Provox® and ProTrach® HMEs

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1 Products

This literature review concerns the Provox Heat and Moisture Exchanger (HME Normal, HiFlow and XtraHME), Provox FreeHands HME Flow,), Provox FreeHands HME Moist, Provox FreeHands FlexiVoice, Provox Micron HME, ProTrach XtraCare HME, ProTrach DualCare HME, ProTrach HME DigiTop and the HME DigiTop O_2 and related accessories all manufactured by ATOS Medical, and devices that are similar to the new Provox Micron HME that combine the HME function with a Filter (HMEF manufactured by GE Healthcare and HUMID-VENT manufactured by Gibeck).

The searches were conducted using these product names as keywords and using their generic names as keywords in the Medline search engine and Cochrane library. Additionally, our own company database with publications on these products was screened for relevant publications.

2 Introduction

During a total laryngectomy, the entire larynx is removed, which leads to a permanent disconnection of the upper and lower airways and a permanent tracheostoma in the neck (see Figure 1). These anatomical changes lead, among other things, to changes in voice production, breathing, and olfaction. In this review the changes in breathing after a total laryngectomy and the influence of HMEs on pulmonary and psychosocial functioning are discussed.

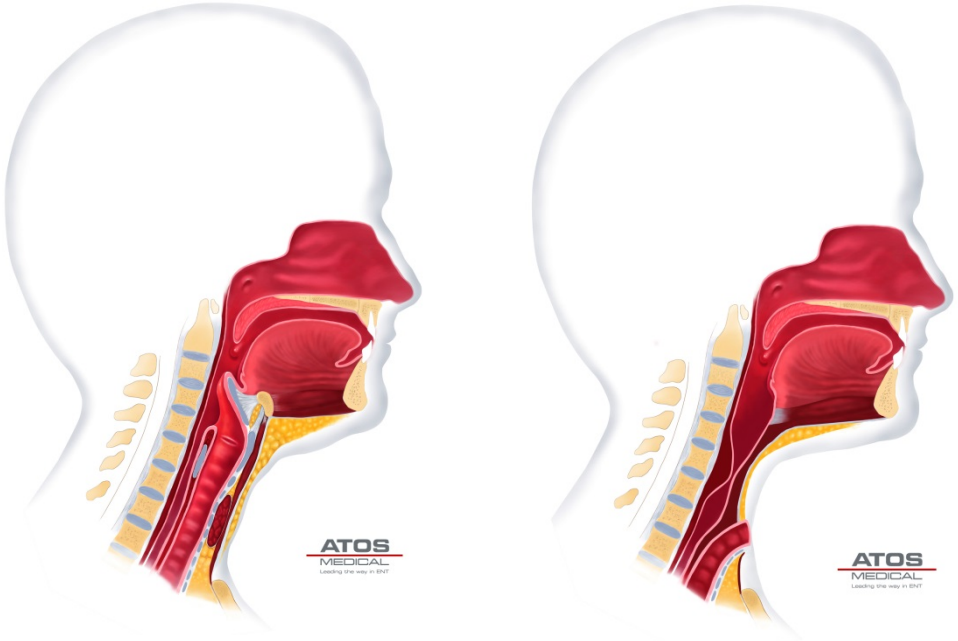

Figure 1 Schematic drawing of normal anatomical situation (A) and the anatomical situation after total laryngectomy (B). In the normal situation the patient can inhale and exhale through the nose and mouth. After total laryngectomy, the upper airways are bypassed and breathing takes place through the tracheostoma in the neck.

A tracheotomy – the creation of a temporary or permanent tracheostoma (see Figure 2) – is performed for different indications than a laryngectomy, examples being upper airway obstruction or a neurological condition. Unlike the tracheostoma of a laryngectomized patient, this stoma requires a tube to ensure the connection between the lower airways and outside world stays open. However, these tracheotomized patients do not necessarily have a total disconnection of the upper and lower airway; the patency of the (connection to the) upper airway differs from patient to patient. Still,

because the resistance through the tracheostomy is much lower than through the upper airways, the upper airway will mostly be bypassed when breathing. This means that breathing is affected in a similar way as in laryngectomized patients, which is why tracheotomized patients have similar complaints and require the use of an HME as well. Therefore the respiratory consequences for laryngectomees apply to tracheostomees as well. In this review the influence of HMEs on pulmonary functioning of tracheostomees specifically is also discussed.

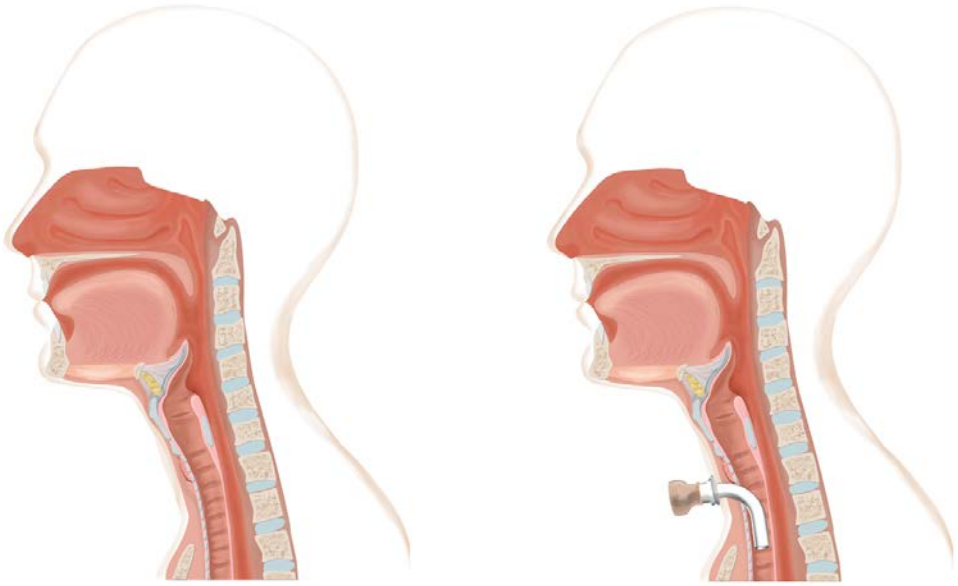

Figure 2 Schematic drawing of normal anatomical situation (A) and the anatomical situation after a tracheotomy, with a tracheostomy tube in place (B). In the normal situation the patient can inhale and exhale through the nose and mouth. After a tracheotomy, the upper airways are mostly bypassed and breathing mainly takes place through the tracheostoma in the neck.

3 Pulmonary function with a tracheostoma

3.1 Humidification and moisturization

During normal nasal inspiration of a healthy individual with an unaltered anatomy, ambient air of, for example, 22°C and 40% Relative Humidity (RH) is conditioned to 29°C and 20 mg H_2O/L (70% Relative Humidity (RH)) in the nose and is further heated to approximately 32°C and 36 mg H_2O/L (100% RH) at the subglottic level[1-4]. As the inspired air passes further through the respiratory tract it reaches the isothermal saturation boundary (ISB) at body temperature (44 mg H2O/L (100% RH) at 37°C) in the small peripheral airways[4].

After a total laryngectomy or tracheotomy, the patient breathes in and out through the tracheostoma in the neck, instead of through the nose and mouth. Therefore, the functions of the upper airways of warming, humidifying, and filtering of the inhaled air are lost, and the upper airway resistance is lost. Inspiration through a tracheostoma leads to a shift in the ISB towards more peripherally located airways, leaving a large part of the airways at suboptimal humidification levels[4]. Ambient air of, for example, 22°C and 40% RH is only conditioned to 27-28°C and 50% RH at the level of the upper trachea. Both temperature and humidity have a significant impact on the ciliary activity in the trachea. Studies in a rabbit model have shown that at body temperature (37°C) the cilia stop beating when the RH drops below 50%. If RH lowers to 60% there already is a reduction in mucociliary frequency of 30%[5, 6].

3.2 Filtration

During normal breathing, besides being humidified and heated, the inhaled air is also being filtered of all types of airborne particles, especially by the nose[7]. This filtration is important for multiple reasons. One is that the airborne spread of viral and bacterial disease requires, among other things, that infectious particles are inhaled by susceptible individuals and deposited at effective sites within the respiratory system[8]. The risk of infection is directly related to the infectious dose of a pathogen[9], the number of particles needed to start an infection. Filtration can help prevent the number of particles inhaled, thus reducing the chance the infectious dose is reached. The other reason that filtration by the upper airway is important, is that not only airborne bacteria and viruses are filtered, but also other particles such as allergens, pollen, dust and Particulate Matter (PM)[7]. PM refers to small ambient airborne particles from various sources[10-13] and is the pollutant that affects the most people worldwide[14]. It is the most harmful fraction of air pollution[15] and has no threshold below which it is not harmful[16]. Even exposure at levels below the latest standards contributes to hospital admissions, ER visits, and is linearly associated with all-cause mortality[17-21]. Literature suggests that a reduction in exposure to PM can be expected to improve health almost immediately and that this should be taken into account for cost-benefit analyses, as PM has also been shown to place a heavy burden on worldwide healthcare financially[21, 22]. The filtration of air is a complicated subject and depends for example on tidal volume, breathing frequency, air flow velocity, and diameter of particle size[8, 23]. In laryngectomees and tracheostomees, the filtration function of the upper airways is lost due to tracheostomal breathing. This means they are expected to have a much higher deposition of all types of particles in the lower airways, which is why they would be at higher risk of respiratory infections or the consequences of other inhalable airborne particles, such as PM.

