The Montgomery Thyroplasty Implant System: A 360° Assessment

Desuter, G.R.R.

Author: Desuter, G.R.R.
Title: The Montgomery Thyroplasty Implant System: A 360° Assessment
Issue Date: 2020-01-21

The Montgomery Thyroplasty Implant System:
A 360° Assessment

Gauthier René Raymond DESUTER

Financial support for distribution was provided by:

SOLUVOS b.v., BESS Group Inc., and XION-Medical GmbH.

Colofon

Lay-out and Printing by:

Universitair Facilitair Bedrijf , Leiden

Cover illustration: Ornella Furnari & Thierry Duprez MD.

The Montgomery Thyroplasty Implant System:
A 360° Assessment

Proefschrift

Ter verkrijging van

de graad van Doctor aan de Universiteit Leiden,

op gezag van de Rector Magnificus prof. mr. C.J.J.M. Stolker,

volgens besluit van het College voor Promoties

te verdedigen op dinsdag 21 januari 2020

klokke 11.15 uur.

door

Gauthier René Raymond Desuter

Geboren te Berchem-Sainte-Agathe, Brussel

in 1968

Promotor:

Prof. dr. P.P.G. van Benthem

Copromotor:

Dr. E. V. Sjögren

Leden promotiecommissie:

Prof. dr. G.J. Fleuren

Dr. M. M. Hakkersteegt (Erasmus Medisch Centrum)

Dr. A.P.M. Langeveld

Prof. dr. H. F. Mahieu (Meander Medisch Centrum)

Prof. dr. I. M. Verdonck- de Leeuw (Vrije Universiteit Amsterdam)

To my father, Roland M.J.J.G. DESUTER (†)

Table of contents

ABBREVIATIONS THESAURUS

AA	Arytenoid Adduction
AP	Arytenoid Pexy
CUSL	Cliniques unniversitaires Saint-Luc, Brussels
ESGP	Estimated Sub-glottic Pressure
F0	Fundamental Frequency
IL	Injection Laryngoplasty
LCA	Lateral Crico-Arytenoid Muscle
LEMG	Larynx electromyography
LUMC	Leids Universitair Medisch Centrum
MPT	Maximum Phonation Time
MeAF	Mean Airflow
MT	Medialization Thyroplasty (all techniques and type of implants)
MTIS	Montgomery Thyroplasty Implant System
PCA	Posterior Crico-Arytenoid Muscle
PQ	Phonatory Quotient
RLN	Recurrent Laryngeal Nerve
TA	Thyro-Arytenoid Muscle
UVFP	Unilateral Vocal Fold Paralysis
VHI	Voice Handicap Index
X	The Vagus nerve

CHAPTER 1

General Introduction and Thesis Outline

Unilateral Vocal Fold Paralysis

and the Montgomery Thyroplasty Implant System

The unilateral vocal fold paralysis (UVFP)

UVFP patients and impact on their quality of life

UVFP with the paralyzed vocal fold in an abduction position results in glottic leakage during phonation.

Patients presenting with a UVFP and glottic air leakage will complain about the following symptoms:

- Breathy Voice
- Disability to project their voice, or in severe cases, even no voicing at all
- Shortness of breath when speaking (phonatory dyspnea)
- Dysphagia, mostly with liquids, due to inability to securely close the glottis during swallowing
- Inefficient cough due to glottic incompetence
- Constipation, due to inability to exert a Valsalva maneuver

The majority of the studies in the literature focus on voice symptoms, but these are not the only ones to consider. There is also a need for patient centered studies, that focus on patients' complaints and needs.

Dysphonia represents a significant disability that is comparable to conditions such as angina pectoralis, sciatica and chronic sinusitis. UVFP patients present the highest level of pre-treatment disability among dysphonic patients [1]

Hogikyan et al. investigated Voice-related Quality of Life (V-RQOL) following medialization thyroplasty (MT) for UVFP [2]. UVFP patients showed very low overall V-RQOL scores (32, 59 /100) in comparison to normal controls (97.95/100). After treatment with MT, the V-RQOL scores of UVFP patients, although improved, could not match the control group reaching a 73, 62/100 overall V-RQOL score.

Basic physiology

Voice produced by a human transmitter, is energy transferred through a gas - the air - that will hit the tympanic membrane of a human receptor. This energy is produced by the lungs mobilizing and expelling air. This pressurized air will encounter a resisting obstacle represented by the closed vocal folds within the larynx and results in a buildup of pressure beneath the glottic plane. The sub-glottic air pressure increases up to the moment it forces the obstacle. The myoelastic properties of the vocal folds then come into play. These properties will alternatively open and close the glottis according to the Bernoulli's law. This will chop the air flow into pressure waves. These elementary acoustic waves are later modified within the resonance cavities of the upper respiratory tract into complex harmonics [3].

Vocal folds consist of a multilayer structure: (1) a surface epithelium, (2) a soft tissue space -the Reinke's space- (3) a lamina propria, a complex structure composed of collagen and elastin fibers (4) a vocal ligament (5) and a muscle, composed mainly of the vocalis portion of the thyro-arytenoid muscle. The integrity of this multi-layer disposition is key to the myoelastic oscillation of the vocal fold and also an important condition for successful voice production.

