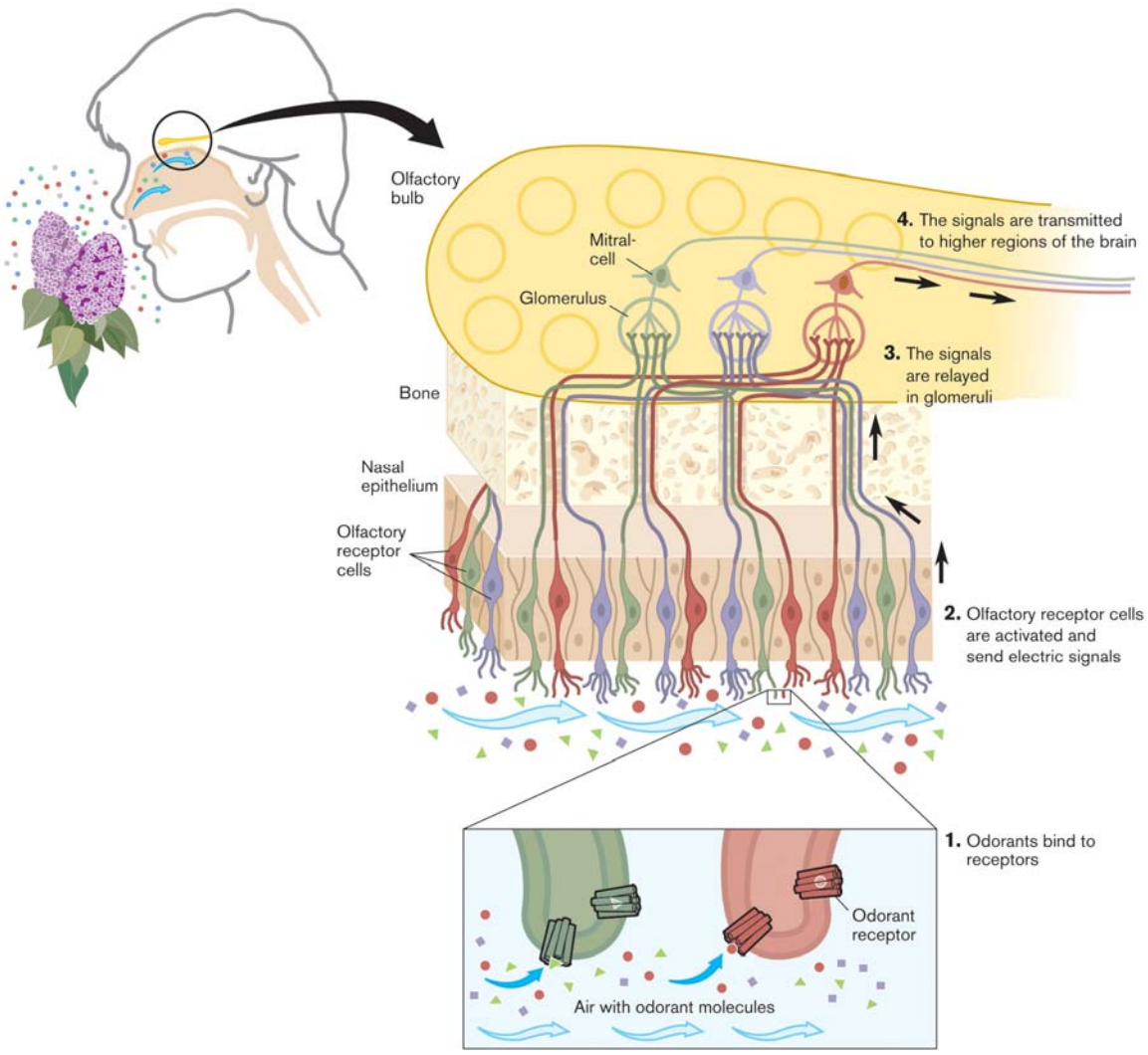

Figure 2. *http://nobelprize.org/nobelprizes/medicine/aureates/2004/press.htm*

Different ways of smelling

Orthonasal and retronasal olfaction

The ability to smell is a natural function that is permanently and unconsciously ongoing. Breathing in and out through the nasal cavity is a major part of this process. The odorant molecules automatically reach the olfactory epithelium in two ways during breathing: through the anterior nasal entrance via the inspiratory airflow (i.e. by orthonasal olfaction), or through the posterior nasal entrance via the expiratory airflow (i.e. by retronasal olfaction), Figure 3. Adequate delivery of the odor molecules via the nasal airflow to the peripheral olfactory epithelium is crucial for stimulation of the orthonasal olfaction. In normal situations there is “passive” smelling during passive orthonasal breathing, and “active” smelling by deeper orthonasal breathing through the nose [11]. Sniffing increases the volume and flow rate of the incoming air augmenting sense of smell in the nose and to the olfactory region [12]. The positive correlations between orthonasal airflow and various olfactory parameters, e.g. estimation of odor intensity [13], percentage of correctly recognized odors [14], and magnitude of activated odorant receptors [15], is well documented.

Smelling may also occur on an expiratory airflow from the oral cavity via the nasopharynx to the olfactory epithelium when breathing out, swallowing or chewing [16, 17]. This is called the retronasal olfaction and plays an important part in identifying the gustation [18]. Chewing to intensify retronasal olfaction can be compared to sniffing for intensifying orthonasal olfaction (Figure 3).

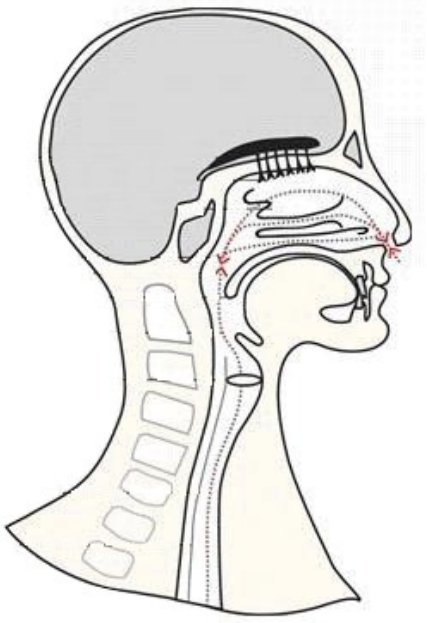

Figure 3. *Normal smelling with orthonasal and retronasal airflow. The anatomical image by courtesy of Atos Medical AB.*

Olfaction – Cranial Nerves

Odorant molecules may also stimulate free nerve endings of three cranial nerves: the trigeminal nerve (CN V), glossopharyngeal nerve (CN IX), and vagus nerve (CN X). A chemo sensation is perceived as irritation, tickling, burning, warming, cooling and stinging [19]. These nerves are, therefore, considered as protecting against irritating odors [20].

Reduced sense of smell

Reasons for reduced (hyposmia) or complete loss (anosmia) of olfactory function may be perceptive or conductive. A perceptive olfactory disorder is caused by damage to the olfactory epithelium, the olfactory bulb or the cerebral nerves involved in the olfactory function, and is therefore usually irreversible. Possible causes for perceptive disorders are, for instance, trauma, toxic chemicals (cytostatic drugs), radiation, virus infection, or disease states like Parkinson's and Alzheimer's diseases [21, 22].

An olfactory disorder caused by a physical obstruction of the orthonasal airflow is conductive. Potential reasons for conductive disorders may be swollen nasal mucosa, e.g. as a consequence of virus infection or allergy, nasal polyps or other tumors, chronic rhinosinusitis, or a deviated nasal septum.

Furthermore, several studies have shown that increasing age is associated with perceptive olfactory dysfunction [23, 24]. In a recent Swedish study the ability to smell was deteriorated in more than 20% of persons older than 60 years [25]. Moreover, there is a widespread belief that smoking has adverse effects on detection sensitivity and perceived intensity for certain odors, however, results from scientific evaluations are conflicting [26, 27].

These factors are also related to laryngectomized patients as the majority of the patients are male, former or present smokers, of older age (> 60 years) and often have received radiotherapy and/or chemotherapy.

Gustatory system

The sense of taste is also described as a chemical sense. The sensation of taste occurs when tastant molecules are released from food, dissolved in saliva and reach taste receptors in the taste buds on the surface of the tongue and on the soft palate, pharynx, larynx, epiglottis, uvula and upper oesophagus [28]. We are able to perceive thousands of taste sensations and these are based on different combinations of the five basic tastes: salt, sour, sweet, bitter, and umami [28, 29]. The role of gustation is important for nutritional intake, nutritional regulation (e.g. sodium, salt) [30], as well as for protection of the body against external toxins

(e.g. bitter taste). Reduced taste is referred to as hypogeusia, whereas ageusia is complete loss to perceive taste.

