Dear Dr. and Mrs. Myers; dear Gene and Barbara. Dear Dr. Woodson; dear Gayle. Dear members of the Academy, ladies and gentlemen. First of all, I would like to thank Dr. Gayle Woodson and Dr. Jeffrey Myers for their honorable invitation to deliver this year’s Eugene N Myers MD International Lecture on Head and Neck Cancer.
SLIDE 2. Looking at the impressive list of predecessors, many of whom have been role models for me, as Gene himself is already for a long time, I am still astonished to be this year’s presidential choice. Maybe that is because Gayle and Jeffrey know that the topic they asked me to talk about has fascinated me ever since I started my career in HN. It has taken up a major part of my clinical research time over the last 35 years and covers some 40% of my contributions to the literature.
SLIDE 3. Such continuity in research would never have been possible without an optimal professional climate and therefore I would like to acknowledge here the inspiring work environment the Netherlands Cancer Institute always has offered. It’s not surprising to me that an independent Irish source has recognized that excellence, and as we heard yesterday from Dr. Morris in his John Conley Lecture, we are all Irish, and thus it must be true. Moreover, this would never have been possible without the great collaboration with my surgical and allied health colleagues in our Institute over those years, all sharing a keen interest in care and rehabilitation of patients treated for advanced larynx cancer. And I also would like to acknowledge here the contributions of the Dutch Laryngectomee Society and our patients, who have been very supportive towards our clinical research over all those years.

In this lecture I will discuss topics that for some HN surgeons, also here in the USA, might have faded into the background of their clinical attention. That concerns the rehabilitation of the impaired functions resulting from advanced tumor growth and/or surgical or organ preservation treatment in advanced laryngeal cancer.
SLIDE 4. Treatment-related impairments can be unavoidable due to the necessary anatomical sacrifices, as obviously is the case with total laryngectomy. The organ is removed and its functions are lost and consequently need to be substituted. Ever since the first laryngectomy for cancer by Billroth in 1873, these function losses were self-evident and thus received extensive attention of HN surgeons and allied health professionals.
Unfortunately, contrary to expectations, organ preservation does not necessarily mean function preservation!

SLIDE 5. Less impairment was expected from organ preservation treatment of advanced laryngeal cancer, because it was assumed that aside from tumor-induced deficits, the anatomy and thus function would remain more or less unchanged. Unfortunately, contrary to these expectations, we now know that organ preservation does not necessarily mean function preservation. One almost could say that the functional impairments after organ preservation therapies have caught us by surprise. One of the reasons might have been that the leading specialists were no longer the HN surgeons, but radiation and medical oncologists, not similarly familiar with the complexity of the HN functions we are dealing with.
Prerequisites for optimal care and rehabilitation HN cancer patients

• The involvement of the head and neck surgeon should not stop at the surgical (e.g. voice restoration) procedure itself, but should be continued long after to optimally support the involved allied health professionals

• Just like the regular multidisciplinary tumor board, there should be a multidisciplinary rehabilitation board dealing with short- and long-term rehabilitation issues; and the HN surgeon should be a key member of this board