The primary condition for the myoelastic theory to occur however consists of adduction of both vocal folds in the midline in the glottic area.

Vocal folds could be seen as two sails. Their free edge can be fully deployed to offer a greater resistance to air -when voicing- or can be fully reefed when no resistance to the air passage -when breathing- is sought. These two sails, horizontally deployed, have a common fixed point anteriorly and a different mobile anchoring point posteriorly. The position of the posterior anchoring points will determine their respective degree of deployment. The anterior fixed point of the vocal folds corresponds to the anterior commissure located approximately at mid-height within the thyroid cartilage. Both mobile posterior points correspond to the vocal processes of the arytenoid cartilages.

In conclusion, the respective positions -in the three dimensions- of the vocal folds depend entirely on the positioning of the arytenoid cartilages.

The arytenoid cartilages are of particular interest. They are constantly in equilibrium on the articulatory facet of the cricoid cartilage. This equilibrium is maintained by tone and contractions of two antagonist muscles.

The Posterior Arytenoid Muscle (PCA) contraction pulls the arytenoid postero-medially. As a result, the vocal process will move externally and open the glottis or, reduce the sail surface to refer to our previous analogy. It will also slightly uplift the vocal fold posteriorly.

LCA

Inversely, the Lateral Crico-arytenoid (LCA) pulls the arytenoid antero-laterally. As a result, the vocal process will move inwards and close the glottis or unfold the sail. It will also slightly lower the vocal fold posteriorly. The LCA acts in conjunction with the inter-arytenoid muscle and the Thyro-arytenoid muscle (TA) that closes the posterior part of the glottis during high pitch voicing and airway protection.

The neurological control of these two antagonistic muscles (LCA and PCA) is remarkable as well as unique in the human body. Both muscles are innervated by the same branch of the Vagus nerve (X): the recurrent laryngeal nerve (RLN). Approximately 30% of the RLN neurons innervate the PCA, while 70% of the RLN neurons innervate the LCA-TA complex. Accordingly, there is clearly a predominance of adductive innervation within the RLN [4].

During voicing, the adducting LCA-TA complex is activated through the RLN to close the glottis. Inversely, during breathing the abducting PCA is activated through the same RLN to allow air passage.

Coordination between breathing and voicing, as well as symmetrical coordination of vocal folds motion depend on motor cortex, pontine reticular formation and brainstem nuclei control (nucleus solitarius and nucleus ambiguous) [5].

Definition of vocal fold paralysis

According to Rosen et al., a vocal fold paralysis is defined as "*an immobile vocal fold due to a neurogenic etiology, the cause can be either a central nervous system pathology (i.e. lateral medullary infarct) or peripheral nervous system abnormality (X or RLN)*" [6].

In common clinical practice, the neurogenic origin of UVFP is supported by the clinical history. The history will reveal the presence of pathology or a medical intervention affecting the neural control of the affected side of the larynx [7]. Laryngeal electro-myography (LEMG) may be useful to confirm the neurogenic origin of UVFP, specifically when medical history does not provide evident causes of neurogenic damage or when a Crico-arytenoid joint pathology is suspected.

The etiology case mix of UVFP will largely depend on local disease incidence, treatment pathways and referring patterns.

Up to 75% of UVFP can be of iatrogenic origin [8].

Figure 1 represents the case mix of etiologies of patients that benefited of a MT at the cliniques universitaires Saint-Luc (CUSL) in Brussels between 2004 and 2018 (n:75).

It is important to note that 82% of the iatrogenic labelled etiologies were related to cancer surgery (esophagus, pulmonary and thyroid gland cancer).

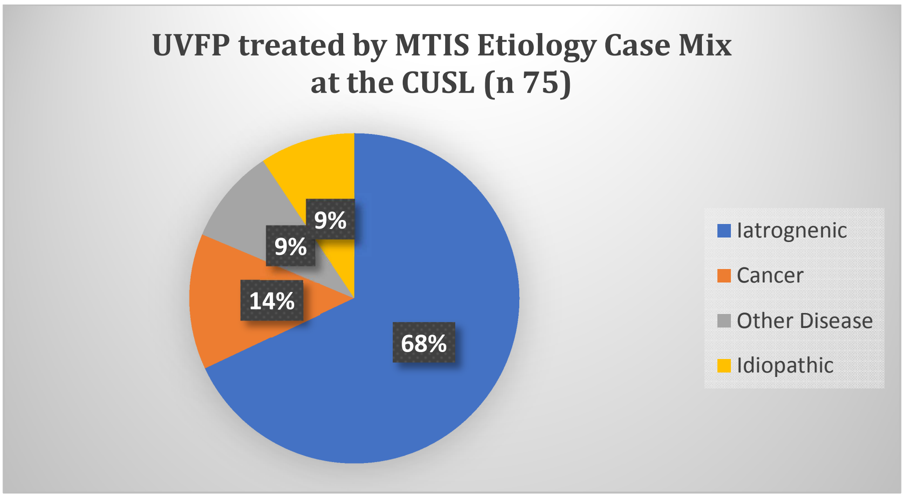


Figure 1: MTIS etiology case mix at the CUSL between 2004 and 2018.