Smell and taste

During eating, a combination of smell and taste including texture and temperature of the food contribute to the perception of flavors. Of the two senses, smell is the main determinant of a flavor [31]. While taste of food, as mentioned above, is limited to the five basic tastes, the smell of food is potentially limitless. Consequently, impaired olfaction affects perception of flavor more than impaired gustation [31]. In contrast to taste, a smell can be detected at a far distance. Pleasant and unpleasant memories with associated emotions can be recalled by the sense of smell, e.g. experiences with unpleasant flavor from food combined with nausea [32]. Similarly, pleasant flavor from food may lead to food preferences [33, 34].

Olfaction following total laryngectomy

Total laryngectomy results in a permanent disconnection of the upper and lower airways with breathing through a permanent opening in the throat, a so called stoma (Figure 4). Consequently, the natural orthonasal airflow will be considerably decreased or totally missing. Olfactory acuity is regarded as a function of nasal airflow, and therefore the reduction in nasal airflow is considered as the key contributing factor to impaired olfaction following laryngectomy [14, 19, 35, 36]. This theory is supported by the fact that when nasal airflow, resembling natural breathing, and sniffing is re-established using puffs of air from squeeze bottles [35] or prosthetic devices (e.g. larynx bypass) that reconnect the nose and the lungs [14, 36], improvement in olfactory acuity is evident. However, histological examination of the olfactory mucosa in laryngectomized patients has shown various degrees of epithelial degeneration [37]. Miani et al concluded that it is the combination of loss of nasal airflow and degenerative phenomena of the epithelium that contributes to the olfactory deficits in patients following total laryngectomy. Obviously, as mentioned before the laryngectomees' sense of smell may also be affected by age, gender and environmental factors.

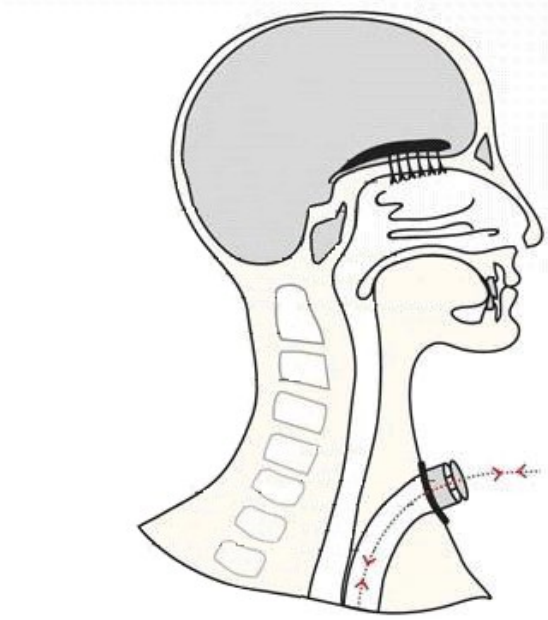

Figure 4. *Breathing post-laryngectomy through a permanent stoma. (Nasal airflow is missing). The anatomical image by courtesy of Atos Medical AB*

Gustation following total laryngectomy

Following total laryngectomy the sense of taste is also impaired, however not to the same extent as the sense of smell. According to a study by Ackerstaff et al [38], including a structured interview with 63 laryngectomized patients, 15% of the patients reported a decreased sense of taste (dysgeusia) while 52% of them had hyposmia. However, smell and taste were closely related as a significant correlation was found between hyposmia and dysgeusia ($r=0.43$, $p<0.001$), where all patients with a taste problem also reported reduced sense of smell. These findings are in concordance with those found by Finizia et al [39] where 21% of the laryngectomized patients reported reduced taste perception and 50% reduced smell perception according to the EORTC QLQ-H&N35 questionnaire.

Methods to restore olfaction after total laryngectomy

Prosthetic devices

Several prosthetic devices for establishing nasal airflow are presented in the literature. However, they are inconvenient to handle and therefore unlikely to be used outside the clinical setting. Bosone [40] was the first to describe a simple device, *the nipple tube*, to improve olfactory function after laryngectomy (Figure 5). Furthermore, Knudson et al [41] introduced *an oral tracheal breathing tube* enabling the patient to inhale and exhale through the nose in the same manner as used with the larynx bypass (Figure 6).

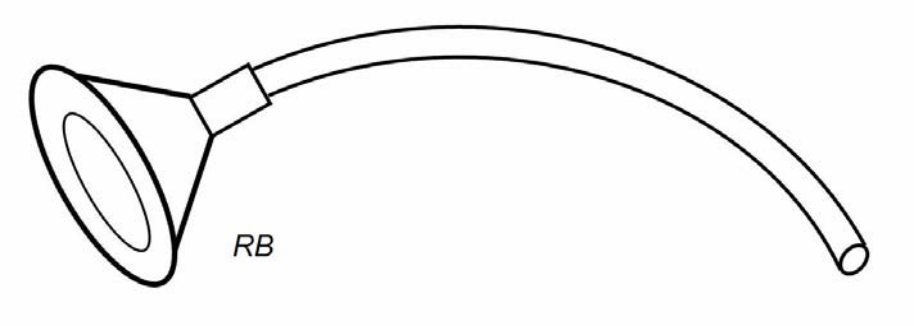

Figure 5. *Nipple tube*

Larynx bypass

The larynx bypass consists of a plastic tube that connects the sealed tracheostoma to the mouth with a mouthpiece (Figure 6). With lips sealed around the mouthpiece a negative pressure, developed in the lungs, leads to orthonasal airflow through the nose where odorant receptors may be stimulated. Goktas et al. [42], having studied the efficacy of this device, showed that laryngectomees examined with a larynx bypass had a better sense of smell than those without an aid. Even if smelling by using a larynx bypass is troublesome and unpractical in everyday life it can be used as a screening method to exclude anosmia in laryngectomees.

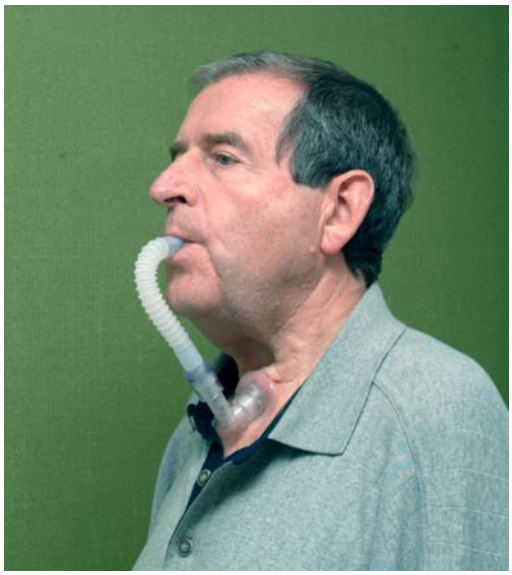

Figure 6. *Smelling by the use of a larynx bypass. Photo taken by Jan Persson with the permission of the patient*

Maneuvers

Various maneuvers to detect odors have been developed for laryngectomees. The principle is to create an inflow of air through the nose by changing volume in the oral cavity and oropharynx while the lips are closed. Examples of these maneuvers are glossopharyngeal press, buccopharyngeal sniffing, and buccopharyngeal maneuver [14, 35]. However, these maneuvers have not been incorporated into routine rehabilitation methods, nor have their effectiveness been systematically evaluated [36].

Nasal Airflow-Inducing Maneuver

Several authors had previously discovered that laryngectomized patients who perceived smell were more active in using face and neck muscles compared to patients not able to smell [7, 14, 35]. As a result from observations of actions and methods applied by these patients, Hilgers and his co-workers [6] developed a new technique for smelling, The Nasal Airflow-Inducing Maneuver (NAIM) or "Polite Yawning Technique." This rehabilitation technique creates a negative pressure in the oral cavity and oropharynx to induce orthonasal airflow, thus enabling odorous substances to reach the olfactory epithelium. Patients are instructed to make an extended yawning while keeping their lips closed and simultaneously lowering their jaw, floor of the mouth, tongue, base of tongue and soft palate (Figure 7**)**. To increase effectiveness, the movement has to be repeated rapidly while breathing has to be calm and independent of the movement. As a second step the patient may try a refined polite yawning technique to make the maneuver less conspicuous in public. This could be achieved by isolated pumping movements of the back of the tongue and the floor of the mouth to eliminate lowering of the jaw. The first intervention study, performed on 33 laryngectomized patients categorized as non-smellers, showed a success rate of 46% after a single 30-minute NAIM therapy session [6]. Evidently, this technique is more patient-friendly than the earlier described maneuvers.