3.3 Effects of lost functions of the upper airways

Breathing through a tracheostoma and the loss of the upper airway functions lead to a wide range of pulmonary complaints such as coughing, excessive sputum production, crusting, and shortness of breath[24-30]. A large number of patients (54%) complain of increased chest infections[31], which is most probably due to the loss of the upper airway functions of heating, humidification and filtration as well. Extensive histological changes (squamous metaplasia of the respiratory ciliary epithelium and chronic inflammatory changes of the lamina propria) have been observed in the trachea at the level of the carina[32, 33]. The pulmonary symptoms develop and increase during the first 6 to 12 months after initial surgery and then tend to stabilize[24, 34].

Laryngectomized patients experience the physical consequences of having a stoma (frequent phlegm production from the stoma and its interference with social activities) as the most severe side effect of their surgery[35]. The respiratory symptoms significantly affect the quality of life of the patient: correlations were found between the respiratory symptoms and perceived quality of voice, aspects of daily life, anxiety and depression[29]. As tracheotomized patients represent a more varied group than laryngectomees – due to a large variety of indications for tracheotomy and a much larger distribution in age – there is no literature looking at the quality of life or social consequences of surgery for *all* tracheostomees. However, due to the similarity in the alteration of the anatomy and subsequent physiological changes, similar effects with regards to quality of life and social and psychological consequences can be expected.

4 HMEs

An HME has three physical properties: 1) heat and moisture exchanging capacity; 2) resistance; and to a small extent 3) filtering particles[36]. The basic component of a heat and moisture exchanger is foam, paper, or another substance, which acts as a condensation and absorption surface. In order to enhance the water-retaining capacity, the material is often impregnated with hygroscopic salts such as CalciumChloride[37]. The HMEs used for laryngectomees and tracheostomees are mostly

hygroscopic and might have been impregnated with a bactericide solution in order to control bacterial colonization[38, 39]. HMEs add a flow rate dependent resistance to the airway resistance. The outcomes of studies that have measured the airflow resistance of HMEs are not consistent[38, 40, 41], but in general, the airflow resistance of an HME is lower than the airflow resistance of the nasal airway. The effect of the increased resistance (compared to stoma breathing without HME) in laryngectomees is still poorly understood[36]. With regards to the filtering function, it is believed that HMEs filter out larger particles to a small extent, but , due to their large pore size, do not filter microorganisms, pathogens or other small particles to a significant degree[36].

5 Benefits of HME use

In 1960, Toremalm described the benefits of HME use for tracheotomized patients: in comparison to nasal breathing, a person breathing through a tracheostoma loses about 500 ml of water. By using an HME it is possible to retain 250 to 300 ml of this water loss in the respiratory system[42, 43]. In the early seventies, the use of Heat and Moisture Exchangers for conditioning of the inhaled air during anaesthesia is described[44, 45].

In 1990, Ackerstaff and colleagues were the first to publish results on the use of an HME in laryngectomized patients[46]. They studied the influence of an HME on respiratory symptoms in 42 laryngectomized patients. The HME (Stomvent) was found to significantly reduce sputum production, reduce forced expectoration in order to clear the airways, and reduce stoma cleaning after using the device for 6 weeks[47]. This reduction in respiratory symptoms led to an improvement in quality of life; symptoms of fatigue and malaise decreased significantly and social contacts improved[47]. Patients using a tracheoesophageal voice prosthesis benefited less from the device used in this study than patients using esophageal or artificial larynx speech since they experienced difficulties in occluding the device for speaking[47]. The HME and baseplate tested in this study could not be separated which led to a relatively large number of problems with loosening of the adhesive due to coughing[47]. Also, with this kind of HME the device will always need to be removed for stoma and tracheoesophageal voice prosthesis cleaning.

In a later study a device was tested in which the HME and baseplate could be separated (Freevent)[48]. Patients were randomized into a treatment (N=24) and control (N=24) group and additionally 15 patients that participated in the previous study were included to compare the two devices. The results of this study showed that the HME user group showed significant reductions in the incidence of coughing, the mean daily frequency of sputum production, forced expectoration, and stoma cleaning. Also significant improvements were found in shortness of breath, fatigue and malaise, sleeping problems, anxiety, depression, and perceived voice quality. Pulmonary function tests showed significant improvements in inspiratory flow and volume values following the use of an HME. Despite the fact that the HME and base plate could be separated, loosening as a result of coughing still occurred frequently because the stoma was still not accessible for cleaning due to two crossed plastic bars blocking the entrance. Also, this device was still difficult to occlude for tracheoesophageal speech. In a multi-centre study in the Netherlands[49] the same HME (Freevent) was tested in 59 new patients that were enrolled in the study after postoperative or postradiotherapy wound healing was complete. Patients were interviewed at 3 months and 6 months of using the HME. The results of this study showed that significant improvements over time were found for forced expectoration, perceived voice quality, social anxiety, social interactions, and in feelings of anxiety and depression.

In a study by Keck[50], it was shown that the tracheal climate rapidly changed after application and removal of an HME. The use of an HME increased the temperature from 27-28°C to 29-30°C and increased the RH from 50% to 70%.

Jones[51] compared pulmonary complaints between HME-users and a placebo group. Their results showed that the subjective respiratory parameters coughing, number of chest infections, mucus production and shortness of breath at rest were all improved in the HME group.

McRae[52] reported that the use of an HME with increased breathing resistance, approximating the normal upper airway resistance, has a positive influence on tissue oxygenation. However, the validity of their measurement technique and results have been questioned, and later research showed that there is no evidence that the use of a high-resistance HME leads to increased tissue oxygenation in laryngectomees[53]. Based on their results, Zuur[53] conclude that due to the fact that high-resistance HMEs cause patient discomfort, HMEs with a convenient breathing resistance can be the first choice.

Zuur et al.[36] reviewed the physiological rationale of HME use and included both in vitro and in vivo studies in this comprehensive overview. Lorenz and Maier[54] conducted a review that assessed the effects of HME cassettes on the conditioning of respiratory air, lung function and psychosocial problems. In both reviews, the conclusion is that an HME works mainly because of the heating and humidification of inhaled air, and that possibly the added breathing resistance and slight particle filtration further benefit the respiratory system. However, Zuur et al.[36] do elaborate that it is not expected that an HME significantly compensates for the loss of upper airway filtration of smaller particles such as bacteria and viruses; the pores of the HME filter are large and there are no effective mechanisms to help capture and trap particles. Kramp et al.[55] conclude that the use of HMEs does not effectively decrease colonization of the lower respiratory tract by pathogenic microorganisms, but that it does not endanger the health of patients through exposure to pathogenic microorganisms, either.

Icuspit et al[56] reported in their article that the use of HME devices decreases the effect of sputum production, the need for ongoing suctioning, and the formation of stomal crusting.

Benefits of HMEs in laryngectomees apply to tracheostomees as well, but there are many reports on the beneficial effects of HMEs in trachetomized patients specifically, besides the two studies by Toremalm[42, 43] that were mentioned earlier.

Primiano et al.[57] reported that a Hygroscopic Condenser Humidifier (HCH) – a different term for HME – conditioned the air in the trachea of a ventilated tracheotomized patient better than mouth breathing would have done, but not as well as nose breathing would have done.

Vitacca[58] et al. reported that in spontaneously breathing tracheotomized patients a HCH improved viscosity and coloring of secretions, prevented further bacterial colonization, heated the inspiratory flow, and helped to improve the functional outcome.

Thomachot et al.[59] showed that in spontaneously breathing tracheotomized patients, in an intensive care unit, an HME provided satisfactory heating and humidification of inspired gasses, similar to that of a heated humidifier.

Rozsasi et al.[60] reported that passive airway humidification in tracheotomized patients, with an HME, is effective within a very short time of use. Ten minutes after placing an HME on a tracheostoma, the evaporative heat exchange and total respiratory heat loss decreased significantly.

6 Provox HME – Clinical Effects

The Provox HME was developed to address the issues with the early HMEs: decreased compliance due to difficulties with adherence of the base plate and troublesome combination with a voice prosthesis. Development was guided by the remarks from patients in the two previous studies. The Provox HME consists of a separate HME cassette and a self-adhesive baseplate available in two different shapes and four different materials to accommodate different skin types in stoma shapes. The Provox HME (see Figure 3) is available in Normal and HiFlow. The HiFlow cassette has a lower resistance than the Normal cassette. The HME substance that is used is a CalciumChloride impregnated polyurethane foam. The HME has a spring type valve that can easily be occluded by finger for tracheoesophageal speech. The air openings are at the side of the HME such that possible occlusion by clothes or sheets is avoided. Removal and insertion of the HME from and into the base plate is easy and after removal the patient has open access to the stoma to clean the area and the voice prosthesis.

Figure 3 Provox HME with adhesive baseplates

In a first study by Hilgers et al.[61] the feasibility of the device was investigated in 19 patients. The results showed that all patients were positive about the valve closure mechanism. They reported that voicing was considerably facilitated and intelligibility improved. Also, the problems with loosening of the baseplate due to phlegm were much decreased. Balle et al.[62], in a study in Denmark in 18 patients found similar positive results as well after a trial period of 3 weeks. Most patients found stoma occlusion with the Provox HME easier and more hygienic, and 11 found that their speech ability and intelligibility had greatly improved. Five patients experienced less coughing and sputum production, while the others reported it was unchanged (12) or more (1). This was less good than the results in previous studies and the authors contribute this to the trial period of only 3 weeks. The majority of patients used one adhesive per day and 1-2 HME cassettes per day. Most patients did not experience a change in airway resistance (11) and 7 found it to be increased. Less skin irritation was reported for the OptiDerm adhesive.