Type of nerve lesions and natural history of re-innervation

Only a relatively a small percentage of UVFPs has a central nervous origin. In most cases the lesion is to be found in the peripheral nerve. Three types of peripheral nerve damage of increasing gravity can be distinguished: (1) neurapraxia, (2) axonotmesis and (3) neurotmesis.

- neurapraxia consists of temporary damage of the myelin sheath. The axons themselves are intact and thus nerve conduction will usually recover within the six weeks. LEMG shows reduction of action potential amplitude.

- axonotmesis consists of more severe damage to the axons and the myelin sheath but the perineural infrastructure consisting of the endoneurium, perineurium and epineurium is preserved. LEMG performed two-three weeks after injury, shows signs of de-innervation such as fibrillation potentials and sharp action potential waves. Recovery appears usually after 6 to 9 months.

- neurotmesis consists of severe damage of axons and myelin sheath associated with a severe injury of the nerve infrastructure. It has a poor prognosis, usually with incomplete or no nerve function recovery at all.

In all these types of nerve injuries there will be a spontaneous tendency toward re-innervation. Once the nerve disruption is overcome, the nerve will regrow at a pace of 2 – 4 mm/day [9].

Whether this reinnervation will be complete and result in appropriate nerve function and movement, remains uncertain. The more severe the nerve lesion is, the smaller the chance of recovery will be.

In clinical practice the severity of the nerve damage is seldom known. Arviso et al. described the natural history of a cohort of 42 patients presenting with a UVFP (2/3 of iatrogenic origin, 1/3 of idiopathic origin). All patients were treated with early (< 3 months) TA injection laryngoplasty (IL) with a temporary material. Twenty-four percent (24%) recovered a full vocal fold motion, 10% recovered a partial vocal fold motion, 40% recovered no vocal fold motion but had a satisfactory compensated voice and finally 29% had no recovery of motion or voice [10].

From Arviso's paper, we can conclude that the natural history of the re-innervation is highly unpredictable. Nevertheless, it is fair to assume that, after UVFP, approximately one third of patients will recover vocal fold motion, one third of patients will recover a satisfactory "compensated voice" with no motion and one third of the patients will not recover motion nor voice.

Young et al. confirmed this concept of "compensated voice" accounting for 21% of their patients, recovering a normal VHI-10, despite lack of recovery of motion. [11]

Mau et al. recently published a study investigating time as a prognostic factor for UVFP recovery [12]. They published a large case series with a de novo mathematical model. The novelty was to take severity of nerve damage into account. A mathematical recovery model based on nerve damage severity was compared to the natural history of 44 UVFP patients that recovered voice. They distinguished neurapraxia lesions, in which the nerve is stretched but the sheath remains intact, from other more severe nerve damage. They postulated that neurapraxia patients' recovery would follow a deterministic bell shape curve with a small dispersion, centered on a 2-3 weeks post-injury latency. In the other group of patients with a more severe nerve lesion, the new nerve sprouts have to cross the site of injury. This occurrence of this "cross-over" stage will follow a probabilistic decreasing recovery/time curve. In a second stage, a neural grow to the target muscle will follow a deterministic bell-shaped recovery/time curve with a larger dispersion centered on a 3 months post-injury latency. The fusion of all these three curves matched completely with the voice recovery latencies – with or without vocal fold motion- of this group of 44 UVFP patients.

Figure 2 shows the camel back-shape (in red) of this time to recovery curve.

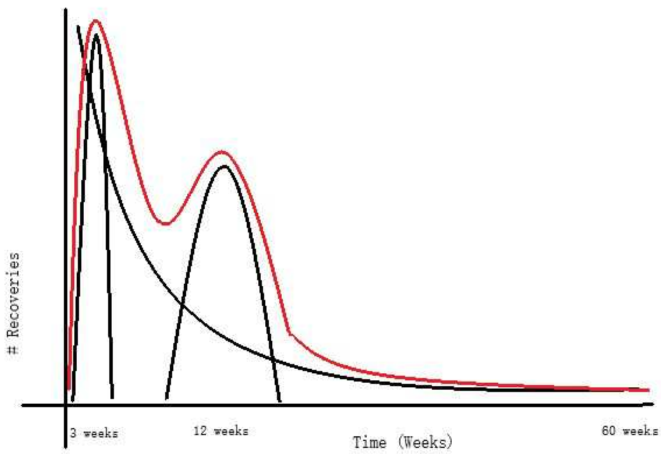


Figure 2: Voice recovery versus time (weeks) after nerve lesion. According to T. Mau et al. Laryngoscope 2018

They concluded that their model predicts that 86% of patients that will eventually recover a voice after UVFP will recover within 6 months, and 96% within 9 months.

No recovery of vocal fold motion could be observed after 7.5 months.

UVFP Treatment options

The basic principle of UVFP treatment is to medialize the paralyzed vocal fold in order to improve glottic closure during phonation.