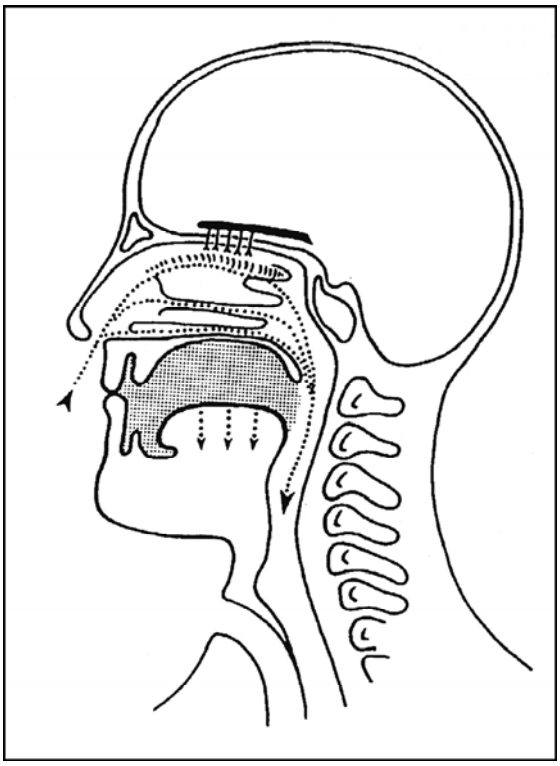

Figure 7. *NAIM – Nasal Airflow-Inducing Maneuver ("polite yawning"). The anatomical image by courtesy of Atos Medical AB*

Methods to restore gustation after total laryngectomy

Although little can be done to restore sensation of taste if permanently affected after radiation or surgical damage, there are ways to optimize residual taste function and flavor perception. This can be achieved by instructing patients to use intensive chewing and back and forth movements of food in the mouth [11]. An increased chewing results in increased release of odorant molecules from food that will lead to an increased oral airflow that enhances the retronasal olfaction [11, 43]. In addition, chewing with lips closed is thought to result in transient increases in the closed oral cavity volume. This generates transient negative pressures, inducing nasal airflow, and thus also encourages orthonasal olfaction [11, 43]. Considering that flavor perception is an integration of taste, smell, temperature and texture, altering the texture or temperature of food may further enhance the sensory experience of oral intake and stimulate enhanced flavor perception.

TESTING OF OLFACTION

Psychophysical olfactory tests

A multitude of psychophysical olfactory tests have been developed for clinical use in various cultural settings. They can be divided into different subgroups and some of these are listed here:

- *Odor threshold or detection test:* Measures the ability of the olfactory system to detect low concentrations of an odor e.g. The Butanol Odor Detection Test [44].
- *Odor identification test:* Measures the ability to identify different odor stimuli out of predetermined alternatives e.g. The Scandinavian Odor Identification Test (SOIT) [45] or The Smell Diskettes Test [46].
- *Odor discrimination test:* Measures the ability to discriminate one odor that is different from a set of three stimuli with the same odor, e.g. part of the olfactory function test “Sniffin´ Sticks” [47].
- *Odor memory test***:** Measures the ability to remember a presented odor stimulus e.g. The Odor Recognition Memory Test [48].

To correctly identify and categorize anosmic, hyposmic and normosmic patients the recommendation in clinical settings is to use a combination of olfactory tests, for example CCCRC (odor threshold test and identification test) and “Sniffin´ Sticks” (odor threshold, odor identification and odor discrimination tests).

In the present studies the odor identification test SOIT was used as it predominantly tests the presence of normal orthonasal airflow, which is crucial for evaluating NAIM rehabilitation. Furthermore, the SOIT includes odorants familiar to a Scandinavian population and has demonstrated satisfactory reliability and validity in earlier clinical use [45].

Neurophysiological tests

It is also possible to measure the olfactory function using neurophysiological tests. These are methods for studying the effects of odorants on human electrophysiological responses by using an olfactometer. Two examples are the Human Electro-Olfactogram (HEOG) and the Olfactory Event-Related Potential (OERP). Results from scientific evaluations are conflicting. According to Doty [49] these methods are not yet as reliable as the psychophysical methods for olfactory measuring but can still be used in clinical research, as in a recently published study by Brämerson et al [50]. Despite poor reliability a combination of electrophysiological measures and psychophysical tests are suggested when assessing olfactory function in several disorders, such as congenital anosmia, head trauma and Alzheimer's disease [51].

AIMS OF THE PRESENT STUDY

The overall aim of this thesis was to increase our knowledge of olfactory impairment and evaluate the effect of NAIM rehabilitation, HRQL and communication in patients with total laryngectomy.

The specific aims of the present studies were:

- To examine and describe the olfactory function in Swedish patients having undergone total laryngectomy (Study I).
- To evaluate the results of repeated interventions with the odor rehabilitation NAIM (Study I).
- To assess the long-term results of olfaction training with NAIM 6 and 12 months after primary treatment (Study II).
- To assess changes in olfaction, HRQL and communication during a 3-year period in laryngectomized patients having received olfactory rehabilitation with NAIM (Study III).
- To develop a reliable and easily administered protocol to be used by SLPs in daily clinical practice to assist in early identification and improvement of patients´ NAIM technique (Study IV).

MATERIALS AND METHODS

Subjects

Patients who had undergone total laryngectomy at least five months prior to study start and living in the catchment area (i.e. western part of Sweden) were identified (n=35, Table 2). Conditions for study inclusion were a mental and physical condition good enough to cope with the intervention and a proficiency in Swedish not requiring an interpreter. Eleven patients (all men) could not participate due to poor general health (n=6); lack of motivation (n=3); and residing outside the catchment area at the time of the study (n=2). Thus, 24 patients (21 males, 3 females, mean age 68) served as subjects in study I and II.

Table 2. *Clinical data*

Characteristic	**Study patients (n=24)**	**Nonparticipating patients (n=11)**
Time since radiotherapy		
Median years (range)	9 (1-30)	8 (1-32)
Time since laryngectomy		
Median years (range)	7 (0.4-29)	10 (0.4-32)
Use of voice device or technique; n (%)		
Voice prosthesis	16 (67)	7 (64)
Electrolarynx	6 (25)	3 (27)
Oesophageal voice	2 (8)	1 (9)
Smoking; n (%)		
Ex-smoker	20 (83)	10 (91)
Smoker	1 (4)	1 (9)
Nonsmoker	3 (13)	0

The laryngectomized patients in study III and IV were initially included in the rehabilitation program from 2002 through 2005. All patients still alive (n=18) accepted to attend a follow-up appointment and participate in study III, whereas 21 of 24 patients with evaluable video documentations were included in study IV.

Furthermore, for comparison of HRQL and communication an age- and gender-matched control group with laryngeal cancer treated with radical radiotherapy and preserved larynx was recruited from the clinical records at the Department of Otolaryngology, Sahlgrenska University Hospital, Göteborg and used in study III. The control group was only examined once. In this study EORTC QLQ-C30 results from the study group were also compared to those of a reference group, i.e. a random sample of 234 men aged 70-79 in the Swedish population drawn from a population-based registry (SEMA) including all Swedish inhabitants born between 1918 and 1979 [52]. Summary information about study I, II, III and IV are shown in Table 3.

Table 3. *Type of studies, patients, methods and analyses in study I-IV*

Type of study	Patients	n (male/ female)	Mean age (Range)	Methods	Analysis
I Intervention	Study patients	24 (21/3)	68 (53-83)	Flexible nasal endoscopy	Olfactory obstruction
	Nonparticipating patients	11 (11/0)	72 (51-84)	Semi-structured interview	Olfactory function
				Larynx bypass	"
				SOIT	"
				Manometer	NAIM feedback
				Video	"
				Questionnaire:	
				QOTA	Olfactory function
				EORTC	Global QoL/Senses
				HAD	Mental distress
				S-SECEL	Communication
II NAIM follow-up				SOIT	Olfactory function
				Manometer	NAIM feedback
				Video	"
6 months	Study patients	23 (20/3)	68 (53-83)	*Questionnaire:*	
12 months	Study patients	24 (21/3)	69 (54-84)	QOTA	Olfactory function
				EORTC	Global QoL/Senses
				HAD	Mental distress
				S-SECEL	Communication
III NAIM follow-up				SOIT	Olfactory function
				Video	NAIM feedback
36 months	Study patients	18 (15/3)	71 (57-83)	*Questionnaire:*	
				QOTA	Olfactory function
	Control patients	18 (15/3)	72 (52-82)	EORTC	HRQL
				HAD	Mental distress
				S-SECEL	Communication
IV NAIM Evaluation	Study patients	21 (18/3)	68 (59-83)	Revised protocol (Hilgers et al 2002)	NAIM evaluation
				Videotape	"

Examinations

Clinical examinations were performed by speech-language pathologists at five different hospitals (Sahlgrenska University Hospital; Södra Älvsborg Hospital; Kärnsjukhuset, Skaraborg Hospital; Norra Älvsborg Hospital; Varberg Hospital) in the western part of Sweden. Collection of data was carried out at the Department of Otolaryngology, Head and Neck Surgery, Division of Logopedics and Phoniatrics, Sahlgrenska University Hospital, Göteborg.