In a long-term compliance study of the Provox HME in 69 patients from Ackerstaff et al.[63], 63% of the patients reported that voicing was facilitated, 55% reported that their intelligibility had improved, 65% reported that respiratory symptoms had diminished, 94% reported a considerable overall benefit of the device, 78% of the patients used the device on a regular daily basis, 6% used it irregularly and 16% did not use the device. There was an obvious relationship between the length of use of the device and pulmonary complaints. The longer the device was used, the more the pulmonary complaints (coughing, forced expectoration, sputum production) decreased.

These results are confirmed by similar studies in Spain[64] and the US[65] indicating that results can be expected to be similar across cultures and climates. For example, the study performed in the US[65] showed that compliance was 73%, and that 68% of the patients reported a decrease in coughing, 73% reported decreased sputum production, 60% reported decreased forced expectoration, and 52% reported decreased need for stoma cleaning. The daily cough-expectoration frequency decreased significantly. In this study, the patients also reported improvements in voice quality, pitch, loudness, and intelligibility. A study conducted in Poland[66] noted similar results. Compliance is crucial and pulmonary problems decrease significantly with HME use, and related aspects such as speech and sleeping tend to improve, regardless of country or climate. Masson et al.[67] concluded in their study conducted in Brazil that the use of an HME over a 6 week time period reduced cough and expectoration of patients; however the HME did not have any influence on the vocal quality of these laryngectomized patients.

Dassonville et al.[68] published the results of a randomized controlled trial including 60 patients, who were randomized between a control group that used no device of this type and a group equipped with the Provox HME. After 3 months of using the device, a notable improvement was found which was statistically significant with regard to cough and to bronchorrhoea, and very close to achieving significance with regard to breathing effort in the HME group.

Merol et al.[69] assessed the immediate postoperative airway humidification after total laryngectomy (TLE), comparing the use of an external humidifier (EH) with humidification through a Provox HME. In a randomized controlled trial 53 patients were randomized into the standard (control) EH or the experimental HME arm. Compliance, pulmonary and sleeping problems, patients' and nursing staff satisfaction, nursing time, and cost-effectiveness were assessed with trial-specific structured questionnaires and tally sheets. Compliance and patients' satisfaction were significantly better, and the number of coughing episodes, mucus expectoration for clearing the trachea, and sleeping disturbances were significantly less in the HME arm. This was also the case for nursing time and nursing staff satisfaction and preference. Authors concluded that the study shows the benefits of immediate postoperative airway humidification by means of an HME over the use of an EH after TLE and also underlines that HMEs presently can be considered the better and more cost effective option for early postoperative airway humidification after TLE.

A study comparing finger occlusion directly on the stoma and finger occlusion on top of the Provox HME (within patient comparison) has demonstrated that maximum phonation time and dynamic loudness range improved in the condition where the patient was occluding on top of the HME[70]. This can probably be attributed to better, airtight, occlusion and better distribution of occlusal forces (reducing force on the voice prosthesis and voice producing segment in the esophagus).

An Airway Climate Explorer for testing of temperature and humidity effects of HMEs in laryngectomized patients has been developed at the Netherlands Cancer Institute[71]. Assessments of the influence of the Provox HME in standard room conditions on tracheal temperature and humidity in laryngectomees shows that the HME modifies temperature and humidity[72]. Zuur et al.[72] concluded that "the presence of an HME increases the intra-tracheal humidity and decreases the intra-tracheal temperature. The calculated relative humidity suggests that not the moisture retention but the thermal capacity is the limiting factor for the heat and moisture exchange efficiency. Therefore, an increase in the thermal capacity may result in a further improvement in the clinically beneficial effect of the tested HME". In another study Zuur et al.[73] concluded that in a cold environment, presence of an HME significantly increases both inspiratory and expiratory temperature and humidity values. In a warm environment, however, presence of an HME has a cooling effect on the temperature while it still humidifies the inspired air[4]. A further study on endotracheal temperature and humidity completed by Scheenstra et al.[74] found that an HME leads to a shortened Inhalation Breath Length which enhances the HME effect. Scheenstra et al.[75] conducted another study of endotracheal

temperature and humidity and tidal volumes in 11 laryngectomized patients with Provox HME Normal, Provox HME HiFlow, and without HME. Both HMEs significantly improved tracheal climate. The Normal HME has better moistening properties and a small but significant positive effect on tidal volume. Therefore, if the higher resistance is tolerated, the Normal HME is the preferred pulmonary rehabilitation device. The HiFlow HME is indicated if lower breathing resistance is required.

The objective of a study completed by Brook et al.[76] was to investigate long-term aspects of HME use in laryngectomized patients. A questionnaire was sent to 195 laryngectomees, and 75 questionnaires were returned. More than 85% of the respondents used an HME, of whom 77% were compliant users (ie, use for more than 20 hours per day). The incidence of pulmonary illnesses (either before or after surgery) was about 25%. More than 90% of the respondents were heavy smokers before laryngectomy. One third of the respondents are regularly exposed to dusty environments. Compliant HME users tended to make less use of external humidifiers, vaporizers, and sleeping medication, and had better pulmonary status and lower health-care costs.

Pedemonte-Sarrias et al.[77] studied the compliance of HME-use in patients and found that 90 of their 115 patients used an HME consistently. Most common reasons for not using the HME compliantly were adhesion problems due to mucous and skin irritation). Of the voice prosthesis users 90% used HME consistently. Authors found that the use of a voice prosthesis and an early start with HME use after TLE ($p<.01$) were factors significantly related to compliant HME use.

In a study conducted by van den Boer et al.[78] the authors aimed to develop a simple method to measure the ex vivo HME performance and compared those results with previous in vitro and in vivo results. The HMEs were weighed at the end of inspiration and at the end of expiration at different breathing volumes. Four Provox HMEs with known in vivo humidity and in vitro water loss values were tested. Results showed that HME performance can be determined by measuring the weight difference between end-inspiration and end-expiration using a regular balance and a standard spirometer. Results correlate well with earlier in vivo measurements using complex custom-built equipment to measure intra-tracheal humidity, and with in-vitro values provided by the manufacturer based on 24-hour ISO 9360-2:2001 assessments.

Several studies that discuss the Provox XtraHME-series as well as the Provox Normal and HiFlow HMEs, are discussed in the section on the Provox XtraHME-series.

7 Provox XtraHME – Clinical Effects

The Provox XtraHME was developed as the new generation of HME cassettes and is designed to have improved function and characteristics when compared to the Provox HME. The Provox XtraHME was introduced to the market in February 2010 and is available in two versions: XtraMoist HME and XtraFlow HME.

Figure 4 Provox XtraHME

The XtraMoist HME is designed to have capacities close to normal nasal function. The humidification is improved compared to the Provox HME and is designed to keep good airflow for easy breathing. The XtraFlow HME is designed with focus on having superior airflow and to be used when exercising

and when adapting to the breathing resistance after having been without an HME for a longer time. Compared to the Provox HME, the XtraHME has 50% more HME media (in volume), which acts as a spring. The XtraHME also has a 1.4 mm lower profile than the Provox HME, and a rim on the lid to guide the correct finger position for occlusion. In Figure 5 the differences between the Provox HME and the Provox XtraHME are shown.

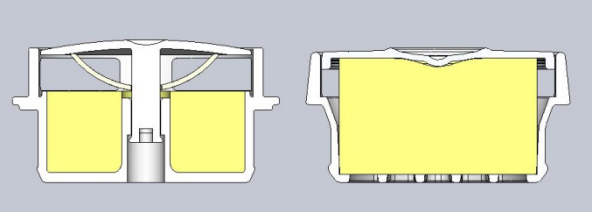

Figure 5 Schematic representation of Provox HME (left) and Provox XtraHME (right)

Scheenstra et al.[79] assessed the short-term endotracheal climate and clinical effects of two newly designed heat and moisture exchangers and compared outcomes with the regularly-used Provox HME and an older design (Stomvent). The new HMEs (Rplus with regular breathing resistance, and Lplus HME, with lowered breathing resistance) showed considerable humidification improvement over the RHME, without the associated temperature decrease of the latter. During a 3-week observation period, 7/13 patients (54%) reported noticeable lowered mucous production with the new HME's. Authors concluded that newly designed HME's show both heating and humidification improvement compared to the R-HME. Although the appearance of the HMEs used in this study is different from the Provox XtraHMEs, the HME media used in the HMEs tested in this study is the same as the HME media used in the XtraHMEs. These newly designed HME's are nowadays marketed as the XtraHMEs (XtraMoist and XtraFlow).

In a study by van den Boer et al.[80] a feasibility study was conducted to determine whether the new Provox HMEs (XtraMoist and XtraFlow) have a better water exchange performance than their predecessors (Normal and HiFlow). Results demonstrated that the XtraMoist HME shows a significantly better water exchange performance than its predecessor.

In a randomized controlled trial Herranz et al.[81] studied the clinical differences between the Provox HME and the Provox XtraHME. Forty-five patients, who were already using an HME, participated in a prospective, randomized cross-over clinical study in which each HME was used for 6 weeks. Results showed that for most parameters studied, the second generation HME performed equally well or better than the first generation HME. The improvement in tracheal climate translated into patients reporting significantly less tracheal dryness with the second generation than with the first generation.

