Novel approaches to performance assessment of heat and moisture exchangers for pulmonary protection and rehabilitation in laryngectomized patients
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Chapter 1

General introduction
INTRODUCTION

Total laryngectomy: indication and consequences

Total laryngectomy is one of the treatment options for (advanced) laryngeal cancer, which is one of the most frequent malignancies in the head and neck region. The incidence of laryngeal cancer varies considerably between European countries, and in the last decade the lowest rates are found in Scandinavian countries (3-4 per 100,000), and highest rates in Central and Southern countries (9-10 per 100,000).\(^1\) The main histology of laryngeal cancer is squamous cell carcinoma. Larynx cancer is highly associated with smoking and excessive alcohol consumption.\(^2,3\) In the Netherlands incidences are declining because of decreased smoking. Males are considerably more frequently affected than females.\(^1,4\)

Before 1990, patients with advanced laryngeal carcinoma were in general treated with total laryngectomy (TLE), whereas after 1990 cisplatin-based chemoradiotherapy (CRT) as well as radiotherapy alone are increasingly used as an organ preserving therapy option.\(^5,6\) Total laryngectomy, according to many head and neck surgeons, is still indicated as primary treatment for T4 laryngeal cancer, in case of salvage surgery for recurrent (laryngeal) disease after (C)RT, in case of 2\(^{nd}\) primary tumour, and in case of a dysfunctional larynx after previous (C)RT.\(^7\)

During total laryngectomy the entire larynx is removed, resulting in a permanent disconnection of the upper and lower airways. Figure 1 shows the respiratory anatomy before and after total laryngectomy. This short-cut does not only affect the breathing condition, but also has consequences for patient’s voice and speech and for smell and taste, all requiring extensive rehabilitation. Fortunately, voice and speech rehabilitation presently can be managed quite well with a voice prosthesis.\(^8\) In essence, this is a one-way valve implanted in a puncture tract in the tracheoesophageal party wall. This device, whilst protecting against aspiration, enables air from the trachea to be diverted into the pharyngoesophageal segment, provoking mucosal waves and thus sound, thereby restoring pulmonary driven voice and speech (see Figure 1).\(^9\) The sense of smell is impaired due to the lack of nasal airflow, since the patient is breathing through a permanent stoma. Mostly,
this issue can be rehabilitated using the oral cavity as a vacuum pump, applying the so-called Nasal Airflow Inducing Manoeuvre or ‘Polite Yawning’ method.\textsuperscript{10}

![Lateral view of respiratory anatomy](image)

**Figure 1.** Lateral view of respiratory anatomy before (A), after (B) total laryngectomy, and (C) voicing with a voice prosthesis in the tracheoesophageal party wall (by courtesy of Plural Publishers; from *Head and Neck Cancer: Treatment, Rehabilitation, and Outcomes.* Ward and van As-Brooks eds.).

The new breathing condition after TLE has a major impact on pulmonary protection. Temperature and humidity of the inspired air are lower due to the short cut of the upper airways and a longer segment of the tracheobronchial epithelium is exposed to relatively cold and dry air. Normal temperature and humidity values at the subglottic level are known since the early fifties of the last century from the intratracheal climate measurements in healthy young male volunteers.\textsuperscript{11} These values, however, are not fully representative for the values in older head and neck cancer patients, as was shown by Scheenstra et al.\textsuperscript{12} That in vivo study of patients with a temporary tracheotomy has shown that the end-inspiratory humidity during stoma breathing instead of nose breathing is decreased from 29.3 mg/L to 21.1 mg/L, and that the end-inspiratory temperature drops from 31.1 °C during nose breathing to 28.3 °C during stoma breathing (at room conditions of 7 mg/l; 24 °C).\textsuperscript{12}

These permanent respiratory climate changes lead to damage of the tracheal epithelium in laryngectomized patients, such as loss of ciliated cells, goblet cell hyperplasia and metaplasia, and an impaired mucociliary clearance, although available literature on these issues is limited.\textsuperscript{13,14} Impaired mucociliary clearance
leads to mucus hypersecretion and coughing in an attempt to compensatively clear the mucus containing inhaled particles such as bacteria and viruses.\textsuperscript{15} Patients with decreased mucociliary clearance are more susceptible to pulmonary infections.\textsuperscript{16} Long-term evaluation with lung function tests after TLE have shown the presence of obstructive deterioration that might increase over months irrespective of the preoperative conditions and this may attribute to inflammatory changes of the lower airways.\textsuperscript{17} Thus it is not surprising that the reported clinical complaints from stoma breathing are daily excessive coughing and mucus expectoration, increased shortness of breath and a decreased quality of life.\textsuperscript{18, 19}

\textit{Pulmonary rehabilitation after total laryngectomy}

Pulmonary rehabilitation after total laryngectomy presently is best achieved with a so-called ‘heat and moisture exchanger’ (HME), which can (partly) restore the loss of air conditioning. In addition to restoring airway resistance and filtration, an HME passively exchanges heat and moisture in the breathing air. Water condensates on the surface of the HME material during exhalation and is evaporated into the inspired air. The device is placed in front of the tracheostoma mounted in an adhesive or tube and is basically a (plastic) case containing core material such as paper or foam (see Figure 2).
Most HMEs contain core material impregnated with a hygroscopic substance to enhance their heat and moisture exchange function. Some examples of HME devices are shown in Figure 3.
Clinical studies describing the effect of HMEs in patients have reported a significant decrease in frequency of daily coughing and mucus expectoration, chest infections and an improvement of quality of life. Only in one study, a significant improvement of pulmonary function, using spirometry, was found after use of an HME. Here, it must also be noted that most of laryngectomized patients are ex-smokers and part of them have pre-existent chronic airways disease, such as COPD. Also part of laryngectomized patients underwent radiation therapy in the (supraclavicular) neck area including the tracheostoma, which damages the mucosa of the cranial part of the trachea as well. These factors influencing tracheal mucosa cannot be restored by the use of an HME.