Pre-inventory interview

Pre-inventory a semi-structured interview was conducted by SLPs at the first study visit. It comprised two questions on patients´ self-estimation of olfaction and gustation before and

after laryngectomy and, in addition, one question about deterioration of olfaction and gustation after laryngectomy. The patients were also asked whether they used any technique to influence the ability to smell. Whenever possible video documentation was used at the pre-inventory interview and repeatedly at each rehabilitation session (Study I), as well as at long-term follow-up (Study II and Study III).

Pre-inventory flexible nasal endoscopy

All patients underwent a flexible nasal endoscopy to rule out nasal obstruction that could prevent nasal airflow to stimulate the olfactory epithelium in the nasal cavity. Anatomical and neurological deficits that might interfere with lip closure, intra- and extraoral mobility or swallowing were evaluated.

Assessment of olfaction

Olfaction was tested before intervention with a larynx bypass. An odor was brought to the first visit by the patient (a well-known odor e.g. perfume or after shave), which was applied in front of the nose while a nasal airflow was induced by means of a larynx bypass [14]. Olfaction was also tested with the odor identification test SOIT.

The SOIT

The SOIT consists of 16 different odors (pine-needle, peppermint, juniper berry, violet, anise, clove, vanilla, almond [bitter], orange, cinnamon, lemon, lilac, vinegar, tar, ammonia, and apple) with 4 response alternatives per odor to choose from with no time limit for answering procedure (Figure 8). Three of the odors - peppermint, vinegar and ammonia – are trigeminal stimulants. The smell consists of five milliliters of odor stimulus placed in a 10 ml glass jar. The test has age- and gender-related cut-off scores (Table 4). According to results of the sense of smell patients can be categorized as having normosmia, hyposmia or anosmia. The SOIT was used at each of the three intervention sessions (Study I) and at long-term follow-up (Study II and III) for testing olfactory acuity and intervention results (Figure 9).

Figure 8. *The Scandinavian Odor Identification Test developed by Nordin et al [45]. Photo taken by Jan Persson*

Figure 9. *Olfaction tested with SOIT Photo taken by Jan Persson with the permission of the patient*

Table 4. *SOIT. Olfactory diagnoses dependent of age- and gender cut-off scores [45]*

Age (years)	Normosmia	Hyposmia (-2SD)	Anosmia (-4SD)
15-34	13-16	10-12	< 9
35-54	12-16	9-11/10-11 *	< 8/< 9 *
55-74	11-16	8-10	≤ 7

* Men/women

Video recordings

Video recordings of the NAIM technique were made in studies I, II and III on Mini Digital Video Cassettes (FujiFilm, Japan) with a Sony DCR-PC8E video camera (Sony Corporation, Japan) in a clinical setting. For best visualization patients´ NAIM performance was recorded in lateral position. The recordings were used for real-time biofeedback during olfactory training and follow-up sessions (studies I, II and III), and for evaluation of different aspects and overall performance of the NAIM (Study IV).

In study IV video samples of >10 seconds in random order from the first (baseline) and third (after treatment) intervention sessions and from follow-up 6 and 12 months after primary intervention were evaluated. Raters were three SLPs educated and trained in NAIM rehabilitation and with many years professional experience working with laryngectomized patients. Prior to evaluation, the raters attended a training session to become accustomed to the protocol and the response alternatives. Evaluation was made on a protocol sheet, one for each video sample.

Olfactory rehabilitation

The olfactory rehabilitation (Study I) consisted of restoring sense of smell with the NAIM. Aim of the maneuver is to create orthonasal airflow through the nose by creating a negative pressure in the oral cavity and oropharynx, while keeping the lips closed, the soft palate relaxed and simultaneously actively lowering the base of the tongue and the floor of the mouth. This could easiest be explained as an extended polite yawning. A water manometer (Figure 10) was consistently used for real-time visual feedback during practice and long-term follow-up (Study I and II). The manometer training was performed correctly when the fluid fluctuated in the manometer and moved towards the nose of the patient. For memorizing the technique the patients received a written program with instructions on the NAIM technique and how to perform the maneuver with the manometer. The patients were instructed to actively use the maneuver as often as possible between interventions and to try to integrate the NAIM technique into daily life situations. The manometer in our study, accepted for use in Sweden, was designed by a Swedish SLP (Claes Österlind) involved in the study.

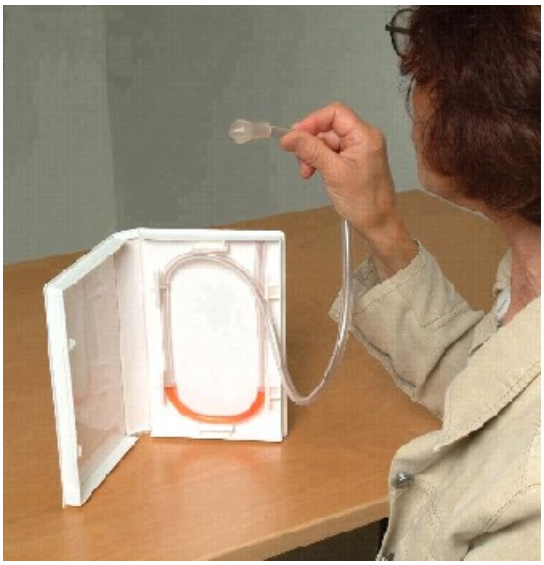

Figure 10. *Manometer with nose tube and colored water for better visualization of the movement. Photo taken by Jan Persson*

Questionnaires

Patients completed all questionnaires during each clinical session.

Questionnaire on Odor, Taste and Appetite

The Questionnaire on Odor, Taste and Appetite (QOTA) [53, 54, 55] (Study I, II and III) consists of several multiple-choice questions addressing the situation both before and after laryngectomy as well as the present situation.

Questions are divided into five scales: 1) present odor perception (POPS, 3 items, score range from 3 to 15); 2) present odor perception compared with past (3 items, score range from 3 to 15); 3) present taste perception (8 items, score range from 8 to 40); 4) appetite (6 items, score range from 6 to 30); 5) daily feelings of hunger (9 items, score range from 9 to 45). A low score indicates bad function or that these scales have deteriorated compared to pre-operative or previous test situations. Conversely, a higher score indicates good function or improvement in these domains.

The QOTA questionnaire was translated into Swedish in 2002, using a formal method of forward-backward translation by two independent bilingual translators. The wording of some of the items in the final QOTA version was slightly modified to avoid ambiguity in Swedish. The translated Swedish version has been pre-tested in 22 laryngectomized patients and none found the questions upsetting, disturbing or hard to understand [56, unpublished data]. Translation was carried out with permission from the authors [55].

EORTC QLQ-C30 and QLQ-H&N35

The European Organization for Research and Treatment of Cancer (EORTC) study group on quality of life has developed a modular measurement system for evaluating health-related quality of life in cancer patients. We used the EORTC QLQ-C30 (Study I, II and III) consisting of 30 questions to assess the patients´ general physical and psychosocial functioning and symptoms [57, 58]. This questionnaire incorporates five functional and three symptom scales, a global QoL scale, and six single items.

To address additional symptoms we used the EORTC QLQ-H&N35 (Study I, II and III), a supplement to the QLQ-C30 consisting of questions relevant to head and neck cancer patients [59, 60]. Both the QLQ-C30 and the QLQ-H&N35 have demonstrated good reliability and cross-cultural validity. These questionnaires can distinguish between patient groups differing in clinical status, as well as detecting changes in patients over time. All scale and item scores range from 0 to 100, where higher scores for functioning scales and global quality of life represent better functioning. For symptom scales and items a higher score corresponds to more severe symptoms. In general, score changes over time of at least 10 points could be interpreted as indicating clinically important changes [61]. In study I & II only the scales and items most relevant for smell and taste are presented (i.e. global quality of life scale, senses scale and single items for taste and smell).