SLIDE 6. There might be another reason why rehabilitation in case of advanced larynx cancer has faded out of the center of HN surgeon’s attention. That is, that once the basic principles of tracheoesophageal voice restoration were established, the speech language pathologists, most notably in here the US, take over most, if not all of the day-to-day care and responsibilities for voice rehabilitation, often substantially decreasing the participation of the HN surgeons. In the present changing landscape of increased application of organ preservation treatment, however, the still needed salvage surgeries have made the outcome of TL less predictable. And thus, also postlaryngectomy rehabilitation has met new challenges. By not being involved in everyday care and outcomes, and thereby leaving the SLP struggle sometimes too long alone with the occasional unavoidable problems, rehabilitation results might not always be optimal. Therefore, my recommendation is that the involvement of the HN surgeon should not stop at the surgical procedure itself, but should continue long after, in order to optimally support the TL patient together with the involved allied health professionals. Just like the now common regular multidisciplinary tumor board, there is a place for a multidisciplinary rehabilitation board dealing with short- and long-term rehabilitation issues; and the HN surgeon is certainly a key member of this multidisciplinary team. Renewed interest in the patho-physiology of function impairments following HN cancer treatment, irrespective of the treatment modality, should be in the center of the HN surgeon’s attention and thus also be an essential topic in the fellowship program. I will come back to this later in my talk.
SLIDE 7. The most obvious function impairment caused by removal of the voice box is loss of pulmonary-driven speech, which, as said, has received extensive attention already from the first TL by Billroth on new-year’s eve in 1873. Ever since that early start of surgical voice restoration there has been a long-lasting surgeon-driven search for restoring pulmonary-driven speech with adequate aspiration prevention. However, when there is a long list of ‘inventors’, as shown on the slide, one can be sure that no one has found the perfect solution for this vital larynx function. That’s why esophageal speech and later electrolarynx speech emerged as substitutes for pulmonary-driven speech. And only with the invention of prosthetic one-way valve devices, this aspiration prevention problem was adequately solved.
SLIDE 8. Mozolewski, an innovative Polish Otolaryngologist has to be recognized as the first to develop such a device and publish clinical results in 1973. His misfortune was that, although the paper contained an abstract in English, he published in Polish during a political climate that prevented his work from receiving the attention and recognition it deserved. However, in 1978 he presented his work at a surgical voice restoration conference in Boston, and that undoubtedly has inspired participants to follow this line of clinical research. And obviously, with the creation here in the US of the first commercial VP by Singer and Blom, and through their long-term teaching efforts, surgical prosthetic voice restoration has gained widespread recognition as the gold standard for postlaryngectomy voice rehabilitation. Also relevant for this success was that Singer and Blom showed that the device could be inserted through a simple, straightforward tracheoesophageal puncture/TEP, which made surgical voice restoration technically less complicated than ever before. And as already indicated, a major factor in this success also has been that generations of SLPs here in the US and elsewhere have devoted so much time and effort to make this essential component of laryngectomee rehabilitation work.
SLIDE 9. In Europe, except in the UK, the development was slightly different from that in the US. From the start, HN surgeons were leading, also because not infrequently SLPs, but especially Laryngectomee Societies were reluctant to accept surgical voice restoration as an alternative to their usual esophageal and electrolarynx speech. Moreover, not all countries had a similar availability of SLPs as the in that respect more favorable US medical system, an additional factor for switching from the original method of
   – secondary TEP with catheter-stent and delayed non-indwelling voice prosthesis insertion
to
   – primary TEP with immediate indwelling VP insertion*

* Annyas et al. Clin Otolaryngol Allied Sci. 1984 (ENT Department, Groningen University Medical Center, The Netherlands)
SLIDE 10. With respect to our own journey in surgical voice restoration, in 1979 we just had started with the Staffieri procedure, one of the then still promising surgical voice restoration methods. Although that technique also fell short in aspiration prevention, it resulted in a series of 11 patients with great voices. Encouraged by that impressive improvement in voice and speech quality as compared to esophageal or electrolarynx speech, I immediately saw the potential of the non-indwelling prosthesis of Singer and Blom, when I first came across that. That was at the meeting of the American Society of Head and Neck Surgery in the spring of 1980 in San Francisco, where Mark Singer gave an inspiring lecture on their first results in 60 patients, published later that year. At the end of his talk, I was able to speak with him, and that enthusiastic conversation led to a significant change of plans for my first tour through the US.
The key was that I could convince Agnes, 5 months pregnant of our second daughter Tessa, to stay behind in NY with our 2.5 half year old daughter Maartje, while I would fly to Indianapolis to accept Mark’s invitation to see the procedure and meet their patients. In 2 days Mark showed me all the tricks of the trait, and I went back to Amsterdam with a generously filled bag of non-indwelling VPs, which we used to salvage our leaking Staffieri fistulas.
After that, surgical voice restoration progressed quickly in our Institute. There was a short intermezzo of using the Panje prosthesis, which had the advantage that, unlike the original BS duckbill device, it had a retention collar and thus was better retained in the TEP tract. But already in the same year the Groningen group presented their first indwelling VP that was specifically designed to be implantable without prior stenting the TEP with a catheter. This was from a surgical point of view the logical next step. Why trouble the patient with a temporary stenting catheter and delayed-awake VP insertion, when one can finalize the whole procedure while the patient is under general anesthesia. With the added advantage that voice rehabilitation can commence right after wound healing is completed. This gives a tremendous psychological boost to the patient, being able to speak the first words without having to first tolerate removal of the catheter, sizing for the right size of the VP, and then having that inserted in a still sore operative area, before being able to start the first voicing attempt. It still amazes me that a method that had its clear logic and merits at the start, the first non-indwelling BS device, as said, did not have a retention collar and could not have been inserted primarily, has so long survived in the US. I am pretty sure that when HN surgeons more often would have joined the SLP at the first VP insertion session, the transition to primary TEP and immediate VP fitting would have been made much earlier. Colleagues that made this change in the nineties, like Brendan Stack, then in St Louis, now in Little Rock, and John Saunders, Dr. Harada, and Barbara Messing in Baltimore, and more recently Brian Burkey and Joann Kmiecik in the Cleveland Clinic, have never gone back to the stenting method. And it only requires an indwelling device irrespective of the brand, as Dan Deschler showed in 2009.
SLIDE 13. The Cleveland Clinic group has recently evaluated their results as shown here. There were no significant differences between primary TEP with primary fit or secondary fit for postoperative stomal breakdown, pharyngocutaneous fistula rate, and voice outcomes, also not in radiated patients. However, primary TEP with primary fit required significantly less postoperative Emergency Department visits and patients tended to have less pain at the stoma/TEP site. Additionally, the need to downsize the VP in length during the first 2 months, always a burden after a catheter stent, has diminished considerably. They conclude that this study provides clear evidence that primary TEP with primary VP fit is a safe alternative to secondary TEP or primary TEP with secondary VP fit. Not surprisingly, some 250 hospitals are estimated now to use this method here in the US.
SLIDE 14. Modern VP development is a long and tedious process and requires not only interested clinicians, but also an industrial companion that is willing to invest in what by many is considered one of the tiniest of niches in the medical device market. This especially holds true in this time and age of increasing use of organ preservation therapy, where many predicted that TL soon would be a procedure of the past. However, in the mean time we know that TL is here for a long time to stay, because with respect to optimal survival, advanced T4 laryngeal cancer is still considered to be a surgical disease, also according to the guidelines here in the US. Moreover, TL is still needed frequently for salvage, not only for oncological, but also for functional reasons. The tissue damage caused by organ preservation therapy in combination with the destruction by the tumor, not-seldom leads to a nonfunctional organ with severe dysphagia and intolerable aspiration, requiring a tracheotomy and feeding tube. And, this more unfavorable tissue environment requires ever more sophisticated surgical and material technical solutions.