Many treatments, based on different approaches, have been proposed in the literature to treat UVFP:

- **Approach #1**: injecting a substance into the TA muscle and thus augmenting the paralyzed side. This is called **Injection Laryngoplasty (IL)**. There are numerous substances available on the market, both permanent and transient.

- **Approach #2**: surgical modification of the larynx cartilaginous framework.

    - **Medialization Thyroplasty (MT) or Isshiki's Type 1 Thyroplasty** consisting of creating a window within the thyroid cartilage and pushing the vocal fold inward to close the glottic gap. An implant allows the permanency of this framework modification. Many materials have been proposed by many authors in the past. They are listed below.

      Medialization Thyroplasty can be complemented by arytenoid procedures such as:

        - Arytenoid adduction (AA) consisting of suturing the arytenoid to the anterior portion of the thyroid ala in order to rotate the posterior anchor of the VF and thus close the (posterior) glottic gap. AA can be combined with IL or reinnervation as well.

        - Arytenoidopexy (AP) consisting of suturing the crico-arytenoid joint in order to modify the position of the posterior anchor of the VF and thus close the glottis gap. AP can be combined with IL or reinnervation as well.

      The need for such complimentary approaches is still debated and appears to depend on the medialization technique or implant that is used [13-15].

- **Approach #3**: restoring tonus by non-selective or selective reinnervation of TA. Several techniques have been proposed:

    - End to end suturing of proximal and distal stumps of the injured nerve (X or RLN) [16]

    - Anastomosis between the Ansa Hypoglossi and the distal stump of the injured nerve (X or RLN). This anastomosis can be non-selective (on the common trunk of the distal stump of the RLN) or selective, with separate grafting of the PCA (abductory) branch and the TA branch [17,18].

    - Muscle (Omo-hyoid muscle) and nerve (Ansa Hypoglossi) "en bloc" grafting into the PCA or the TA [19].

Arytenoid procedures can also be combined with re-innervation procedures [20]

- **Approach #4**: guiding inevitable re-innervation so that abductory impulse will eventually activate the abductory muscle (PCA), and adductory impulses will activate the adductory muscles (LCA-TA). Experiments have been performed injecting neutropic agents and stem cells supposedly secreting neutropic agents in the target muscle (PCA or TA) [21].

- **Approach #5:** electric stimulation by pacers has been attempted within the frame of research protocols [22].

- **Approach #6:** voice therapy has been proposed as treatment for UVFP. Results, however, remain modest and do not match surgical approaches results in terms of Maximum Phonation Time (MPT) and modified Voice Handicap Index (VHI-10) improvement [23]. Drawing conclusions about voice therapy efficiency for UVFP remains difficult because of lack of outcome indicators and interventions standards [24].

Approaches number 1, 2 and 3 have been the subject of numerous publications showing their benefits and can be considered as gold standards of treatment. Siu et al. published, in 2015, a systematic review that compared outcomes in surgical interventions of UVFP [25]. According to this review there is no evidence suggesting superiority of any of these approaches in terms of voice outcomes. They also conclude that reinnervation may be best reserved for infants and children.

Table 1 summarizes the strengths and weaknesses of each approach according to Siu et al.

Approach	Strengths	Weakness
IL	can be performed office-based, does not impeach later MT (temporary measure)	may require multiple injections
MT	instantaneous result, simple technique	long-term result may fade away due to progressive vocal fold atrophy, requires operating room time
AA or AP	may be useful correcting large posterior horizontal or vertical glottic gaps	technically challenging, more risk of complications compared with MT
Reinnervation	prevent TA atrophy long-term results are good	technically challenging long latency before voice result, requires operating room time

Table 1: Strengths and weakness of UVFP treatments. (IL: injection laryngoplasty, MT: medicalization thyroplasty, AA: arytenoid adduction, AP: aytenoidopexy, TA: thyro-arytenoid muscle)

Approaches 4 and 5 are not considered as gold standards. Larynx pacing and use of neurotrophic agents remains largely experimental to date.

Approach 6 is mostly considered as a support effort to the IL, MT and reinnervations procedure. Efficiency of voice therapy as sole intervention remains uncertain and is subject to further investigations.

Medialization thyroplasty

Techniques

As mentioned earlier, MT, also called Type 1 Thyroplasty referring to Isshiki's classification [30, 31], represents a standard treatment for paralyzed vocal fold in abduction [32].

The basic principle of MT consists of pushing the paralyzed vocal fold inwards through a fenestration created of the lateral ala of the thyroid cartilage. Many materials have been proposed over the years since the first interposition of cartilage performed by Dr Payr in 1915 [33].

Table 2 summarizes the different materials used around the world. Some materials need larger or smaller cartilage fenestration. Some are pre-molded and provided by the industry, others are self-carved per-operatively by the surgeon. Finally, some are self-anchored others need stitches in order to be stabilized.