Van den Boer et al.[82] conducted a study that aimed to: 1) assess the water exchange performance of commercially available HMEs for laryngectomized patients, 2) validate these results with absolute humidity outcomes, and 3) assess the role of hygroscopic salt present in some of the tested HMEs. Results showed a wide variation in water exchange performance. It was shown that water exchange correlates well with the end-inspiratory absolute humidity outcome, which validates the ex vivo weight change method[78]. Wet core weight is a predictor of HME performance. Hygroscopic salt increases the weight of the core material. Considerable differences in performance between the different HMEs were found. The Provox XtraMoist HME was shown to have a statistically significantly higher water exchange than all other tested HMEs.

Van den Boer et. al[83] also designed an additional study to assess the residual water uptake capacity of used HMEs (XtraMoist, XtraFlow, Normal and HiFlow) by measuring the difference between wet and dry core weight. The study results demonstrated that the water uptake capacity of hygroscopic HMEs

is clinically acceptable although no longer optimal after 24-hour tracheostoma application. From a functional point of view, the guideline for daily device replacement is therefore justified.

Van den Boer et al.[84] also studied the effect of the XtraMoist and XtraFlow HMEs on tracheal mucociliary clearance in laryngectomees in more detail. They concluded that long-term use of these HMEs helps restore tracheal ciliated cells and helps prevent their loss.

8 Provox FreeHands HME – Clinical Effects

In addition to the Provox HME that requires finger occlusion, a system has been developed that enables hands-free speech: The Provox FreeHands HME (see Figure 6). This system combines the Provox FreeHands HME automatic speaking valve with the Provox FreeHands HME cassette. Upon speech-exhalation, the membrane of the speaking valve closes off automatically, enabling the pulmonary air to be diverted through the voice prosthesis into the esophagus. This system is developed specifically for prosthetic tracheoesophageal speakers. The unique features of this system are the combination of an HME-cassette and hands-free valve (valve cannot be used without the HME-cassette), an adjustable cough relief valve that allows the air that is built up during coughing to escape, an on-off position that allows the patient to switch off the speech valve function when closing of the valve is not desired, and the availability of the speech membranes in three different strengths to accommodate different speaking pressures.

Figure 6 Provox FreeHands HME in StabiliBase plate and Provox FreeHands HME cassette

In a first study by Hilgers et al.[85] the feasibility of this device was investigated in 20 laryngectomized speakers of whom 5 already used an existing automatic speaking valve. Five patients discontinued using the device during the study due to problems with adherence of the base plate to the skin. Of the remaining 15 patients, 11 users used the device on a regular daily basis. The study showed that maximum phonation time and dynamic loudness range using the Provox FreeHands HME were lower than with a regular Provox HME, but higher than with another hands-free device. The finding that the use of hands-free devices results in less good phonation times can be attributed to the fact that when using a hands-free device some of the speaking air is consumed for closing the valve mechanism. The finding that the dynamic loudness range is smaller can be attributed to the fact that more air pressure is required to close the valve.

In a subsequent multi-center study[86], compliance, quality of life, and voice quality aspects of the Provox FreeHands HME were studied in 79 laryngectomized patients. Eight of them were regular users of another hands-free device, 58 had used another hands-free device unsuccessfully, and 13 had never used a hands-free device. After a trial period of 6 months, 19% of the patients used the device on a daily basis (average of 5 hours), 57% used it irregularly, for example at special occasions or for a limited number of hours per day. Maximum phonation time and dynamic loudness range

were found to be better than with another automatic speaking valve, but worse than with the regular Provox HME.

Tervonen et al.[87] compared the Provox FreeHands HME with the regular Provox HME in 14 patients and also found that speaking characteristics were less good when using an automatic speaking valve. Compared to the Provox HME that is occluded by finger, speaking with the FreeHands HME was more difficult in 50% and easier in 21%; breathing was heavier in 64% and easier in 14%; and subjective voice quality was worse in 29% and better in 21%. Despite its limitations, 13 out of the 14 patients continued to use the device; one of them continuously and 12 of them occasionally. The one patient that discontinued its use had difficulties with the adhesive. During this study the XtraBase adhesive was tested that was developed especially for hands-free speech. The base of this adhesive is more rigid and gives more support to the peristomal area. Both when used with a regular HME and with the FreeHands HME, on average the patients rated the skin adherence of the XtraBase as better than that of the 'conventional' (OptiDerm, Regular, FlexiDerm) adhesives.

Hamade et al.[88] performed perceptual and acoustic analysis to compare speech with manual stoma occlusion and with the Provox FreeHands HME in four patients. The objective analyses showed that maximum phonation time, intensity of read speech, and percentage pause time were all significantly decreased when using the automatic speaking valve and that random noise in the speech signal increased and extraneous noise caused by the valve increased when using the hands-free device. These results were not confirmed by the perceptual evaluations. Data from a questionnaire and patient diary suggested that the main advantage of the device is the ability to speak hands-free when performing a manual task, the main disadvantage was problems with base plate seal.

Lorenz et al.[89] studied the FreeHands HME in 24 laryngectomized patients. Seven discontinued its use (three due to recurrence, four due to skin adherence problems). Ten out of the remaining 17 patients used the device daily; on average 8.4 hours each day. In total, 88% of the patients considered it a great advantage to be able to speak hands-free. A long-term follow-up to this study conducted by Lorenz et al.[90] found that 76% of the 17 patients considered the FreeHands to be a great advantage.

In a study by Brook et al.[76] it was shown that regarding quality of life, patients who use a FreeHands device tended to have more frequent social contacts ($r = 0.251$; $p = 0.030$).

Published research into the Provox FreeHands HME system focuses on the properties of the speaking valve and its benefits. Based on equivalence with the existing HMEs used in both tracheotomized and laryngectomized patients, data from the literature support the HME-performance of the Provox FreeHands HME system as well.

9 Provox FreeHands FlexiVoice

A second device has been developed that enables hands-free speech in prosthetic tracheoesophageal speakers: the Provox FreeHands FlexiVoice (see Figure 7). This system combines the new Provox FreeHands FlexiVoice automatic speaking valve with the new Provox FreeHands HME Flow and Provox FreeHands HME Moist cassettes. The speaking valve has two settings. In one setting, the membrane of the speaking valve is always in the opened position; useful during physical activity. In the other setting, the speaking valve is bias-open, meaning the membrane is normally in the opened position and only closes upon relatively strong exhalation. This allows pulmonary air to be diverted through the voice prosthesis into the esophagus, for tracheoesophageal speech. The Provox FreeHands FlexiVoice comes with three different strengths of membranes (each strength a separate device), to accommodate different speaking pressures. The membrane also acts as a pressure relief valve, which allows the air to escape when coughing. The design of the speaking valve also allows for

speech through digital occlusion, by placing a single finger over the front opening. The speaking valve cannot be used without an HME-cassette, meaning the system functions as a full-time HME. There are two versions of HME-cassettes available for the Provox FreeHands FlexiVoice: Provox FreeHands HME Flow, with lower resistance, and Provox FreeHands HME Moist, with better moisture return properties.

Figure 7 The Provox FreeHands FlexiVoice speaking valve

As the device was introduced in 2014, there are no published articles discussing the device as of yet. Preliminary results were presented at the Global Postlaryngectomy Rehabilitation Academy in Rome in 2014[91]. These results showed that the FlexiVoice was used more days per month and more hours per day than the FreeHands, and that patients preferred its appearance, its overpressure function, its ease of speech and its voice quality, over those of the FreeHands. Based on equivalence with the Provox FreeHands HME system and existing HMEs used in both tracheotomized and laryngectomized patients, data from the literature support the performance of the Provox FreeHands FlexiVoice system.

10 Provox Micron HME – HME and filtration

The Provox Micron HME combines a Heat and Moisture Exchanger with an electrostatic filter (see Figure 8). The electrostatic filter provides protection for the laryngectomized patient from small particles and airborne microorganisms and pathogens (>99% Bacterial and Viral Filtration Efficiency).

Figure 8 Provox Micron HME

The clinical effect of the Provox Micron HME in laryngectomized patients was investigated by Scheenstra et al.[92] in a short-term feasibility study. They assessed the new Provox Micron HME for short-term endotracheal climate changes in 13 patients and feasibility in daily practice in 16 patients. Compared to open stoma breathing, the Provox HME Normal increases minimum endotracheal humidity values and the Provox Micron HME also increases end-inspiratory and end-expiratory temperature values. Patients spontaneously reported a further reduction in pulmonary complaints compared to the use of the normal Provox HME.

In a study by Brook et al.[76], in a group of users of Provox Micron, 33% stated that they had reduction in common cold symptoms, flu symptoms, asthmatic symptoms and allergy symptoms, and 39% stated that they had a reduction in amount of secretions and coughing frequency since they started using Provox Micron.

There are also some similar devices on the market that are used in ventilator dependent patients and during anesthesia that have both Heat and Moisture Exchanging and Filtration capacities (HUMIDVENT, Gibeck; HMEF, GE Healthcare). The use of an HME with filter has been found to decrease the incidence of Ventilator Associated Pneumonias (VAPs) in ventilated patients on the intensive care unit (ICU) in comparison with Heated Humidifiers[93, 94]. A review in 1988 by Subayi et al.[95] showed that HMEFs decrease the rate of nosocomial pneumonias in comparison with heated humidifiers. In a study that was carried out in guinea pigs, a bacterial and viral filter was found to successfully protect the pigs from sensitization to aerosolized Natural Rubber Latex[96]. Also, the use of HMEFs during anesthesia prevents bacterial migration from the patient to anesthesia circle systems[97, 98].