Medical device research is increasingly time consuming: from start research project to publication

- **Provox: 1988 – 1990**
  - Hilgers & Schouwenburg. Laryngoscope 1990
  - Hilgers, Cornelissen, Balm. Eur Arch Otolaryngol 1993

- **Provox2: 1995 – 1997**

- **Provox ActiValve: 1998 – 2003**
  - Soolsma, van den Brekel, Ackerstaff, Balm, Tan, Hilgers. Laryngoscope 2008

- **Provox Vega and Smart Inserter: 2006 – 2010**
  - Hilgers, Ackerstaff, van Rossum, Jacobi, Balm, Tan, van den Brekel. Acta Otolaryngol 2010
  - Hilgers, Ackerstaff, Jacobi, Balm, Tan, van den Brekel. Laryngoscope 2010

- **Provox Vega Puncture Set: 2008 – 2013**
  - Hilgers, Lorenz, Maier, Meeuwis, Kerrebijn, Vander Poorten, Vinck, Quer, van den Brekel. Eur Arch Orl. 2013
  - Lorenz, Hilgers, Maier. HNO. 2013
Disclosure Statement

• The Netherlands Cancer Institute receives a Research Grant (RG) from Atos Medical Sweden, which contributes to the existing infrastructure for health-related quality of life research of the department of Head and Neck Oncology and Surgery

• All reported research, including studies carried out in relation to this RG, has been approved by the institutional Medical Ethical Review Board