Type of implant & technique	Designer (if applicable)	Reference article
Medtronic Silastic Implant™	J.L. Netterville	**Netterville** JLStone RE, Luken ES, Civantos FJ, Ossoff RH (1993) Silastic medialization and arytenoid adduction: The Vanderbilt experience. A review of 116 phonosurgical procedures. Ann Otol Rhinol Laryngol 102;413-424
Hard Silicone MTIS™	W. Montgomery	**Montgomery** WW, Blaugrund SM, Varvares MA (1993) Thyroplasty: a new approach. Ann Otol Rhinol Laryngol 102:571-579
Hydroxyapatite VoCom™ implant	C. W. Cummings	**Cummings** CW, Purcell LL, Flint PW (1993) Hydroxylapatite laryngeal implants for medialization. Preliminary report. Ann Otol Rhinol Laryngol 102:843-851
Titanium implant™	G. Friedrich	**Friedrich** G (1999) Titanium vocal fold medialization implant: introducing a novel implant system for external vocal fold medialization. Ann Otol RhinolLaryngol 108: 79-86
Gore-Tex™ (Polytetrafluoroethylene)	None/ surgeon-specific technique	**McCullogh** TM, Hoffman HT. (1998) Medialization laryngoplasty with expanded polytetrafluoroethylene. Ann Otol Rhinol Laryngol 107:427-432
Self-carved Silastic block	None/surgeon-specific technique	**Benninger** MS, Manzoor N, Ruda M.(2015) Short and Long-term Outcomes after silastic medialization laryngoplasty: are arytenoid procedures needed? J Voice, Vol. 29N 2, 236-40 Shingal T, **Anderson J**, Chung J, Hong A, Baratha A Effect of medialization on glottic airway anatomy: cadaver model (2015)J Voice Vol 30, N6, 757.e1-757.e6

Reports reveal good results for all the materials described in table 1, showing low re-intervention rates.

Unfortunately, the lack of standardized voice outcome indicators impedes proper comparison between materials and techniques so that, to our best of knowledge, none of these can be declared to be superior to others [25].

In 2018, the choice of the technique and material that is used for a MT is left to the discrepancy of the surgeons. Their choice is usually based on their own experience and training.

The Montgomery Thyroplasty Implant System (MTIS)

The pioneer, entrepreneur and generous spirit of William W. Montgomery MD

William W. Montgomery MD

Proctor VT, 1923 - Brookline, MA 2003

William W. Montgomery was a Harvard surgeon and an innovator. This is how he was he described in his New York Times Obituary the 15th of November 2003[26].

He was also fond of sharing his knowledge and inventions with anyone who asked for it. As Joseph B. Nadol Jr, one of his former residents, stated in The Lancet in 2004, he had a "*rather uncanny ability to make things seem simple…his hypotheses were always how to make surgery better, safer, more reliable…and easier*" [27].

These principles were followed when developing the MTIS [28,29].

It was all about developing a system that was reliable, safe as well as easy to use. Its easiness of use was aimed at being able to share the technique as widely as Dr. Montgomery possibly could. From a patient's perspective, the larger the number of surgeons performing MTIS is, the better the accessibility to the technique will be.

W. Montgomery was also a woodcrafter and his first prototypes were simply crafted in Vermont's maple wood (FIGURE 3). As a former war-surgeon during the nineteen-fifty Korean conflict, his motto could certainly be stated as "keep it simple and efficient".

The reality of this philosophy will be tested by this thesis.

FIGURE 3: Original Montgomery's Implant carved by William W. Montgomery in maple wood. (Courtesy of S. Montgomery)

The Medialization Thyroplasty technique known as the Montgomery Thyroplasty Implant System™ (MTIS).

This technique and type of implant is widely used and available all over the world. Its frequency of use is increasing with its reported short learning curve and excellent post-operative voice outcomes. The MTIS provides not only a pre-molded hard silicone implant, but also a step-by-step operative procedure.

<u>The MTIS procedure:</u>

The procedure is performed under light sedation and local anesthesia. Particular attention is offered to overweight and/or apneic patients for which sedation must be titrated in order to avoid any tongue ptosis causing apnea and desaturation. An anesthesiologist is present within the OR during the entire procedure. Oxygen and cardio-pulmonary parameters are monitored continuously.

The patient lies on his back with a neutral positioning of the head. Oxygen is administrated through a nasal probe fixed with tape.

In our experience, we do not systematically use visual feed-back of the larynx with simultaneous trans-nasal video-endoscopy. The patient's voice is the sole feed-back indicator. Video-endoscopic feed-back is reserved for difficult or unclear cases.

All surgical steps correspond to the step-by-step surgical procedure described by Dr. Montgomery's initial paper and provided with the implants, sizer set and surgical instrument set by Boston Medical Inc. [34]. These steps are filed at the Federal Food & Drugs Administration (FDA) and have not been modified since their initial filing .

Rationale and outline of the thesis

At the time of starting this work, a review of the literature focusing on MTIS for UVFP retrieved fifteen studies [36-50]. Only 2 teams have published large series evaluating the results of MTIS for treatment of UVFP, one of which was performed by Montgomery himself. Both teams concluded that MTIS represented an efficient, safe, reliable and reproducible technique that superseded the results with Gore-Tex. Laccourreye et al. also evaluated the results after 2 years of follow-up and found that the good results were maintained over this period.

One of the unwritten but outspoken criticisms, on MTIS is the following: "How could the individual shape of individual larynges be addressed sufficiently with only six sizes of implants per gender made available?" Some laryngologists also complain about the incidence of re-do surgeries they have been confronted with after MTIS surgeries. Nevertheless, a growing number of MTIS implants are used in the US each year [35].