11 ProTrach XtraCare HME – HME and filtration

The ProTrach XtraCare HME is a device with 15 mm ISO connector, intended for all patients that breathe through a tracheostoma, combining a Heat and Moisture Exchanger with an electrostatic filter (see Figure 9); an HMEF. The HME provides a return of exhaled heat and moisture. The electrostatic filter provides patients with a tracheostoma with protection from small airborne particles, such as pollen, mold, smoke and Particulate Matter (>98% Particle Filtration Efficiency (100 nm)) and from airborne bacteria and viruses (>99% Bacterial and Viral Filtration Efficiency). This means the device helps compensate for the lost heating, humidification and filtration functions of the upper airway. The ProTrach XtraCare has an optional O_2-adaptor, which can be fitted over the device, after which O_2 can be administered through the HMEF.

Figure 9 ProTrach XtraCare HME

As the device was introduced in 2014, there are no published articles discussing it as of yet. There are no other devices on the market that combine an HME and an electrostatic filter for spontaneously breathing tracheotomized patients. Based on equivalence with the Provox Micron HME and existing HMEs and HMEFs used in both tracheotomized and laryngectomized patients, data from the literature support the performance of the ProTrach XtraCare HME.

12 ProTrach DualCare HME, ProTrach HME DigiTop and HME DigiTop O_2

The ProTrach DualCare HME is a combination of a part-time HME with a part-time speaking valve (see Figure 10). It was developed to allow tracheotomized patients that already use an automatic speaking valve without an HME, or want to use an automatic speaking valve, to do so but still have the benefits of pulmonary rehabilitation of an HME. The system consists of an HME-cassette (available with 15 mm and 22 mm ISO connector) and an automatic speaking valve that fits over the HME-cassette. The speaking valve cannot be used without an HME-cassette. The system has a speaking mode and an HME mode, between which can be switched by means of a 45 degree twist. The speaking mode offers a bias-closed speaking valve that only opens upon inhalation, allowing for hands free speech. The HME mode offers a real HME and a lower breathing resistance. The speaking valve is available in beige and blue (for hospital use).

Figure 10 ProTrach DualCare Speaking Valve with HME 15 Cassette (left) and HME 22 Cassette (right)

As the device was introduced in 2014, there are no published articles discussing it as of yet. Preliminary results were presented at the American Speech-Language-Hearing Association convention in Orlando, Florida in 2014[99]. The results showed that patients that started using the DualCare speaking valve with HME-cassette had statistically significantly better voice and speech sound, less valve noise during speaking, a more natural voice, less dry coughs during the night and less discomfort when breathing dry air, compared to their usual device. Out of the 11 patients trying the redesigned (final design) speaking valve, 100% preferred the DualCare, compared to their usual device. There are no other devices on the market that combine a real HME and a bias-closed speaking valve, for tracheotomized patients. Based on equivalence with existing HMEs used in both tracheotomized and laryngectomized patients, data from the literature support the performance of the ProTrach HMEs in combination with the ProTrach DualCare Speaking Valve.

The ProTrach HME DigiTop and the HME DigiTop O_2 (see Figure 11) are accessories for the DualCare system. Both are covers for the ProTrach HME-cassettes. The ProTrach HME DigiTop is indicated for tracheotomized patients and the HME DigiTop O_2 for all patients with a tracheostoma, so can be used with FreeHands HME-cassettes as well. With its two holes on the sides, both DigiTops allow speech through manual occlusion, and they can be used when sleeping and during the weaning process. The ProTrach HME DigiTop is available in beige and blue (for the hospital), while the HME DigiTop O_2 is only available in blue. The HME DigiTop O_2 offers the same function as the ProTrach HME DigiTop, but also includes a port to connect an oxygen supply to. Both the DigiTop and DigiTop O_2 cannot be used without an HME-cassette and offer a full-time HME-experience.

Figure 11 ProTrach HME DigiTop (top) and HME DigiTop O_2 (bottom)

As the accessories were introduced in 2014, there are no published articles discussing them as of yet. Based on equivalence with existing HMEs used in both tracheotomized and laryngectomized patients, data from the literature support the performance of the ProTrach HMEs in combination with the ProTrach HME DigiTop and HME DigiTop O_2. Furthermore, based on equivalence with HMEs that include a manual occlusion option, data from the literature support the performance of the combination of the ProTrach HME with the ProTrach HME DigiTop and HME DigiTop O_2. And, based on equivalence with the TrachPhone HME that has an O_2 port, data from the literature and from clinical experience do not report any problems with performance of these devices, and as such these data support the performance of the ProTrach HMEs in combination with the HME DigiTop O_2.

13 TrachPhone HME – multifunctional HME for tracheostomees

The TrachPhone HME (also sold under the name MediFlux HCH F6 and TrachVox) is a multifunctional device with a 15 mm ISO connector, intended for tracheotomized patients (see Figure 12). It incorporates a full-time HME, a manually operated speaking valve, an O_2-port and a suction port that doubles as pressure release valve.

Figure 12 TrachPhone HME

Vitacca et al.[58] looked at the performance of the substantially equivalent MediFlux HCH-6V device and found that its use in spontaneously tracheotomized patients improved viscosity and color of secretions, prevented further bacterial colonization of the airway, heated inspiratory flow, and helped improve the functional outcome.

Vitacca et al.[100] also reported that the the substantially equivalent MediFlux HCH-6V device did not induce significant changes in respiratory mechanics and breathing pattern in spontaneously breathing tracheotomized COPD patients.

14 Attachment of HME, FreeHands HME-cassettes, Provox and Provox Micron HME

The HME devices can be attached to the tracheostoma in two different ways: peristomally (base plate) or intraluminally (laryngectomy tube or stoma button).

14.1 Peristomal attachment

For peristomal attachment the different types of Provox HMEs can be attached into a variety of available Provox adhesives (Provox OptiDerm, Regular, FlexiDerm, XtraBase, StabiliBase and StabiliBase OptiDerm). Additionally, some patients may require the use of Provox Silicone Glue to improve the seal of the adhesive to the skin. Other products that are recommended for proper application of the adhesive are Remove (to remove glue from the skin) and SkinPrep (to protect the skin against adhesive and glue and prevent skin irritation).

The most common reported problem with the adhesives is that they can cause skin irritation, and that device life is too short, especially when used with a hands-free speaking device. Successful use of the adhesive depends on stoma characteristics, on how the patient uses the adhesive and with what device the adhesive used.

Tervonen et al.[87] reported that skin adherence with the XtraBase adhesive was perceived as better than that of conventional baseplates when used with the Provox FreeHands. Dirven et al.[101] reported that the combination of FlexiDerm, and extracted base from an XtraBase adhesive and the external neck brace demonstrated to have the smallest outward neck movement during handsfree speech, which would likely increase the time the Provox FreeHands can be used by the patient.

Van der Houwen[102] et al. studied in detail (peri)stomal geometry data of a diverse population of laryngectomized patients in relation to adhesive use. The study revealed a mismatch between patients and adhesives. Authors conclude that based on their data new adhesives can be developed that could help improve rehabilitation after laryngectomy.

These studies show that it is important to look at the individual patient and have a wide choice of adhesives available.The Provox adhesives are the result of incremental changes of a long-standing technology and have been on the market since 1995. During the years, attachment methods have improved and a larger variety of choices is now available to suit individual patient needs.

14.2 StabiliBase and StabiliBase OptiDerm

The peristomal adhesive baseplate StabiliBase was introduced in 2012 and consists of a conically shaped, firm plastic base with vertical stabilizing bars (see Figure 13). The base is welded on its outer rim to the adhesive material, which is similar to that of the existing Provox FlexiDerm and Provox XtraBase adhesives (Atos Medical). The baseplate liner has three removable vertical strips and can be attached to the skin in three steps.

In a prospective study by Hilgers et al.[103] the StabiliBase adhesive for peristomal attachment of HMEs was preferred by three-quarters of the study participants over the baseline adhesive (FlexiDerm or XtraBase). StabiliBase also showed a prolonged lifespan. Also when used with the Provox FreeHands, a londer device life was observed. During this study, it appeared that some patients would benefit from the StabiliBase design, but could not use this adhesive due to skin problems. Therefore, the Stabilibase OptiDerm (see Figure 14) was developed, combining the design of the StabiliBase with the adhesive properties of the OptiDerm (skin-friendly adhesive). The device was introduced to tyhe market in 2014 and no literature is available yet. However, due to its equivalence to both the Stabilibase and the OptiDerm data on these two devices are considered applicable to the StabiliBase OptiDerm.

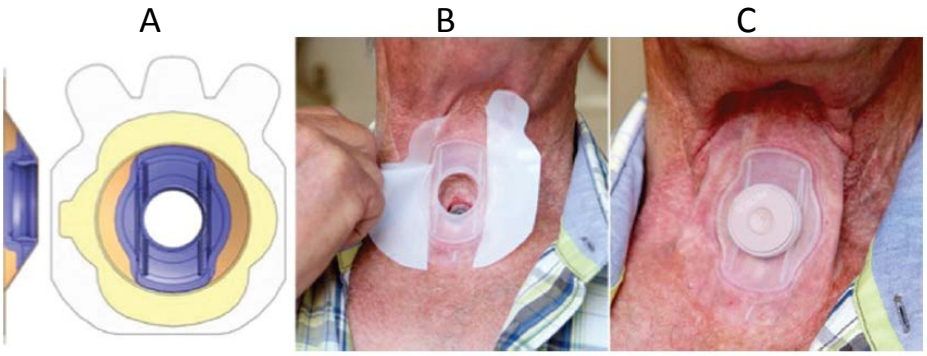

Figure 13 A: Schematic drawing of Stabilibase adhesive. B: pleeling away the sides. C. Attached StabiliBase with HME

Figure 14 StabiliBase OptiDerm adhesive

14.3 Intraluminal attachment

For intraluminal attachment the HME device can be attached into a LaryTube or a LaryButton. The primary goal of using a LaryTube or LaryButton is usually to maintain stoma patency, although more recently a LaryButton has also shown to be beneficial in combination with a hands-free speaking valve.