SLIDE 15. And for that a manufacturer with a long-term perspective is indispensable. Therefore, through what is my usual disclosure slide, I would like to acknowledge here Atos Medical that through their research grants to the Netherlands Cancer Institute over the years significantly has contributed to the infrastructure of the Quality of Life research in our department, which self-evidently always has been scrutinized by the Medical Ethical Review Board of the Institute. And I would like to especially acknowledge here Jan-Ove Persson, the innovative engineer of Atos Medical, who from the beginning in 1987, was the inventor of most of the medical devices we worked on and thereby the ideal sparring partner for our clinical research.
SLIDE 16. An example that we now need ever more sophisticated surgical and material technical solutions was that through our continuous prospective and retrospective evaluations, such as for the PhD project of Bas Op de Coul, we could identify a subgroup of patients with a very short median device life of some 3 weeks. What made this subgroup so interesting was that many of the removed incompetent valves in these patients were not covered with biofilm, the usual reason for valve failure.
SLIDE 17. This lead to the discovery that in this subgroup an under-pressure in the esophagus during swallowing and breathing caused frequent inadvertent opening of the valve, as can be seen in the video. Probably due to material fatigue, that is loss of elasticity, this results in early incompetence of the valve. By applying magnets in the valve and valve seat this under-pressure phenomenon could be counteracted. Longevity also could be improved by constructing the valve and valve seat of a Teflon-like fluoroplastic material that is not susceptible to biofilm eroding. The two pictures at the bottom of the slide show an example of that. This prosthesis was removed after one year in a patient with a median device life for his regular prosthesis of 3 weeks. As can be seen the silicone material is fully overgrown with biofilm, whereas the valve and valve seat are not.
SLIDE 18. This inertness of the fluoroplastic material further could be substantiated in a study just published in Head Neck. On the images on the right, one can see that Candida is invading the silicone material, but that the biofilm covering the fluoroplastic is not invasive, thus leaving the surface ‘unharmed’. The resulting VP has the longest device life in the literature so far. In 3 independent studies, this is over 300 days, which makes this device an attractive solution for this subgroup of patients. This also because antifungal treatment never has been shown to work adequately against the complex biofilm on VPs, in which Candida, along with a myriad of bacterial strains, is just one of the components.
SLIDE 19. Another example of the more sophisticated recently developed technical solutions is the new surgical tool for primary and secondary TEP and immediate VP fitting, which was tested in an extensive multicenter study, conducted in 4 different European countries in 5 HN centers. This Seldinger type dilatation procedure has made TEP easier, faster, and probably also less traumatic than so far possible. These are important considerations in view of the fact, as said, that nowadays laryngectomies increasingly are salvage procedures. As can be seen in the video, primary TEP with primary VP fit takes about a minute. The disposable nature of the tool reassures that its components are in ideal condition, something that not always was the case with the surgical instruments used before, which required maintenance and re-sterilization. As can be seen in the video, the dilator with the pre-mounted VP is attached to the guide wire, next the puncture tract can be carefully dilated, and finally the loop around the VP is delivering the tracheal flange into the trachea.
SLIDE 20. Besides our medical device-related clinical trials, a significant part of the research in our department has been devoted to basic voice and speech studies. The PhD theses of Corina van As and Petra Jongmans concerned postlaryngectomy voice quality and speech intelligibility. The almost finished thesis of Renee Clapham concerns the use of automatic speech recognition tools for intelligibility assessment. The studies in the first two PhD theses improved our insight in the anatomical and physiological parameters influencing voice and speech. The third PhD thesis works towards a solution for the tedious process of perceptual voice quality and speech intelligibility assessment. Although perceptual analysis is still the gold standard, this soon might be replaced with an automated speech recognition tool that within minutes, instead of days and weeks, provides this relevant clinical information. This will make it possible to assess and follow patient’s speech developments on a more objective and regular basis, providing useful, instant, and consistent feedback not only for the patient, but also for the therapist.
Inevitable/direct consequences of total laryngectomy for pulmonary physiology and respiratory functioning

- Disconnection of upper and lower airways: no more conditioning (heating, humidifying, and filtering) of the breathing air

- Decrease in breathing resistance (>50%): ‘equal pressure point’ ➞ more peripheral in pulmonary tract ➞ affects pulmonary physiology (‘alveolar collapse’, blood-gas exchange ↓)

SLIDE 21. The second impairment of TL to address is also an obvious consequence of the disconnection of the upper and lower airways. Pulmonary complications are preprogrammed when the conditioning, filtering and humidification of the breathing air is no longer taking place. And the more than 50% drop in airway resistance affects pulmonary physiology through a shift of the equal pressure point, resulting an increased risk for alveolar collapse and suboptimal blood-gas exchange.
Clinical pulmonary rehabilitation research at the Netherlands Cancer Institute (PhD project AH Ackerstaff)

SLIDE 22. Over the last two decades clinical research, starting with the PhD project of Annemieke Ackerstaff, ...
Phase II and III clinical studies on the positive effects of HME use#