There is a discrepancy, between the frequency of use and the limited number of publications on MTIS. This constituted the trigger of this thesis.

Within the global context of the recent "Implant Files Scandal", the questions we should ask ourselves are: is MTIS a good medialization system? What are its advantages and disadvantages? Is it not high time for a 360° assessment?

Research Questions

Subsidiary Question: How do you assess MTIS voice outcome?

Anyone who would like to compare different treatment modalities of UVFP is confronted by the lack of standardized voice outcome measures and differences in reporting of outcome data [25]. This is also is also true for the MTIS related literature. To evaluate their results, for example, Montgomery and Laccourreye used MPT [42,48], Hartle et al. used acoustic parameters [40], Borel et al. used the VHI score [43], Cesari et al. a new electro-acoustic data set [44] and Almohizea et al. investigated per-operative Peak Direct Subglottic Pressure [36].

Voice outcome indicators had to be chosen to evaluate MTIS performance. Accordingly, a literature review was launched (STUDY 1, chapter 2). The aim of the review was to assess the most frequent Voice Outcome Indicators (VOI) that were used in the recent English literature. Subsequently a second study subjected these frequently used VOIs to the surgeon's opinion (STUDY 2, chapter 3).

Question 1: Is the MTIS a simple technique? What is its "learning-curve"?

In 2015, before the launching of the thesis, G. Desuter reported the results of a retrospective study that focused on MTIS learning curve. MTIS provides good outcomes even when performed by a novice surgeon. Over time with growing experience of the surgeon, operating times shorten and voice outcomes are maintained. [51].

Question 2: does the MTIS offer permanent results?

As Siu's review suggested that voice improvement after MT could fade away with time due to the vocal fold atrophy caused by ageing and that the 2 years follow-up of Laccourrey's paper could not answer this question [25, 42], we launched a European multi-centric cross-sectional study to evaluate very-long term (> 2 years) VHI-30 scores of MTIS patients (STUDY 3, Chapter 4).

Question 3: Does the MTIS make additional arytenoid cartilage surgery unnecessary? In other words, does the MTIS also achieve posterior glottis closure?

The 1993 initial paper of Montgomery stated that "the design of the implant will close the posterior commissure". This closure should be related to optimal voice improvement. Neither data nor technique was available at the time this thesis was started, to be able to test this statement. Considering the progress of medical imagery techniques and pre-operative planning software, we expected an imagery study assessing the relationship between MTIS implants and the arytenoid cartilage. As a matter of fact, an imagery study has now recently been published and shows a positive influence of the arytenoid position and closure using the MTIS [52]. We opted for a non-irradiating approach to assess the posterior glottis. With a team of engineers from the Free University of Brussels, we launched a post-mortem study to evaluate the possibilities of assessing height and position of the vocal process, using a new endoscopic laser-based measuring device (STUDY 4, chapter 6). This work will eventually help evaluate the effect of the Montgomery implant on the posterior glottis.

Question 4: Considering the large variation in laryngeal anatomy, do 6 sizes of implants per gender allow satisfactory treatment of all the UVFP patients?

To answer this question, we launched a study comparing Thyroid cartilage shapes per gender with voice outcomes (STUDY 5, chapter 6)