In contrast to laryngectomees who only in a few cases require a tube to maintain stoma patency, all tracheostomees require a tracheostomy tube to maintain stoma patency, due to the difference in surgery and the difference in the resulting tracheostoma. The HMEs are placed directly or with an adaptor on the tracheostomy tube.

The Provox LaryTube is a so-called laryngectomy tube or tracheostoma tube (see Figure 15). Many laryngectomized patients require a laryngectomy tube to maintain stoma patency, especially in the early postsurgical days and during postoperative radiotherapy[104]. Some patients experience permanent problems with stoma patency, requiring permanent use of a laryngectomy tube[104]. The unique feature of the Provox LaryTube is that it is the only laryngectomy tube available that holds an HME. The LaryTube can hold Provox HMEs or Provox Freehands HMEs. The LaryTube is held in place with a tubeholder (neck tie) or it can be clicked into a baseplate (model with Blue Ring). For patients using a voice prosthesis, a fenestrated LaryTube is available.

Figure 15 Three different types of LaryTubes. Left: with blue ring; Middle: regular; Right: fenestrated.

Laryngectomy tubes are considered a necessary part of laryngectomy care. A stoma that is too small causes difficulties in breathing and changing the voice prosthesis. There are no studies available on LaryTube or laryngectomy tubes in general.

The Provox LaryButton is a so-called laryngectomy button or stoma button (see Figure 16). A stoma button is primarily used in stoma's that are shrinking and that have a tight 'lip' or 'rim' that holds the button in place[104]. The LaryButton can hold an HME or FreeHands HME. Studies have shown that the use of a stoma button increases successful use of a hands-free speaking valve[105]. The unique features

of the LaryButton are that it, in contrast to other available models, is more stoma and patient friendly in design (rounder edges, softer materials) and that it can be held in place by using an additional neck tie or LaryClips (small adhesives combined with Velcro-attached hooks). These additional features enlarge the number of patients that is able to use the device. The need for a tight 'lip' or 'rim' to hold the button in place is less important.

Figure 16 LaryButton with LaryClips

A study on the use of the LaryButton and LaryClips[106] demonstrated that the system was appreciated by the majority of the patients and that its use led to increased success with usage of hands free speaking valves. Lewin et al.[107] describe how the LaryButton and other trachea buttons with the intraluminal attachment have become a preferred method for securing hands-free speaking valves to the stoma. These are effective because they eliminate the need for adhesives and glues that are often ineffective in sustaining a peristomal seal during hands-free TE speech production.

15. References

(1) McFadden ER, Jr., Denison DM, Waller JF, Assoufi B, Peacock A, Sopwith T. Direct recordings of the temperatures in the tracheobronchial tree in normal man. *J Clin Invest* 1982;69(3):700-705.

(2) Ingelstedt S. Studies on the conditioning of air in the respiratory tract. *Acta Otolaryngol Suppl* 1956;131:1-80.

(3) Keck T, Leiacker R, Heinrich A, Kuhnemann S, Rettinger G. Humidity and temperature profile in the nasal cavity. *Rhinology* 2000;38(4):167-171.

(4) Scheenstra RJ, Muller SH, Hilgers FJ. Endotracheal temperature and humidity in laryngectomized patients in a warm and dry environment and the effect of a heat and moisture exchanger. *Head Neck* 2011;33(9):1285-1293.

(5) Mercke U. The influence of varying air humidity on mucociliary activity. *Acta Otolaryngol* 1975;79(1-2):133-139.

(6) Mercke U, Toremalm NG. Air humidity and mucociliary activity. *Ann Otol Rhinol Laryngol* 1976;85(1 Pt 1):32-37.

(7) Schwab JA, Zenkel M. Filtration of particulates in the human nose. *Laryngoscope* 1998;108(1 Pt 1):120-124.

(8) Hatch TF. Distribution and deposition of inhaled particles in respiratory tract. *Bacteriol Rev* 1961;25:237-240.

(9) Tellier R. Aerosol transmission of influenza A virus: a review of new studies. *J R Soc Interface* 2009;6 Suppl 6:S783-S790.

(10) Kelly FJ, Fussell JC. Air pollution and airway disease. *Clin Exp Allergy* 2011;41(8):1059-1071.

(11) Particulate matter: Basic Information. http://www.epa.gov/pm/basic.html . 2014. US EPA (United States Environmental Protection Agency).
Ref Type: Online Source

(12) McGarry P, Morawska L, He C et al. Exposure to particles from laser printers operating within office workplaces. *Environ Sci Technol* 2011;45(15):6444-6452.

(13) Invernizzi G, Ruprecht A, Mazza R et al. Particulate matter from tobacco versus diesel car exhaust: an educational perspective. *Tob Control* 2004;13(3):219-221.

(14) Air quality and health – Fact sheet N°313. http://www.who.int/mediacentre/factsheets/fs313/en/ . 2014. WHO (World Health Organization).
Ref Type: Online Source

(15) The World Health Report 2002 – Reducing Risks, Promoting Healthy Life. http://whqlibdoc.who.int/publications/2002/9241562072.pdf . 2002. WHO (World Health Organization).
Ref Type: Online Source

(16) WHO Air quality guidelines for particulate matter, ozone, nitrogen dioxide and sulfur dioxide, Global update 2005, Summary of risk assessment. http://whqlibdoc.who.int/hq/2006/WHO_SDE_PHE_OEH_06.02_eng.pdf WHO/SDE/PHE/OEH/06.02. 2005.
Ref Type: Online Source

(17) Anderson HR, Spix C, Medina S et al. Air pollution and daily admissions for chronic obstructive pulmonary disease in 6 European cities: results from the APHEA project. *Eur Respir J* 1997;10(5):1064-1071.

(18) Brunekreef B, Holgate ST. Air pollution and health. *Lancet* 2002;360(9341):1233-1242.

(19) Jongeneel WP, Straatsen BAM, van Kempen EEMM, Fischer PH. Gezondheidseffecten van wegverkeer: een quickscan. http://www.ggdkennisnet.nl/?file=5785&m=1319011665&action=file.download RIVM Briefrapport 630800001/2008. 2008.
Ref Type: Online Source

(20) Villeneuve PJ, Chen L, Rowe BH, Coates F. Outdoor air pollution and emergency department visits for asthma among children and adults: a case-crossover study in northern Alberta, Canada. *Environ Health* 2007;6:40.

(21) Lepeule J, Laden F, Dockery D, Schwartz J. Chronic exposure to fine particles and mortality: an extended follow-up of the Harvard Six Cities study from 1974 to 2009. *Environ Health Perspect* 2012;120(7):965-970.

(22) Anderson JO, Thundiyil JG, Stolbach A. Clearing the air: a review of the effects of particulate matter air pollution on human health. *J Med Toxicol* 2012;8(2):166-175.

(23) Heyder J, Rudolf G. Deposition of aerosol particles in the human nose. *Inhaled Part* 1975;4 Pt 1:107-126.

(24) Harris S, Jonson B. Lung function before and after laryngectomy. *Acta Otolaryngol* 1974;78(3-4):287-294.

(25) Natvig K. Influence of different climates on the peak expiratory flow in laryngectomees. *J Laryngol Otol* 1984;98(1):53-58.

(26) Todisco T, Maurizi M, Paludetti G, Dottorini M, Merante F. Laryngeal cancer: long-term follow-up of respiratory functions after laryngectomy. *Respiration* 1984;45(3):303-315.

(27) Togawa K, Konno A, Hoshino T. A physiologic study on respiratory handicap of the laryngectomized. *Arch Otorhinolaryngol* 1980;229(1):69-79.

(28) Torjussen W. Airway obstructions in laryngectomized patients. A spirometric investigation. *Acta Otolaryngol* 1968;66(1):161-170.

(29) Hilgers FJ, Ackerstaff AH, Aaronson NK, Schouwenburg PF, van ZN. Physical and psychosocial consequences of total laryngectomy. *Clin Otolaryngol Allied Sci* 1990;15(5):421-425.

(30) Usui N. Ventilatory function in laryngectomized patients. *Auris Nasus Larynx* 1979;6(2):87-96.

(31) Jay S, Ruddy J, Cullen RJ. Laryngectomy: the patient's view. *J Laryngol Otol* 1991;105(11):934-938.

(32) Griffith TE, Friedberg SA. HISTOLOGIC CHANGES IN THE TRACHEA FOLLOWING LARYNGECTOMY. *Ann Otol Rhinol Laryngol* 1964;73:883-892.

(33) Roessler F, Grossenbacher R, Walt H. [Condition of the tracheobronchial mucous membrane in patients with long-term tracheostomy. A scanning electron microscopy study]. *Laryngol Rhinol Otol (Stuttg)* 1988;67(2):66-71.

(34) Ackerstaff AH, Hilgers FJ, Balm AJ, van ZN. Long-term pulmonary function after total laryngectomy. *Clin Otolaryngol Allied Sci* 1995;20(6):547-551.