- Improvement of pulmonary issues: decreased coughing, stoma cleaning, sputum production, forced expectoration, and shortness of breath
- Improvement of associated physical and psychosocial problems: fatigue, sleep, anxiety and depression, and social contacts
- Improvement of voice quality
- Improvement of pulmonary function
- Prevention of pulmonary problems with early start
- Prevention of loss of ciliated cells in the trachea
- Decrease in tracheobronchitis and pneumonia
- HMEs are Cost-effective


SLIDE 23. ... has shown that consistent 24/7 use of HMEs results in a significant improvement of the inevitable pulmonary issues, such as excessive mucus production and frequent forced expectoration, many laryngectomized patients are bothered with. Moreover, this consistent 24/7 HME use results in an improvement of many quality of life dimensions and in an improvement of voice quality. Furthermore, pulmonary function improves significantly and early postoperative start with such devices can to some extent prevent the development of these unfavorable respiratory side effects of TL. Recently we also could show that long-term HME users have significantly more ciliated cells in the trachea than non-HME users. Besides that, there has been a reduction of tracheobronchitis since the introduction of these devices, which also turn out to be cost-effective in the European healthcare systems studied, and thus, most likely, in many comparable countries, as well.
SLIDE 24. Additionally, in a recent randomized clinical trial together with French colleagues we could show that immediate postoperative start with an HME is significantly more effective than traditional external humidification in compensating for the lost air conditioning function of the upper respiratory tract. HME use showed significant better outcomes regarding compliance, coughing, phlegm production, need for suctioning, sleep, and patient satisfaction. Moreover, nursing time and costs were significantly lower with HMEs as compared to external humidification. Certainly, additional compelling arguments to consider this early compensation for the lost upper airway functions with HMEs as an interesting and cost-effective alternative to external humidification.
SLIDE 25. The in vivo and ex vivo physical data of the HME-effects on tracheal climate are more recently obtained. In three successive PhD projects of Karel Zuur, Renske Scheenstra and Cindy van den Boer, these effects have been unraveled.
SLIDE 26. For that it was necessary to develop custom-made equipment, the Airway Climate Explorer, short ACE, which enabled precise humidity and temperature measurements in the first centimeter of the trachea with open stoma and right behind the HME. The essential ACE component was the internal heating system for condensation prevention. The temperature had to be well-above body temperature, and in this case 40°C turned out to be optimal. Without that condensation prevention technology, the data obtained with the ACE would not have been reliable, as could be shown in the first validation study.

The complicated probe construction needed for preventing condensation is depicted in more detail here. In an internal tube with a diameter of only 2.2 mm, 6 electrical wires for temperature control and heating, and a temperature probe had to be integrated, still leaving enough room for allowing pre-defined air sampling. Moreover, the tube had to be externally insulated and could not exceed a diameter of 6 mm in order not to cause un-physiological air turbulences in the trachea. Ultimately the probe fulfilling all these requirements was 5 mm in diameter.

ACE air sample catheter:
- Length 30 cm
- Total diameter 5 mm
- Inner diameter 0.8 mm
- 4 heating wires
- 2 control wires
- Silicone and air isolation

Continuous air sampling: 600 ml/min.

SLIDE 28. With this fully validated technology, under cold room conditions the first generation HMEs appeared to function as expected, but much to our surprise, under normal room temperature conditions they functioned differently. Although there was also then a highly significant increase in humidity at end-inspiration, there was also a slight decrease in temperature due to evaporative cooling, which obviously is not optimal. Since a much bigger special filter HME did not have that problem, the logical conclusion was that the thermal capacity of the first generation HMEs apparently was insufficient under normal room temperature conditions, and thus should be increased. This led to the development of the second generation HMEs, where this unfavorable effect could be solved without the device becoming too big, as can be seen on the slide.

Overview of HME effects on humidity: significant Upper Respiratory Tract compensation in all tested HMEs, up to almost physiological levels with the best humidifying version of 2nd generation HMEs (XtraMoist)