HADS

The Hospital Anxiety and Depression Scale questionnaire (HADS) is a tool detecting mood disorders in somatically ill patients [62] and has frequently been used in cancer studies, for example lung cancer [63] and head and neck cancer [64, 65]. The two-factor structure has been confirmed in many studies [66, 67]. The Swedish version has been documented in a study by Sullivan et al [68]. HADS consists of 14 items on a four-point response scale ranging from 0-3. The summary scale scores for anxiety (7 items) and depression (7 items) thus range from 0-21. Each person is also grouped according to a clinically tested classification of psychiatric morbidity. A scale score < 8 is within the normal range, a score 8-10 indicates a possible and a score >10 indicates a probable mood disorder.

S-SECEL

The original Self Evaluation of Communication Experiences after Laryngectomy (SECEL) was developed to assess communication dysfunction in laryngectomized patients and has demonstrated satisfactory psychometric properties [69]. The Swedish version (S-SECEL) was adapted for use in patients receiving different treatments for laryngeal cancer. It has proved to be reliable and shown both convergent and discriminant validity, as well as, satisfactory internal consistency [70, 71, 72, 73]. S-SECEL consists of 35 items addressing communication experiences and dysfunction in patients receiving different treatments for laryngeal cancer. Thirty-four of the items are aggregated into 3 subscales to measure general (5 items; score range 0-15), environmental (14 items; score range 0-42) and attitudinal (15 items; score range 0-45) communication experiences, as well as a total scale (score range 0-102). Each item is rated on a four-point scale ranging from 0 (never) to 3 (always) and addressing the last 30 days. Scoring of subscales and a total scale is carried out by simple addition (0-102). A higher score indicates greater perceived communication dysfunction. Item no. 35: “Do you talk as much now as before your laryngeal cancer?” is answered by three response categories (Yes/More/Less), and is not included in the scoring system. Appendix I.

NAIM protocol

The NAIM protocol used in study IV is a revision of the original protocol used by Hilgers et al [74]. The original protocol consisted of only dichotomized variables (Yes/No) that may lack in both sensitivity and reliability. For example, when evaluating item *lowering floor of the mouth* a positive score could represent a perfect execution as well as a partially acceptable

execution. With the purpose of increasing the sensitivity to detect change we therefore revised the protocol by adding response options wherever possible.

Response alternatives are Totally correct/Partly correct/Totally incorrect (question 1a and 2) and Tense/Partly tense/Relaxed (question 1d). Response alternatives for items 1b-c are dichotomized (Yes/No). Calculated scores range between 0-22 (item 1a-d) and 0-2 (question 2), with higher scores representing better NAIM technique. Appendix II.

STATISTICAL ANALYSIS

Study I, II and III

As data in our studies were on ordinal scale level and not normally distributed we have only used nonparametric tests. Pearson correlation coefficient was calculated for all correlation analyses and formally tested with Pitman´s nonparametric permutation test. For comparison between groups the Fisher nonparametric permutation test was used. For comparison over time within groups the Fisher nonparametric permutation test for matched pairs was used. The subjects were their own controls. All tests were 2-tailed and conducted at a 5% significance level [75]. When estimating clinical significance in the EORTC questionnaires, changes over time within the study group and differences in mean scores between groups were assessed according to recommendations by Osoba, where a difference in HRQL scores of 10 points or more is regarded clinically significant [61].

Study IV

For comparison between groups Wilcoxon´s paired sign rank test and Sign test were used and conducted at a 5% significance level. The interrater reliability of the perceptual evaluations of questions 1-11 in the protocol was calculated with Spearman's rank order correlation coefficient (Spearman rho). This coefficient calculates a value from -1 to +1. The higher the positive value is the better interrater reliability. Cohen's kappa was used for measuring intrarater reliability of questions 1-11 in the protocol. A kappa coefficient < 0.20 indicates that agreement between raters is non-existing or very low; 0.21-0.40 low; 0.41-0.60 moderate; 0.61-0.80 good; and 0.81-1.00 very good [76].

ETHICS

The studies were approved by the Ethical Committee for Human research at Sahlgrenska University Hospital and were conducted in accordance with the Declaration of Helsinki.

RESULTS

Study I

The purpose of this study was 1) to examine and describe olfactory function in Swedish patients having undergone total laryngectomy, and 2) to evaluate the results of repeated interventions with the odor rehabilitation NAIM. All patients reported having normal sense of smell before laryngectomy. After laryngectomy, before NAIM intervention, olfactory testing with a larynx bypass enabling orthonasal airflow revealed that only 5 patients were unable to smell with the tube. However, a majority of the patients considered their sense of smell to have deteriorated compared to pre-surgery.

According to SOIT, 18 of 24 patients (75%) had impaired sense of smell before NAIM rehabilitation (baseline). After NAIM rehabilitation 72% with impaired sense of smell improved (Figure 11). Of the 14 non-smellers, 7 converted to smellers after only one intervention session, resulting in a success rate of 50% after a single session. Of the remaining 7 non-smellers, 3 converted to smellers after repeated sessions, while 4 non-smellers showed no improvement. Moreover, 75% of the patients with hyposmia converted to normosmia after 1, 2 and 3 interventions, respectively. Of the 5 patients with larynx bypass not able to smell before intervention, 2 were categorized as smellers after NAIM rehabilitation. The SOIT score significantly improved ($p=0.005$) for non-smellers after intervention. In addition, the non-smellers' subjective estimation of their olfaction and gustation were significantly higher compared to before treatment ($p<0.001$ and $p=0.02$ respectively). Although not statistically significant, non-smellers showed an improvement according to the smell item on QLQ-H&N35. In addition, based on their subjective estimation smellers had significantly better sense of smell ($p=0.03$), and significantly better appetite ($p=0.03$), and taste ($p=0.47$) according to QOTA.

Study II

The aim of this study was to assess long-term results of the NAIM by re-examining the patients 6 and 12 months after primary rehabilitation. One patient could not be examined at the 6-month follow-up due to concomitant disease but participated in the 12-month follow-up (Figure 11).

At the 6-month follow-up 83% were smellers. Based on their subjective estimation both non-smellers and smellers had significantly better sense of smell at the 6-month follow-up ($p< 0.001$ and $p=0.004$, respectively) compared to before intervention. However, sense of smell according to SOIT scores was significantly better only for non-smellers ($p= 0.004$).

At the 12-month follow-up rehabilitation results were further improved, with only 3 patients (12%) remaining non-smellers (Figure 11). Again, according to their subjective estimation, both non-smellers and smellers had better sense of smell at the 12-month follow-up ($p=0.004$ and $p=0.003$, respectively) compared to pre-intervention. Furthermore, 88% were active users of the NAIM with 8 patients using it on a daily basis, 7 using it frequently but not daily, and 6 patients using it infrequently. The 3 patients never having used NAIM prior to the 12-month follow-up were all non-smellers.

Study III

The purpose of this study was to assess long-term results in laryngectomized patients concerning olfactory function, HRQL and communication 36 months after primary NAIM rehabilitation (study group n=18). In addition, we wanted to compare results between the study group and an age- and gender-matched control group (i.e. patients with laryngeal cancer with preserved larynx, control group n=18)

SOIT and QOTA

According to SOIT scores, 78% of the study group was categorized as smellers (Figure 11). Twelve of the 18 patients (67%) used the NAIM technique “automatically”, i.e. on a daily basis.

Comparison between the study group and the control group showed that the controls had significantly better sense of smell according to both SOIT and QOTA scores ($p<0.001$ and $p<0.001$, respectively).

EORTC QLQ-C30 and QLQ-H&N35

In general, the score values within the study group were stable over time. However, between group comparisons showed significant differences regarding *Sleep disturbances* and *Senses scale* with less problems in the control group and *Sexuality* with less problems in the study group.

HAD

At all measurement points the study group reported stable and low score values regarding anxiety and depression and no differences were found when compared to the control group.

S-SECEL

There were no significant differences in S-SECEL scores for the study group over time with most communication problems found in the Environmental scale. When dividing the study

group into smellers and non-smellers the total score values showed a deterioration of the communication in non-smellers over time whereas smellers improved. The study group, as a whole reported more problems with speech and communication than the control group (Table 6).