(35) Mohide EA, Archibald SD, Tew M, Young JE, Haines T. Postlaryngectomy quality-of-life dimensions identified by patients and health care professionals. *Am J Surg* 1992;164(6):619-622.

(36) Zuur JK, Muller SH, de Jongh FH, van ZN, Hilgers FJ. The physiological rationale of heat and moisture exchangers in post-laryngectomy pulmonary rehabilitation: a review. *Eur Arch Otorhinolaryngol* 2006;263(1):1-8.

(37) Thomachot L, Viviand X, Arnaud S, Boisson C, Martin CD. Comparing two heat and moisture exchangers, one hydrophobic and one hygroscopic, on humidifying efficacy and the rate of nosocomial pneumonia. *Chest* 1998;114(5):1383-1389.

(38) Grolman W, Blom ED, Branson RD, Schouwenburg PF, Hamaker RC. An efficiency comparison of four heat and moisture exchangers used in the laryngectomized patient. *Laryngoscope* 1997;107(6):814-820.

(39) Brusasco C, Corradi F, Vargas M et al. In vitro evaluation of heat and moisture exchangers designed for spontaneously breathing tracheostomized patients. *Respir Care* 2013;58(11):1878-1885.

(40) Verkerke GJ, Geertsema AA, Schutte HK. Airflow resistance of airflow-regulating devices described by independent coefficients. *Ann Otol Rhinol Laryngol* 2001;110(7 Pt 1):639-645.

(41) Verkerke GJ, Geertsema AA, Schutte HK. Airflow resistance of heat and moisture exchange filters with and without a tracheostoma valve. *Ann Otol Rhinol Laryngol* 2002;111(4):333-337.

(42) Toremalm NG. The daily amoung of tracheo-bronchial secretions in man. A method for continuous tracheal aspiration in laryngectomized and tracheotomized patients. *Acta Otolaryngol Suppl* 1960;158:43-53.

(43) Toremalm NG. A heat-and-moisture exchanger for posttracheotomy care. An experimental study. *Acta Otolaryngol* 1960;52:461-472.

(44) Shanks CA, Sara CA. A reappraisal of the multiple gauze heat and moisture exchanger. *Anaesth Intensive Care* 1973;1(5):428-432.

(45) Steward DJ. A disposable condenser humidifier for use during anaesthesia. *Can Anaesth Soc J* 1976;23(2):191-195.

(46) Ackerstaff AH, Hilgers FJ, Aaronson NK, Schouwenburg PF, van ZN. [Physical and psychosocial sequelae of total larynx extirpation and the use of a heat and moisture exchanger]. *Ned Tijdschr Geneeskd* 1990;134(50):2438-2442.

(47) Hilgers FJ, Aaronson NK, Ackerstaff AH, Schouwenburg PF, van ZN. The influence of a heat and moisture exchanger (HME) on the respiratory symptoms after total laryngectomy. *Clin Otolaryngol Allied Sci* 1991;16(2):152-156.

(48) Ackerstaff AH, Hilgers FJ, Aaronson NK, Balm AJ, van ZN. Improvements in respiratory and psychosocial functioning following total laryngectomy by the use of a heat and moisture exchanger. *Ann Otol Rhinol Laryngol* 1993;102(11):878-883.

(49) Ackerstaff AH, Hilgers FJ, Aaronson NK et al. Heat and moisture exchangers as a treatment option in the post-operative rehabilitation of laryngectomized patients. *Clin Otolaryngol Allied Sci* 1995;20(6):504-509.

(50) Keck T, Durr J, Leiacker R, Rettinger G, Rozsasi A. Tracheal climate in laryngectomees after use of a heat and moisture exchanger. *Laryngoscope* 2005;115(3):534-537.

(51) Jones AS, Young PE, Hanafi ZB, Makura ZG, Fenton JE, Hughes JP. A study of the effect of a resistive heat moisture exchanger (Trachinaze) on pulmonary function and blood gas tensions in patients who have undergone a laryngectomy: a randomized control trial of 50 patients studied over a 6-month period. *Head Neck* 2003;25(5):361-367.

(52) McRae D, Young P, Hamilton J, Jones A. Raising airway resistance in laryngectomees increases tissue oxygen saturation. *Clin Otolaryngol Allied Sci* 1996;21(4):366-368.

(53) Zuur JK, Muller SH, Sinaasappel M, Hart GA, van ZN, Hilgers FJ. Influence of heat and moisture exchanger respiratory load on transcutaneous oxygenation in laryngectomized individuals: a randomized crossover study. *Head Neck* 2007;29(12):1102-1110.

(54) Lorenz KJ, Maier H. [Pulmonary rehabilitation after total laryngectomy using a heat and moisture exchanger (HME)]. *Laryngorhinootologie* 2009;88(8):513-522.

(55) Kramp B, Donat M, Dommerich S, Pau HW, Podbielski A. Prospective controlled study of microbial colonization of the trachea in tracheotomized and laryngectomized patients with HME (heat and moisture exchanger). *Acta Otolaryngol* 2009;129(10):1136-1144.

(56) Icuspit P, Yarlagadda B, Garg S, Johnson T, Deschler D. Heat and moisture exchange devices for patients undergoing total laryngectomy. *ORL Head Neck Nurs* 2014;32(1):20-23.

(57) Primiano FP, Jr., Moranz ME, Montague FW, Jr., Miller RB, Sachs DP. Conditioning of inspired air by a hygroscopic condenser humidifier. *Crit Care Med* 1984;12(8):675-678.

(58) Vitacca M, Clini E, Foglio K et al. Hygroscopic condenser humidifiers in chronically tracheostomized patients who breathe spontaneously. *Eur Respir J* 1994;7(11):2026-2032.

(59) Thomachot L, Viviand X, Arnaud S, Vialet R, Albanese J, Martin C. Preservation of humidity and heat of respiratory gases in spontaneously breathing, tracheostomized patients. *Acta Anaesthesiol Scand* 1998;42(7):841-844.

(60) Rozsasi A, Leiacker R, Fischer Y, Keck T. Influence of passive humidification on respiratory heat loss in tracheotomized patients. *Head Neck* 2006;28(7):609-613.

(61) Hilgers FJ, Ackerstaff AH, Balm AJ, Gregor RT. A new heat and moisture exchanger with speech valve (Provox stomafilter). *Clin Otolaryngol Allied Sci* 1996;21(5):414-418.

(62) Balle VH, Rindso L, Thomsen J. Speech rehabilitation by Provox voice prosthesis combined with heat and moisture exchange filters. *Acta Otolaryngol Suppl* 1997;529:251-253.

(63) Ackerstaff AH, Hilgers FJ, Balm AJ, Tan IB. Long-term compliance of laryngectomized patients with a specialized pulmonary rehabilitation device: Provox Stomafilter. *Laryngoscope* 1998;108(2):257-260.

(64) Herranz Gonzalez-Botas J, Suarez T, Garcia CB, Martinez MA. [Experience with the HME-Provox Stomafilter in laryngectomized patients]. *Acta Otorrinolaringol Esp* 2001;52(3):221-225.

(65) Ackerstaff AH, Fuller D, Irvin M, Maccracken E, Gaziano J, Stachowiak L. Multicenter study assessing effects of heat and moisture exchanger use on respiratory symptoms and voice quality in laryngectomized individuals. *Otolaryngol Head Neck Surg* 2003;129(6):705-712.

(66) Bien S, Okla S, van As-Brooks CJ, Ackerstaff AH. The effect of a Heat and Moisture Exchanger (Provox HME) on pulmonary protection after total laryngectomy: a randomized controlled study. *Eur Arch Otorhinolaryngol* 2010;267(3):429-435.

(67) Masson AC, Fouquet ML, Goncalves AJ. Tracheostoma humidifier: influence on secretion and voice of patients with total laryngectomy. *Pro Fono* 2008;20(3):183-189.

(68) Dassonville O, Merol JC, Bozec A et al. Randomised, multi-centre study of the usefulness of the heat and moisture exchanger (Provox HME(R)) in laryngectomised patients. *Eur Arch Otorhinolaryngol* 2011;268(11):1647-1654.

(69) Merol JC, Charpiot A, Langagne T, Hemar P, Ackerstaff AH, Hilgers FJ. Randomized controlled trial on postoperative pulmonary humidification after total laryngectomy: external humidifier versus heat and moisture exchanger. *Laryngoscope* 2012;122(2):275-281.

(70) van As CJ, Hilgers FJ, Koopmans-van Beinum FJ, Ackerstaff AH. The influence of stoma occlusion on aspects of tracheoesophageal voice. *Acta Otolaryngol* 1998;118(5):732-738.

(71) Zuur JK, Muller SH, de Jongh FH et al. A newly developed tool for intra-tracheal temperature and humidity assessment in laryngectomized individuals: the Airway Climate Explorer (ACE). *Med Biol Eng Comput* 2007;45(8):737-745.

(72) Zuur JK, Muller SH, Vincent A, Sinaasappel M, de Jongh FH, Hilgers FJ. Assessment of tracheal temperature and humidity in laryngectomized individuals and the influence of a heat and moisture exchanger on tracheal climate. *Head Neck* 2008;30(8):1072-1082.

(73) Zuur JK, Muller SH, Vincent A, Sinaasappel M, de Jongh FH, Hilgers FJ. The influence of a heat and moisture exchanger on tracheal climate in a cold environment. *Med Eng Phys* 2009;31(7):852-857.