SLIDE 29. As a result these second generation HMEs have an even better humidification effect, almost closing the physiological gap between nose and stoma breathing, as can be seen on this slide.
SLIDE 30. More recently the PhD studies of Cindy van den Boer resulted in a new method to assess the water exchange capacity in a more physiological way than possible with the in vitro technology according to the ISO 9360 standard. This laboratory test uses an artificial lung that, however, cannot fully mimic the in vivo situation. In this novel ex vivo method, the difference in weight of the HME at end-expiration and end-inspiration of the volunteer is a measure for the water exchange capacity of the device. Again, the validation of this method was a long and tedious process, but now it is established, it is certainly easier to duplicate for confirmation studies, and the components are, unlike with the ACE, readily commercially available.
SLIDE 31. With this ex vivo method, it is possible to compare devices and to work on further improvements, without having to bother patients, as was necessary with the in vivo ACE measurements. And as recently could be shown, calling a device an HME not necessarily means it has a significant humidification effect. To paraphrase George Orwell’s ‘Animal Farm’: All HMEs are equal, but some are more equal than others.
The sense of smell is the third function depending on an intact airway and rehabilitation of this sense also has been a research topic in our department. Time does not permit to go into all details, but this project together with our psychologist Frits van Dam, and SLP Corina van As led to the discovery of a simple and effective maneuver, the nasal airflow inducing maneuver or NAIM, by using the oral cavity as a vacuum pump, schematically shown in the animation. The NAIM is also called ‘polite yawning’ technique, because that is the basic feeling you get when executing this maneuver. With the NAIM, a nasal airflow can be created that is strong enough to restore the sense of smell. In our initial studies we found that in the majority of patients olfaction could be regained.
SLIDE 33. In the mean time this line of research has been taken up in other institutes, confirming our findings and showing that results can be further improved with more intensive and prolonged SLP training, while the time investment is not very high. Devoting at follow-up visits regularly a couple of minutes to check whether the technique is still performed correctly and that patients realize that this is an active maneuver never bringing back the passive sense of smell, is enough to stabilize this technique in every day life. Even professional wine sniffing and tasting is possible again, as last year experienced by one of Brendan Stack’s patients, underlined by the great Oregon Pinot, he selected for me. And as we know, this is very relevant skill, because also for our laryngectomy patients, life is too short to drink bad wine.
Dysphagia prevention and treatment after organ preservation approaches

• Initial thought/hope was that organ preservation also meant function preservation, but the reality has sunken in now. Hence the increased efforts to develop preventive and therapeutic options and tools for the inevitable sequels of organ preservation approaches

• Analogy with postlaryngectomy rehabilitation?

The last vital function necessary to address when talking about care and rehabilitation of patients treated for advanced laryngeal cancer is swallowing. Although swallowing also after TL can be impaired and should receive attention in the rehabilitation program, this element of HN rehabilitation has become more in the foreground since the increasing application of organ preservation protocols and the observation that dysphagia is a significant complication that has to be taken care of. As already mentioned, the initial thought and hope was that organ preservation also meant function preservation, but in the mean time reality has sunken in. Hence, the increased efforts for developing preventive and therapeutic methods and tools for the inevitable sequels of the organ preservation approach. And, maybe in analogy with the progress we have made over the last decades in TL rehabilitation, with combined multidisciplinary efforts, we can advance in this field as well.
Dose-effect relationships exist for dysphagia and trismus / MIO (comparable with literature: e.g. * Nuyts et al. (2013), Teguh et al. (2008), Feng et al. (2007), Levendag et al. (2007))