Table 6. *Mean (CI) S-SECEL scores from baseline to 36 months after treatment in study group and control group*

	Mean (95% CI) Score				
S-SECEL	**Study group (n=18)**			**Control group (n=18)**	**p value study/ control**
	Baseline	**6 mo**	**36 mo**		
General*	4.2 (3.0-5.5)	4.8 (3.4-6.3)	4.3 (3.2-5.5)	3.8 (2.8-4.9)	0.55
Environment*	13.4 (11.0-15.9)	12.4 (9.5-15.4)	14.8 (10.7-18.9)	7.6 (4.8-10.4)	0.006
Attitudinal*	7.4 (5.2-9.6)	7.8 (4.3-11.4)	10.7 (6.8-14.7)	1.7 (0.5-2.8)	<0.001
Total*	25.1 (20.2-29.9)	25.1 (19.1-31.2)	29.8 (21.7-37.9)	13.1 (9.2-16.9)	<0.001

Abbreviations: CI =Confidence interval; S-SECEL The Swedish Self-Evaluation of Communication Experiences after Laryngeal Cancer.
*Minimum-maximum: 0-15 (General), 0-42 (Environmental), 0-45 (Attitudinal), and 0-102 (total), low value = better communication
p-value significant at < 0.05, comparison between study group at 36 month and control group

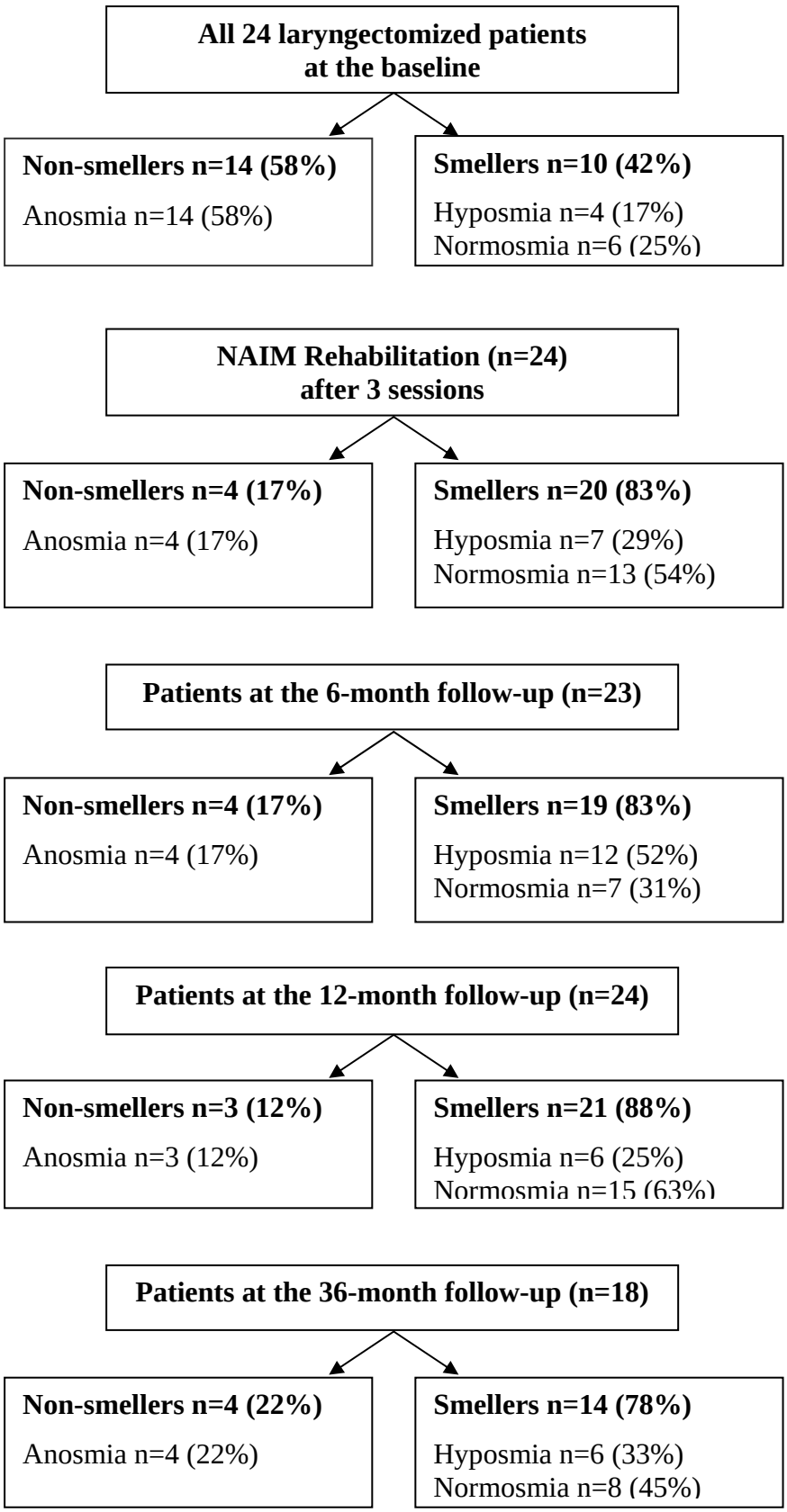

Figure 11. *SOIT results before and after treatment and at 6, 12 and 36 months follow-up*

Study IV

The aims of this study were to: 1) assess variables important for effective execution of the NAIM and 2) develop a structured NAIM protocol for these evaluations to be used by SLP in daily clinical practice.

When assessing execution of the NAIM technique using the protocol a significant improvement compared to baseline was seen throughout the study. The improvement in olfactory technique at different measurement points after intervention was shown both in the summary scores of the first 11 NAIM protocol variables and for the overall technique (item 12). Key variables such as *lowering floor of mouth* and *lowering jaw* improved most. In addition most patients also normalized their breathing over time. Significant improvements in olfactory function compared to baseline were also seen according to SOIT scores (Table 7).

Table 7. *Mean (SD) NAIM and SOIT scores at baseline, after treatment, and at 6 and 12 months follow-up*

	Baseline	**After treatment**	**6 mo**	**12 mo**
NAIM / 1-11*	11.84 (3.69)	13.85 (3.73)	13.85 (3.93)	15.12 (3.06)
p†	…	0.009	0.029	0.001
NAIM / 12**	0.29 (0.46)	0.76 (0.54)	0.86 (0.57)	1.19 (0.60)
p†	…	0.008	0.005	0.001
SOIT	8.86 (2.58)	10.14 (3.23)	9.86 (3.28)	11.57 (3.43)
p†	…	0.015	0.046	0.002

* Minimum -maximum 0-22; ** Minimum-maximum 0-2, for item scoring see Appendix II.
Higher scores = better NAIM function
† Wilcoxon signed rank test, comparison to baseline data

GENERAL DISCUSSION

Impaired olfactory function

One of the major findings in study I was the high prevalence (75%) of impaired sense of smell in patients after total laryngectomy. This finding was independent of time since the operation and in concordance with studies previously described [7, 8].

All 24 patients in our study reported an impaired sense of smell after laryngectomy compared to pre-surgery. However, since olfaction was not measured before the operation these results were not objectively confirmed. In future studies we therefore suggest, as part of the pre-operative examination, systematical psychophysical olfactory testing before laryngectomy to identify patients´ sense of smell.

Other factors that might influence the olfactory capacity are age, gender, smoking, chemo- and radiotherapy. Several studies [23, 25, 77] report an age- and gender-related olfactory dysfunction, especially in elderly people and males. These are factors that probably are relevant also in our study as a majority of the patients were men and over 60 years of age. Furthermore, radiotherapy and exposure to cytostatic drugs might adversely influence the sense of smell [78, 79]. However, the radiation field in laryngeal cancer patient does not involve the olfactory epithelium, which makes any influence on sense of smell in these patients less likely. Whether or not tobacco smoking affects sense of smell is subject for controversy. Some studies have shown negative effects [26, 80] on the olfactory function whereas others [25, 81] have found no such effect.

Olfaction results from NAIM intervention and long-term follow-up

A second important finding in study I was the improvement in olfactory function after NAIM rehabilitation in 72 % of patients with anosmia and hyposmia. After only one intervention session 50% of the non-smellers converted to smellers, this is in line with results also found by Hilgers et al [6]. Despite these promising results, Hilgers et al [6] discussed the possibility if more intervention sessions would further improve the rehabilitation results. Hence, our rehabilitation program was designed to include three interventions within six weeks. This extended program proved advantageous as we did note further improvement in the olfactory function following the second and third intervention session.

In study II and III we confirmed that our treatment regime results, with repeated NAIM-interventions persist 12 and 36 months later. The percentage of smellers was very similar post-treatment in study I (83%) to those in study II (88%) and III (78%). These results are, to some extent, better than those published by Hilgers et al [74]. However, the studies are not

totally comparable as the study design by Hilgers et al, with a single intervention session and one follow-up visit between 4 and 24 months post-intervention differed from ours. Furthermore, we used different olfactory tests. The identification olfactory test SOIT used by our research group seems more discriminatory than the Smell Diskettes olfactory test [46] used by Hilgers et al, due to the use of more test stimuli (16 instead of 8) and with four verbal alternative responses instead of three picture-verbal alternatives. Moreover, the Smell Diskettes olfactory test is only categorizing the patients into two groups (normosmia and hyposmia/anosmia), whereas the SOIT also recognizes hyposmic patients, probably making it more suitable for evaluating NAIM rehabilitation over time.