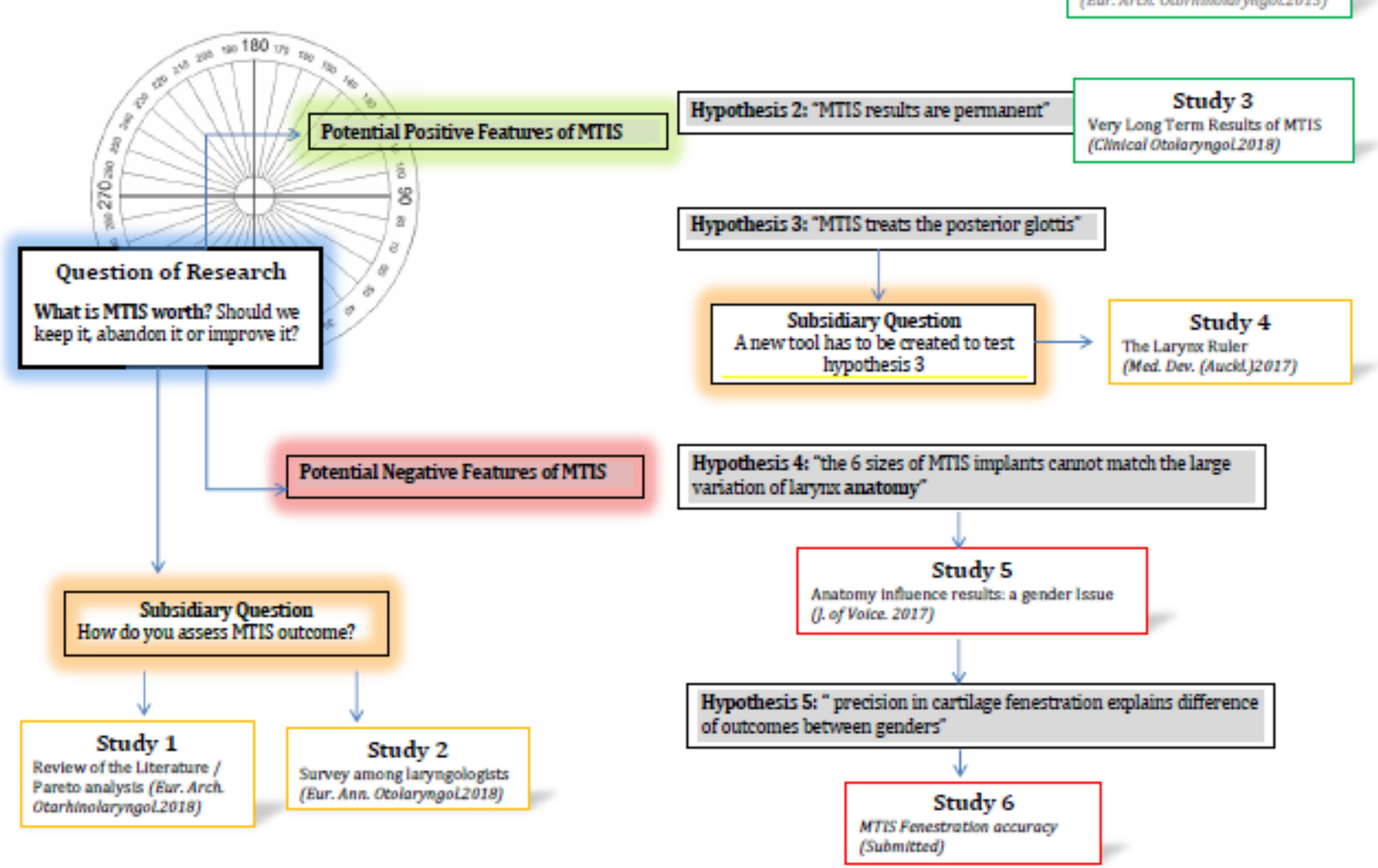
Question 5: What is the accuracy of cartilage fenestration by following the "instruction for use" provided by the MTIS?

As many opinion leading laryngologists complained of having to deal with a significant number of unsatisfied MTIS patients due to wrongly placed implants, we launched a study that looked at the accuracy of MTIS cartilage fenestration and the influence of the position of fenestration on voice outcomes (STUDY 6, chapter 7).

Figure 4 represents a flow chart representing the various questions of research and their rationale.

"The Montgomery Thyroplasty Implant System: A 360° Assessment"

FLOWCHART



Financial disclosure:

The author of this thesis has been proctoring for Bess Inc., Berlin, Germany, in 2015-17.

This allowed the author to enlarge his experience with the MTIS in many different operating theaters and settings around the world.

References chapter 1

1.Benninger MS, Ahuja AS, Gardner G, Grywalski C. Assessing outcomes for dysphonic patients. J Voice. 1998 Dec;12(4):540-50.

2.Hogikyan ND, Wodchis WP, Terrell JE, Bradford CR, Esclamado RM. Voice-related quality of life (V-RQOL) following type I thyroplasty for unilateral vocal fold paralysis. J Voice. 2000 Sep;14(3):378-86.

3.Decker GZ, Thomson SL. Computational simulations of vocal fold vibration: Bernoulli versus Navier-Stokes. J Voice. 2007 May;21(3):273-84. Epub 2006 Feb 28.

4.Sanders I, Wu BL, Mu L, Li Y, Biller HF. The innervation of the human larynx. Arch Otolaryngol Head Neck Surg. 1993 Sep;119(9):934-9.

5.Jürgens U. Neural pathways underlying vocal control. Neurosci Biobehav Rev. 2002 Mar;26(2):235-58. Review.

6.Rosen CA, Mau T, Remacle M, Hess M, Eckel HE, Young VN, Hantzakos A, Yung KC, Dikkers FG. Nomenclature proposal to describe vocal fold motion impairment. Eur Arch Otorhinolaryngol. 2016 Aug;273(8):1995-9. doi: 10.1007/s00405-015-3663-0. Epub 2015 Jun 3. Review.

7.Sulica L, Cultrara A, Blitzer A, Vocal fold paralysis: causes, outcomes and clinical aspects chp3 in Vocal Fold Paralysis Springer-Verlag Berlin Heidelberg 2006

8.Laccourreye O, Papon JF, Kania R, Ménard M, Brasnu D, Hans S. [Unilateral laryngeal paralyses: epidemiological data and therapeutic progress]. Presse Med. 2003 May 17;32(17):781-6. French.

9.Crumley RL, McCabe BF. Regeneration of the recurrent laryngeal nerve. Otolaryngol Head Neck Surg. 1982 Jul-Aug;90(4):442-7.

10.Arviso LC, Johns MM 3rd, Mathison CC, Klein AM. Long-term outcomes of injection laryngoplasty in patients with potentially recoverable vocal fold paralysis. Laryngoscope. 2010 Nov;120(11):2237-40.