In vivo, the performance of HME devices was measured intra-tracheally in laryngectomized patients using a specially developed Airway Climate Explorer (ACE). This test configuration has measured the effect of HMEs on tracheal climate in various ambient conditions. With the application of an HME over the tracheostoma, the more or less constant relative humidity of the inspired air is to a great extent restored. The largest effect of using an HME by patients is found in end-inspiratory humidity levels (increase up to 6.8 mg/L). The effect on end-inspiratory temperature varies due to the trade-off between heat exchange and evaporative cooling and depends on the heat capacity of the device type. In all
climate circumstances the tracheostoma has an HME function itself as well: in a cold environment it warms and humidifies the air and in a warm environment the air is cooled and humidified. This HME effect of the tracheostoma itself is increased by using an HME device. The addition of airway resistance by the HME does probably not influence arterial oxygenation. HME resistance depends on the amount of HME material used and clinically acceptable breathing resistance varies among patients, which is a decisive factor in compliancy. Also, HME occlusion for optimal speech (without air leakage through the stoma), and size of the device are important feasibility factors for patients’ use. The constraints on size and resistance make designing effective HMEs extremely difficult as only a relatively small amount of exchange material can be used.

HMEs were introduced in the early 90’s and are nowadays considered standard treatment for pulmonary rehabilitation in the Netherlands and many other countries, but despite the evidence about the beneficial health effects of HMEs, many countries have not yet covered these devices in their medical reimbursement system.

Outline of this thesis

Although quite extensive knowledge about function and effects of HMEs with respect to pulmonary rehabilitation after TLE exists, several questions still need to be addressed. This thesis is focussing on new techniques to measure the humidification effects of an HME and to further increase our understanding of how an HME functions. The aim for these new techniques is to enable assessment of potential differences in performance between different HME types, and if any, understanding where such differences originate. Another practical question that can be assessed with a new technique is whether an HME still performs efficiently after 24-hour tracheostoma application.

Another relevant question is what effect HME use (due to improved tracheal climate) has on tracheal mucociliary clearance? More specifically: does the tracheal ciliated epithelium recover after HME use and is tracheal mucus transport velocity in HME users higher/better than in non-HME users (long-term)? And, is short-term
(1-hour) removal of the HME (e.g. during tracheostoma cleaning) already affecting mucus transport velocity?

In recent years, our knowledge of HME function has gained substantially through in vivo intra-tracheal climate measurements, but these are technically challenging and not readily available for research groups without (expensive) customized equipment such as the ACE.\textsuperscript{24,33,34} Moreover, presently, there are many different HME types commercially available with differences in size, material, breathing resistance and airtight occlusion for speech, and testing a large series of different HMEs is too burdensome for patients to be involved in. The alternative, the standard in vitro ISO 9360-2:2001 test method, uses a mechanical lung model that is able to evaluate a large number of different HMEs\textsuperscript{35,36}, but this model is probably not completely representative for human lung performance. Moreover, there are pitfalls in the calibration of the various acceptable ISO test set-ups. Chapter 2 presents, as a new alternative, a newly developed ex vivo method that measures the water exchange and humidity performance of an HME by assessment of the HME weight change between end-inspiration and end-expiration. This method is validated with the results of previous intra-tracheal in vivo measurements and in vitro ISO water loss outcomes of similar HME types (chapter 2, and 3). With this method it appears to be easy to test and compare the performance of many different HMEs (chapter 4). This method also facilitates better understanding of the function of the exchange of water in an HME device and the role of hygroscopic salt on the HME core material (chapter 4).

Standard of care is to advise patients to use HMEs for a maximum period of 24 hours because after that period bacterial contamination might become a source of infection, but also because of a potential decrease in water exchange performance. Daily replacement does not cause additional exposure to pathogenic microorganisms\textsuperscript{37} and shows that using an HME for 24-hours is bacteriologically safe. Although in vitro ISO 9360-2:2001 studies have suggested that after 24-hours water loss values are still more or less unchanged, HME performance after 24-hour tracheostoma application, however, never has been tested in patients. Hygroscopic HMEs might loose some of their hygroscopic salt by dilution in (condensed) water during breathing. Therefore, the performance of HMEs used by patients after 24-hour tracheostoma application was assessed (chapter 5).
The physiological long-term and short-term effects of an HME on tracheal mucociliary clearance is investigated by assessing ciliated cell contents in brush biopsies of tracheal epithelium and by measuring tracheal mucus transport velocity by means of scintigraphy scans (chapter 6). Different patient groups are combined in this chapter due to the limited numbers of laryngectomized patients available for this research, especially the limited numbers of non-HME breathing patients in the Netherlands.

In chapter 7, an attempt is made to evaluate the effect of long-term HME use on the number of pulmonary infections among laryngectomized patients using retrospective data (medical records), and a European wide survey among head and neck surgeons.

Chapter 8 discusses the results of the previous chapters and the acquired knowledge about the function of an HME, its effect on mucociliary clearance and pulmonary infections and the different methods that could be used to test HME performance in pulmonary rehabilitation after total laryngectomy. In addition, some suggestions for further research will be given.
REFERENCE LIST