During follow-up, however, there was a fluctuation in the level of sense of smell. In study II, at the 6-month follow-up, the number of patients with normosmia was nearly halved compared to post-intervention results (30% vs. 54%). This might be explained by problems with the NAIM technique or in the implementation of NAIM in daily life and the rather long period between the intensive training episode and the first follow-up. According to Hilgers et al [74], a correct execution of the NAIM is important for creating a sufficient orthonasal airflow leading to improved olfactory function. As with other aspects of post-laryngectomy rehabilitation (e.g. voice, pulmonary status) repeated and intensive training is necessary to gain full control of the technique. It is important for the patient to understand that the NAIM is an active process that needs to be incorporated in the daily activities to reach as normal a sense of smell as possible. Consequently, the increase in number of patients with normosmia, may depend on repetition and improvement of the NAIM technique after follow-up at 6 and 12 months.

Evaluation of treatment

Olfactory test

For several reasons we used the Scandinavian Odor Identification Test (SOIT) when evaluating the NAIM treatment. The SOIT has demonstrated satisfactory reliability and validity in clinical use [25, 45], it includes odorants familiar to a Scandinavian population, and it predominately tests the orthonasal airflow, which is crucial for evaluating NAIM rehabilitation. Based on results from study I, II and III we found the SOIT to be easy to perform, well accepted and the best Scandinavian option when testing olfactory function after NAIM rehabilitation in laryngectomized patients. We therefore recommend the use of SOIT in Scandinavian NAIM rehabilitation programs in laryngectomized patients.

Questionnaires

For evaluation purposes in clinical research it is important to use questionnaires with good psychometric properties. One of the most commonly used validated HRQL instruments are the EORTC questionnaires. However, some studies highlight the need to add more disease specific questionnaires when measuring HRQL, communication and olfaction, especially in laryngectomized patients [73, 82, 83]. Therefore, we complemented the EORTC questionnaires with the QOTA and the S-SECEL. Results from our studies confirm the need for such specific questionnaires in laryngectomized patients.

An interesting finding according to EORTC-H&N35 was the lack of a significant difference in olfaction (the Senses scale; "Problems with smell" and "Problems with taste") between the study group and the control group. We agree with Bindewald et al who suggested that these two items should be analyzed separately since the scale has previously shown low internal consistency [59, 84]. This would be especially relevant in laryngectomized patients due to the varying meaning of the questions for these patients. According to recent studies impaired sense of smell is associated with a deteriorated quality of life [85, 86]. Even if we could not confirm an association between olfaction and HRQL when measured with the EORTC questionnaires, both smellers and non-smellers reported improved quality of life when interviewed about the importance of olfactory rehabilitation in daily situations. All patients stressed the importance of regaining both pleasant and unpleasant odors, e.g. odors in nature, when dealing with food and cooking, and personal hygiene. Furthermore, both smellers and non-smellers seemed motivated to apply NAIM when olfactory training was integrated in daily life and the learning effect was positive and remained even after a long period of time. The six patients in study III who did not use the NAIM regularly were two smellers and four non-smellers. The two smellers reported good olfaction acuity and one of them explained that he was a smeller as a consequence of using oesophageal voice, the other claimed to have a smelling technique of his own similar to the NAIM. Reasons for the non-smellers not to use the NAIM were finding it too conspicuous in public, difficult to apply, bad motivation to learn or poor general health.

One could expect the study group with alaryngeal communication to score higher on the QLQ-H&N35 Speech scale than the control group with laryngeal communication but our results indicated no significant difference. However, the S-SECEL questionnaire indicated to be more sensitive to differences between the alaryngeal speakers with higher levels of reduced conversational abilities than the laryngeal speakers treated with radical radiotherapy. This may be explained by the fact that everyday communication requires adaptation to background noises which are unfavorable to laryngectomized patients, e.g. in a bus or a car,

at a party or over the telephone. In addition, patients categorized as smellers seemed to judge themselves as more successfully rehabilitated regarding communication compared to non-smellers. The three patients who were non-smellers throughout study I-III also demonstrated the highest levels of communication dysfunction among the study patients.

Results from both groups on the HAD scale corresponds well to other studies with laryngeal cancer patients [73, 83, 87]. Only one of the study patients, who had swallowing and communication problems, exceeded the cut-off value (>10) for depression at the 36-months follow-up.

In conclusion, our study group proved to have HRQL scores comparable to those of the controls and better than those reported in previous studies after total laryngectomy [39, 82, 88, 89]. Somewhat surprisingly, both the study group and the control group also reported better HRQL compared to reference data from a general age-matched Swedish population sample [52]. One reason for this may be the time interval between treatment and start of the study which allowed our study patients to recover from anatomic and functional alterations. Additionally, it can be speculated that the improved rehabilitation program now available after total laryngectomy affects HRQL positively (e.g. voice prostheses, hands-free and HME devices).

NAIM protocol

One of the major findings in study IV was that raters were able to reliably evaluate performance of the NAIM technique over time using our revised NAIM protocol. A second important finding was that certain movements, e.g. *closing lips*, *lowering floor of mouth* and *jaw* and *normal breathing*, seem to be more important than others for a successful olfactory rehabilitation with NAIM. There are several reasons for using a protocol in clinical practice, one being to observe and follow performance of such key variables throughout the rehabilitation program. Another reason is to use the protocol to assist in early identification and improvement of the patient´s NAIM technique irrespective of the SLP´s experience working with laryngectomized patients. However, subjective ratings such as visual analyses are not enough to track technique changes but ought to be complemented with olfactory testing.

Limitations

Although the study group included all available laryngectomized patients in our catchment area at start of the study the size of the cohort is relatively small. Also, the majority of the

study group was successfully rehabilitated and had completed their therapy concerning communication, breathing and swallowing which may have influenced the HRQL.

Who will gain?

Patient selection

In accordance with our data, we conclude that the majority of the laryngectomized patients can improve their olfactory function and should be offered NAIM rehabilitation. In study I, even patients categorized as smellers post-inventory became “better smellers”. The improvement was not statistically significant, however, this might be due to ceiling-effects in the SOIT test. In addition, two of the five patients not able to smell with the larynx bypass became smellers after NAIM rehabilitation. Thus, the results from olfactory testing with a larynx bypass may indicate but not predict with certainty if a patient would benefit from olfactory rehabilitation.

Pre-operative counseling

Impaired olfaction in laryngectomized patients and, more importantly, its rehabilitation has not received as much focus as the more obvious consequences, such as changes in voice, pulmonary and swallowing function. Van Dam et al [7] reported that 50% of patients were not even informed during pre-operative counseling about post-operative changes in smell and taste. Furthermore, 91% of the laryngectomees were not given any rehabilitation instructions involving compensation for reduced sense of smell and taste. These results are in line with the outcome in our study where 42% of the patients were not pre-operatively informed about the smell and taste deficits, nor were smell and taste rehabilitation instructions given. In a study by Lennie et al [90], the laryngectomized patients wanted post-operative changes in smell and taste to be discussed during the pre-operative counseling, a finding in line with our clinical experience. Even though patients have a lot of information to cope with in pre-operative counseling, we conclude that information concerning smell and taste is a necessity.

Recommendations

If there are no complications post-laryngectomy, olfactory rehabilitation can be integrated in speech therapy and start 3-4 weeks post-operatively. One of our study patients became an excellent TE-speaker, even using a hands-free speech, during olfactory rehabilitation training. Data from our studies suggest that a minimum of three sessions is recommended, but the exact number of sessions should be in concordance with each patient´s need. Furthermore, we recommend follow-up after 3, 6 and 12 months with further NAIM training for better long-

term results. We also suggest that the number of follow-up sessions can be individualized with regard to the patients´ ability to perform NAIM. Although NAIM is an effective method for improving olfactory function the patient has to be made aware that passive olfaction never returns after total laryngectomy, and that the NAIM is an active procedure that needs repetition and intensive training to be incorporated into the patients´ everyday behavior. Video documentation and a water manometer for use in clinic and home practice are useful tools for technique improvement, making the patient aware of details disturbing the maneuver. Furthermore, we suggest the use of validated questionnaires for evaluation purposes. However, if short of time, a few questions about smell and taste repeatedly asked (i.e. before laryngectomy, before and after NAIM intervention, and at follow-up) can provide important information when combined with the objective olfaction test results.