(74) Scheenstra RJ, Muller SH, Vincent A, Sinaasappel M, Zuur JK, Hilgers FJ. Endotracheal temperature and humidity measurements in laryngectomized patients: intra- and inter-patient variability. *Med Biol Eng Comput* 2009;47(7):773-782.

(75) Scheenstra RJ, Muller SH, Vincent A, Sinaasappel M, Hilgers FJ. Influence of breathing resistance of heat and moisture exchangers on tracheal climate and breathing pattern in laryngectomized individuals. *Head Neck* 2010;32(8):1069-1078.

(76) Brook I, Bogaardt H, van As-Brooks C. Long-term use of heat and moisture exchangers among laryngectomees: medical, social, and psychological patterns. *Ann Otol Rhinol Laryngol* 2013;122(6):358-363.

(77) Pedemonte-Sarrias G, Villatoro-Sologaistoa JC, Ale-Inostroza P, Lopez-Vilas M, Leon-Vintro X, Quer-Agusti M. Chronic adherence to heat and moisture exchanger use in laryngectomized patients. *Acta Otorrinolaringol Esp* 2013;64(4):247-252.

(78) van den Boer C, Muller SH, Vincent AD, Zuchner K, van den Brekel MW, Hilgers FJ. A novel, simplified ex vivo method for measuring water exchange performance of heat and moisture exchangers for tracheostomy application. *Respir Care* 2013;58(9):1449-1458.

(79) Scheenstra RJ, Muller SH, Vincent A, Ackerstaff AH, Jacobi I, Hilgers FJ. A new heat and moisture exchanger for laryngectomized patients: endotracheal temperature and humidity. *Respir Care* 2011;56(5):604-611.

(80) van den Boer C, Muller SH, Vincent AD, Zuchner K, van den Brekel MW, Hilgers FJ. Ex vivo water exchange performance and short-term clinical feasibility assessment of newly developed heat and moisture exchangers for pulmonary rehabilitation after total laryngectomy. *Eur Arch Otorhinolaryngol* 2014;271(2):359-366.

(81) Herranz J, Espino MA, Morado CO. Pulmonary rehabilitation after total laryngectomy: a randomized cross-over clinical trial comparing two different heat and moisture exchangers (HMEs). *Eur Arch Otorhinolaryngol* 2013;270(9):2479-2484.

(82) van den Boer C, Nuller SH, Vincent AD, van den Brekel MW, Hilgers FJ. Ex vivo assessment and validation of water exchange performance of 23 heat and moisture exchangers for laryngectomized patients. *Respir Care* 2014;59(8):1161-1171.

(83) van den Boer C, Vas Nunes JH, Muller SH, van dN, V, van den Brekel MW, Hilgers FJ. Water Uptake Performance of Hygroscopic Heat and Moisture Exchangers after 24-Hour Tracheostoma Application. *Otolaryngol Head Neck Surg* 2014;150(6):999-1004.

(84) van den Boer C, Muller SH, van dN, V et al. Effects of heat and moisture exchangers on tracheal mucociliary clearance in laryngectomized patients: a multi-center case-control study. *Eur Arch Otorhinolaryngol* 2014.

(85) Hilgers FJ, Ackerstaff AH, van As CJ, Balm AJ, van den Brekel MW, Tan IB. Development and clinical assessment of a heat and moisture exchanger with a multi-magnet automatic tracheostoma valve (Provox FreeHands HME) for vocal and pulmonary rehabilitation after total laryngectomy. *Acta Otolaryngol* 2003;123(1):91-99.

(86) Op de Coul BM, Ackerstaff AH, van As-Brooks CJ et al. Compliance, quality of life and quantitative voice quality aspects of hands-free speech. *Acta Otolaryngol* 2005;125(6):629-637.

(87) Tervonen H, Back L, Juvas A et al. Automatic speaking valve in speech rehabilitation for laryngectomized patients. *Eur Arch Otorhinolaryngol* 2005;262(10):816-820.

(88) Hamade R, Hewlett N, Scanlon E. A quantitative and qualitative evaluation of an automatic occlusion device for tracheoesophageal speech: the Provox FreeHands HME. *Clin Linguist Phon* 2006;20(2-3):187-193.

(89) Lorenz KJ, Groll K, Ackerstaff AH, Hilgers FJ, Maier H. Hands-free speech after surgical voice rehabilitation with a Provox voice prosthesis: experience with the Provox FreeHands HME tracheostoma valve system. *Eur Arch Otorhinolaryngol* 2007;264(2):151-157.

(90) Lorenz KJ, Huverstuhl K, Maier H. [Finger-free speech with the Provox FreeHands HME Automatic Tracheostoma Valve system. Clinical long-term experience]. *HNO* 2009;57(11):1090-1098.

(91) de Kleijn BJ, Lansaat L, van den Brekel MWM, van der Laan BFAM. Clinical assessment of a new speaking valve for hands-free speech in laryngectomized subjects: Provox® FreeHands FlexiVoice; short term results. 2014.

(92) Scheenstra RJ, Muller SH, Vincent A, Ackerstaff AH, Jacobi I, Hilgers FJ. Short-term endotracheal climate changes and clinical effects of a heat and moisture exchanger with an integrated electrostatic virus and bacterial filter developed for laryngectomized individuals. *Acta Otolaryngol* 2010;130(6):739-746.

(93) Kirton OC, DeHaven B, Morgan J, Morejon O, Civetta J. A prospective, randomized comparison of an in-line heat moisture exchange filter and heated wire humidifiers: rates of ventilator-associated early-onset (community-acquired) or late-onset (hospital-acquired) pneumonia and incidence of endotracheal tube occlusion. *Chest* 1997;112(4):1055-1059.

(94) Kranabetter R, Leier M, Kammermeier D, Just HM, Heuser D. [The effects of active and passive humidification on ventilation-associated nosocomial pneumonia]. *Anaesthesist* 2004;53(1):29-35.

(95) Subayi L, Chergui K, Beydon L. [Heat and moisture exchanging filters for conditioning of inspired gases in adult anesthesia and resuscitation]. *Ann Fr Anesth Reanim* 1998;17(7):699-708.

(96) Barbara J, Santais MC, Levy DA, Ruff F, Leynadier F. Prevention of latex sensitization in guinea pigs by a bacterial and viral filter used in anaesthesia. *Br J Anaesth* 2005;95(3):349-354.

(97) Boots RJ, Howe S, George N, Harris FM, Faoagali J. Clinical utility of hygroscopic heat and moisture exchangers in intensive care patients. *Crit Care Med* 1997;25(10):1707-1712.

(98) Rathgeber J, Kietzmann D, Mergeryan H, Hub R, Zuchner K, Kettler D. Prevention of patient bacterial contamination of anaesthesia-circle-systems: a clinical study of the contamination risk and performance of different heat and moisture exchangers with electret filter (HMEF). *Eur J Anaesthesiol* 1997;14(4):368-373.

(99) de Klein BJ, Wedman J, van der Laan BFAM. Phase 2 clinical feasibility study of a new Speaking Valve with a heat- and moisture exchanger (ProTrach® DualCare™) for tracheotomized patients.: Dept. of Otolaryngology and Head and Neck Surgery, University Medical Center Groningen (UMCG), Groningen, Netherlands; 2014.

(100) Vitacca M, Clini E, Porta R, Ambrosino N. Breathing pattern and respiratory mechanics in chronically tracheostomized patients with chronic obstructive pulmonary disease breathing spontaneously through a hygroscopic condenser humidifier. *Respiration* 1997;64(4):263-267.

(101) Dirven R, Kooijman PG, Maal TJ, Hilgers FJ, Berge SJ, Marres HA. An external neck brace to support the peristomal fixation of an automatic stoma valve (ASV): 3D stereophotogrammetrical assessment. *Acta Otolaryngol* 2010;130(7):851-858.

(102) van der Houwen EB, van Kalkeren TA, Post WJ, Hilgers FJ, van der Laan BF, Verkerke GJ. Does the patch fit the stoma? A study on peristoma geometry and patch use in laryngectomized patients. *Clin Otolaryngol* 2011;36(3):235-241.

(103) Hilgers FJ, Dirven R, Wouters Y, Jacobi I, Marres HA, van den Brekel MW. A multicenter, prospective, clinical trial evaluating a novel adhesive baseplate (Provox StabiliBase) for peristomal attachment of postlaryngectomy pulmonary and voice rehabilitation devices. *Laryngoscope* 2012;122(11):2447-2453.

(104) Ward EC, Acton LM, Morton A-L. Chapter 11. Stoma Care and Appliances. In: Ward EC, van As-Brooks CJ, editors. *Head and Neck Cancer: Treatment, Rehabilitation, and Outcomes*.San Diego: Plural Publishing; 2007. 289-311.

(105) Lewin JS, Lemon J, Bishop-Leone JK, Leyk S, Martin JW, Gillenwater AM. Experience with Barton button and peristomal breathing valve attachments for hands-free tracheoesophageal speech. *Head Neck* 2000;22(2):142-148.

(106) Hilgers FJ, Ackerstaff AH. Development and evaluation of a novel tracheostoma button and fixation system (Provox LaryButton and LaryClip adhesive) to facilitate hands-free tracheoesophageal speech. *Acta Otolaryngol* 2006;126(11):1218-1224.

(107) Lewin JS, Montgomery PC, Hutcheson KA, Chambers MS. Further experience with modification of an intraluminal button for hands-free tracheoesophageal speech after laryngectomy. *J Prosthet Dent* 2009;102(5):328-331.