SLIDE 35. Radiation oncologists have addressed this issue by trying to diminish the RT dose on structures important for swallowing, such as the pharyngeal constrictor muscles, as is possible with IMRT techniques. In line with the literature, also we found a dose response relationship for dysphagia, maximum inter-incisor mouth opening, and trismus, which means that by defining swallowing structures as “organs at risk” in the treatment planning, as already is done for salivary glands to limit xerostomia, with IMRT swallowing could become potentially less impaired.
SLIDE 36. Although IMRT is relevant and not without effect, the prevention of non-use atrophy as a contributing factor to long-term dysphagia might be at least as relevant, or maybe even more so, for function preservation. Only in recent years we have started to realize the importance of the principles “eat and exercise”/“use it or loose it” as a way to prevent long-term dysphagia. The strong focus on prevention of weight loss and therefore the use of prophylactic tube feeding likely is partly responsible for the increase in dysphagia we have seen. We should not be surprised that after months of non-use the major swallowing musculature has atrophied, making recovery of oral intake extremely difficult and not-seldom impossible. For once, we cannot only blame radiotherapy for that, but should acknowledge our own shortcomings in this respect. Preventive exercising, starting before therapy onset and to be continued during and after tube feeding, if that is unavoidable, seems a valid approach to decrease this dismal side effect of chemoradiotherapy, as also suggested in the recent PhD project of Lisette van der Molen.
In the current follow-up PhD project on dysphagia by Sophie Kraaijenga, the effectiveness of this preventive approach was further strengthened with the finding that all patients of the original preventive study population prospectively followed and still alive at 6-years follow-up, had maintained or regained adequate oral intake. The development of medical devices supporting this preventive and therapeutic approach is also promising, as shown in a recent feasibility study in 10 senior citizens. This approach currently is being tested in a phase II clinical trial.
SLIDE 38. Another example of dysphagia research is our recent feasibility study on the potential value of lipofilling in the treatment of oropharyngeal dysfunction and dysphagia, started by my colleagues Michiel van den Brekel en Ludi Smeele. This study, encompassing 7 patients now, shows promising results with significant swallowing improvements in 4 patients. Two of them were confined to long-term tube feeding, but now are back to oral intake, allowing removal of the feeding tube. These examples show that a close collaboration between HN surgeon and allied health professionals is essential for progress in these functional deficit areas and that HN surgeons should have a keen interest, not only in HN cancer treatment, but also in HN cancer rehabilitation, since together with our allied health colleagues, we have the armamentarium to restore or compensate functions losses. And dysphagia research is only at its infancy in this respect.
SLIDE 39. When we invest similar time and effort in this aspect of HN rehabilitation, as we have done in total laryngectomy rehabilitation, my expectation is that we will be able to solve or at least improve this debilitating aspect of organ preservation treatment better than so far deemed possible. Therefore, it’s mandatory to set up more multidisciplinary HN rehabilitation programs, preferably based on the WHO ICF conceptual model of functioning, disability, and health, and the ICF HN core set proposed by Tschiesner and others. Recently, in the Netherlands Cancer Institute we have been able to establish such an evidence-based program, which therefore is funded within the regular private healthcare insurance we have in the Netherlands. This multidisciplinary HN rehabilitation program, functioning since 2010, shows very promising results, as we recently could conclude in the first evaluation study of this program.

To sum up, over the last decades the increasing use of organ preservation protocols has created new challenges for HN rehabilitation. Besides the traditional rehabilitation of the aftermaths of the lost voice box, that is voice, pulmonary, and olfaction rehabilitation, we now also have to address the functional issues caused by the compromised larynx and pharynx. Function preservation in organ preservation protocols should be more integrated, not only through ever more clever radiotherapy planning, but also through structural incorporation of preventive exercises and tools to avoid non-use atrophy of the swallowing musculature.
Advanced larynx cancer-related research at the Netherlands Cancer Institute
(PhD project AJ Timmermans)

SLIDE 40. Moreover, it has become clear that total laryngectomy still is indispensable as primary treatment modality for advanced (T4) larynx cancer, and for management of recurrent disease and/or debilitating laryngeal dysfunction after prior non-surgical treatment. Several publications in the last decade, including the papers in the just finished PhD project of Jacqueline Timmermans, have shown that. Also postlaryngectomy rehabilitation, thus, remains an essential theme in present-day laryngeal cancer care and rehabilitation. I therefore would like to stress once more that this requires a life long multidisciplinary team commitment. The involvement of the HN surgeon should not stop at the surgical voice restoration procedure itself, but should be continued long after, not leaving the SLP struggle too long alone with the occasional unavoidable problems. Our current knowledge of postlaryngectomy voice, breathing and olfaction patho-physiology, the evidence-base for our present rehabilitation options, should be used to the benefit of all our patients. And fortunately, medical device technology still is progressing, enabling reliable restoration of pulmonary-driven speech, and compensation for lost upper respiratory tract/climate conditioning functions in the majority of cases, despite increasing surgical challenges. And similar developments in dysphagia research are promising.
SLIDE 41. Finally, as an example of the progress we made in the care and rehabilitation of patients treated for advanced laryngeal cancer over the last 30 years, I would like to show you a performance by Salvatore Barile, an Italian musician and music teacher, who had his laryngectomy in 2000. Since his secondary TEP in 2003, he not only has developed excellent TE speech, but due to recent technical improvements now also is able to play his slide trombone with both hands again.

Example of progress in 30+ years of prosthetic voice rehabilitation
Playing a brass instrument after total laryngectomy: a case report.
Cavalot, Schindler, Juliani, Schindler, Cortesina. Head Neck 2009;
Physiology and prospects of bimanual tracheoesophageal brass instrument play. Hilgers, Dirven, Jacobi, van den Brekel. Acta Otorhinolaryngol Ital. 2015
Thank you for your attention