CONCLUSION

The present studies rendered the following conclusions:

- Olfactory impairment is common in patients after total laryngectomy.
- The NAIM is a patient-friendly, easy to learn, inexpensive and effective method for restoring olfactory function after total laryngectomy.
- Long-term improvements were seen following olfactory rehabilitation with NAIM.
- Laryngectomized patients that are successfully rehabilitated regarding smell and communication had an overall good HRQL.
- We recommend that NAIM rehabilitation should be offered to all laryngectomized patients and incorporated into their routine rehabilitation program.
- An odor identification test predominantly testing orthonasal airflow and categorizing sense of smell in olfactory diagnoses, e.g. the SOIT, is suitable for assessment and evaluation of the NAIM technique after total laryngectomy.
- We suggest that validated HRQL questionnaires should be complemented with more diagnose specific questionnaires for evaluation of olfaction and communication after total laryngectomy in clinical research.
- For evaluation of the technique a NAIM protocol is helpful for the SLP to identify important NAIM variables and to assess the progress of the rehabilitation.

FUTURE RESEARCH AND GOALS

Investigation of NAIM rehabilitation prospectively - a multi-center study involving two different University Hospitals (Göteborg and Linköping) with the aim to “normalize” olfaction and gustation in laryngectomees by rehabilitation of sense of smell in direct conjunction with the post-operative rehabilitation. The study includes subjective and objective screening of patients´ sense of smell and taste pre- and post-operatively, early onset of NAIM rehabilitation and a more intensive follow-up regime

NAIM rehabilitation courses for speech language pathologists in the Nordic countries in order to incorporate the NAIM in ordinary rehabilitation programs for laryngectomized patients

Development and evaluation of a standardized video manual

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SUMMARY IN SWEDISH (SVENSK SAMMANFATTNING)

Efter total laryngektomi är övre och nedre luftvägar separerade, vilket resulterar i en rad oönskade effekter såsom avsaknad av andning via näsa och mun, nedsatt förmåga att uppfatta lukt och smak samt förlust av normal röstfunktion. Nyligen presenterades en metod kallad Nasal Airflow-Inducing Maneuver (NAIM) för rehabilitering av luktförmågan efter total laryngektomi. Målsättningen med denna studie var: 1) att beskriva luktförmågan hos laryngektomerade patienter och att mäta luktförmågan efter behandling med NAIM (Studie I); 2) att utvärdera resultaten 6 och 12 månader efter intervention (Studie II); 3) att utvärdera luktförmåga, hälsorelaterad livskvalitet (HRQL) och kommunikation 36 månader efter intervention (Studie III); och 4) att utveckla ett kliniskt protokoll för att följa förändringar i NAIM teknik över tid (Studie IV).

Studiegruppen bestod av 24 laryngektomerade patienter. Luktförmågan utvärderades med hjälp av the Scandinavian Odor Identification Test (SOIT). Utifrån SOIT resultat delades patienterna sedan in i luktare (normosmi och hypsomi) eller icke-luktare (anosmi). Patienternas självskattning av lukt, smak, hälsorelaterad livskvalitet och kommunikation utvärderades med validerade frågeformulär.

Vid lukttestning före intervention hade 18 av 24 patienter (75%) nedsatt luktförmåga. Efter 3 behandlingar med NAIM hade 72% av patienterna förbättrat sin luktförmåga. Vid uppföljning 6 och 12 månader efter avslutad NAIM behandling var 83% respektive 88% luktare enligt SOIT resultaten. Vid uppföljning 36 månader efter avslutad behandling var 78% luktare av de 18 patienter som fortfarande var i livet. Därutöver uppgav patienterna god livskvalitet. Med hjälp av ett strukturerat protokoll var det möjligt att följa förbättrad NAIM teknik över tid.

Slutsatser: Försämrad luktförmåga är vanligt hos laryngektomerade patienter (75%), rehabilitering med NAIM är lätt att lära ut och ger utmärkta långtidsresultat och bör därför inkluderas i existerande rehabiliteringsprogram. För att utvärdera tekniken är ett protokoll med NAIM variabler till god hjälp. Slutligen föreslår vi att livskvalitetsformulären kompletteras med specifika frågeformulär för analys av luktförmåga och kommunikation.

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APPENDIX I S-SECEL

INSTRUCTIONS:
Here are 35 statements about experiences with communication after a laryngectomy.
Read each of the statements carefully and place a firm tick in the box beside each question that describes you NOW or in the last 30 days.

		Always	Often	Sometimes	Never
1.	Are you relaxed and comfortable around other people in speaking situations?	☐0	☐1	☐2	☐3
2.	Would you describe yourself as a low-keyed, calm person?	☐0	☐1	☐2	☐3
3.	Are you an active, ”outgoing,” talkative person?	☐0	☐1	☐2	☐3
4.	Do you admit to the person you are speaking to that you had a laryngectomy?	☐0	☐1	☐2	☐3
5.	Do you think your speech improves with the amount of time you use it?	☐0	☐1	☐2	☐3
6.	Do you find that you frequent clubs, meetings, or lodges less often because of your speech?	☐3	☐2	☐1	☐0
7.	Do you have difficulty getting people´s attention to speak?	☐3	☐2	☐1	☐0
8.	Do you have difficulty yelling or calling out to people?	☐3	☐2	☐1	☐0
9.	Do you find that people are unable to understand you?	☐3	☐2	☐1	☐0
10.	Do you find you have to repeat things a number of times during conversations to be understood?	☐3	☐2	☐1	☐0
	Do you have trouble with speaking:				
11.	- in large groups of people?	☐3	☐2	☐1	☐0
12.	- in small groups of people?	☐3	☐2	☐1	☐0
13.	- with one person?	☐3	☐2	☐1	☐0
14.	- in different rooms of your house (apartment, residence)?	☐3	☐2	☐1	☐0
15.	- in loud or noisy places?	☐3	☐2	☐1	☐0
16.	- on the telephone?	☐3	☐2	☐1	☐0
17.	- in the car, bus or while traveling?	☐3	☐2	☐1	☐0

	Does your speech cause you to:	Always	Often	Sometimes	Never
18.	- have difficulty when attending parties or social gatherings?	☐3	☐2	☐1	☐0
19.	- use the telephone less often than you would like?	☐3	☐2	☐1	☐0
20.	- feel left out when you are with a group of people?	☐3	☐2	☐1	☐0
21.	- limit your social life or personal life?	☐3	☐2	☐1	☐0
	Does your speech cause you to feel:				
22.	- depressed?	☐3	☐2	☐1	☐0
23.	- frustrated when talking to family and friends and they can´t understand you?	☐3	☐2	☐1	☐0
24.	- different or peculiar?	☐3	☐2	☐1	☐0
25.	- Do you hesitate to meet new people because of your speech?	☐3	☐2	☐1	☐0
26.	- Do you get left out of conversations because of your speech?	☐3	☐2	☐1	☐0
27.	Do you avoid speaking with other people because of your speech?				
28.	Do people tend to fill in words or complete sentences for you?	☐3	☐2	☐1	☐0
29.	Do people interrupt you while you are speaking?	☐3	☐2	☐1	☐0
30.	Do people tell you that they can´t understand you?	☐3	☐2	☐1	☐0
31.	Do the people you speak with get annoyed with you because of your speech?	☐3	☐2	☐1	☐0
32.	Do people avoid you because of your speech?	☐3	☐2	☐1	☐0
33.	Do people speak to you differently because of your speech?	☐3	☐2	☐1	☐0
34.	Do your family and friends fail to understand what it´s like to communicate with this type of speech?	☐3	☐2	☐1	☐0
35.	Do you talk the same amount now as before your laryngectomy?	YES ☐	MORE ☐	LESS ☐	

APPENDIX II NAIM Evaluation Protocol

NAIM Evaluation Protocol

Variables used for evaluation of the NAIM technique (revised 2007 from Hilgers et al (2002))

Patient performance of NAIM variables*

	Totally correct	Partly correct	Totally incorrect
1. Lip closure	☐2	☐1	☐0
2. Lowering floor of mouth	☐2	☐1	☐0
3. Lowering jaw	☐2	☐1	☐0

	Yes	No
4. Bite gesture	☐0	☐2
5. Chewing movement	☐2	☐0
6. Facial movements	☐0	☐2
7. Doing something with stoma	☐0	☐2

Type of breathing

8. Sniffing	☐0	☐2
9. Deep	☐0	☐2
10. Normal	☐2	☐0

	Tense	Partly tense	Relaxed
11. Head/neck position	☐0	☐1	☐2

	Totally correct	Partly correct	Totally incorrect
12. Overall rating of NAIM technique**	☐2	☐1	☐0

* NAIM 1-11, execution of 11 NAIM variables, score range minimum-maximum 0-22

** NAIM 12, overall rating of NAIM technique, score range minimum-maximum 0-2