11.Young VN, Smith LJ, Rosen C. Voice outcome following acute unilateral vocal fold paralysis. Ann Otol Rhinol Laryngol. 2013 Mar;122(3):197-204.

12.Mau T, Pan HM, Childs LF. The natural history of recoverable vocal fold paralysis: Implications for kinetics of reinnervation. Laryngoscope. 2017 Nov;127(11):2585-2590. doi: 10.1002/lary.26734. Epub 2017 Jun 13.

13.Benninger MS, Manzoor N, Ruda JM. Short- and long-term outcomes after silastic medicalization laryngoplasty: are arytenoid procedures needed? J Voice. 2015 Mar;29(2):236-40. doi: 10.1016/j.jvoice.2014.07.008. Epub 2014 Dec 12.

14.Chang J, Schneider SL, Curtis J, Langenstein J, Courey MS, Yung KC. Outcomes of medialization laryngoplasty with and without arytenoid adduction. Laryngoscope. 2017 Nov;127(11):2591-2595. doi: 10.1002/lary.26773. Epub 2017 Jul 12.

15.Mortensen M, Carroll L, Woo P. Arytenoid adduction with medialization laryngoplasty versus injection or medialization laryngoplasty: the role of the arytenoidopexy. Laryngoscope. 2009 Apr;119(4):827-31. doi: 10.1002/lary.20171.

16.Chen X, Wan P, Yu Y, Li M, Xu Y, Huang P, Huang Z. Types and timing of therapy for vocal fold paresis/paralysis after thyroidectomy: a systematic review and meta-analysis. J Voice. 2014 Nov;28(6):799-808. doi: 10.1016/j.jvoice.2014.02.003. Epub 2014 Apr 13. Review.

17.Wang W, Chen D, Chen S, Li D, Li M, Xia S, Zheng H. Laryngeal reinnervation using ansa cervicalis for thyroid surgery-related unilateral vocal fold paralysis: a long-term outcome analysis of 237 cases. PLoS One. 2011 Apr 29;6(4): e19128. doi: 10.1371/journal.pone.0019128.

18.Lee SW, Park KN. A long-term comparative prospective study between reinnervation and injection laryngoplasty. Laryngoscope. 2018 Aug;128(8):1893-1897. doi: 10.1002/lary.27140. Epub 2018 Feb 16.

19.Goding GS Jr. Nerve-muscle pedicle reinnervation of the paralyzed vocal cord. Otolaryngol Clin North Am. 1991 Oct;24(5):1239-52. Review.

20.Chhetri DK, Gerratt BR, Kreiman J, Berke GS. Combined arytenoid adduction and laryngeal reinnervation in the treatment of vocal fold paralysis. Laryngoscope. 1999 Dec;109(12):1928-36.

21.Halum SL, Bijangi-Vishehsaraei K, Saadatzadeh MR, McRae BR. Differences in laryngeal neurotrophic factor gene expression after recurrent laryngeal nerve and vagus nerve injuries. Ann Otol Rhinol Laryngol. 2013 Oct;122(10):653-63.

22.Zealear DL, Billante CR, Courey MS, Netterville JL, Paniello RC, Sanders I, Herzon GD, Goding GS, Mann W, Ejnell H, Habets AM, Testerman R, Van de Heyning P. Reanimation of the paralyzed human larynx with an implantable electrical stimulation device. Laryngoscope. 2003 jul;113(7):1149-56.

23.Busto-Crespo O, Uzcanga-Lacabe M, Abad-Marco A, Berasategui I, García L, Maraví E, Aguilera-Albesa S, Fernández-Montero A, Fernández-González S. Longitudinal Voice Outcomes After Voice Therapy in Unilateral Vocal Fold Paralysis. J Voice. 2016 Nov;30(6): 767.e9-767.e15. doi: 10.1016/j.jvoice.2015.10.018. Epub 2015 Dec 3.

24.Desjardins M, Halstead L, Cooke M, Bonilha HS. A Systematic Review of Voice Therapy: What "Effectiveness" Really Implies. J Voice. 2017 May;31(3): 392.e13-392.e32. doi: 10.1016/j.jvoice.2016.10.002. Epub 2016 Nov 15. Review.

25.Siu J, Tam S, Fung K. A comparison of outcomes in interventions for unilateral vocal fold paralysis: A systematic review. Laryngoscope. 2016 Jul;126(7):1616-24. doi: 10.1002/lary.25739. Epub 2015 Oct 20. Review.

26.Mary Duenwald, William W Montgomery, 80, Harvard Surgeon and Innovator, The New York Time Obituary, 2003 Nov 15

27.Oransky I Lancet 2004 Jan 10;363(9403):173

28.Varvares MA, Nadol JB Jr. William W. Montgomery, MD, 1923-2003. Ann Otol Rhinol Laryngol. 2004 Jan;113(1):1-4.

29.Nadol JB Jr. Obituary: William W. Montgomery, MD. Laryngoscope. 2003 Dec;113(12):2228-9.

30.Isshiki N, Morita H, Okamura H, Hiramoto M. Thyroplasty as a new phonosurgical technique. Acta Otolaryngol. 1974 Nov-Dec;78(5-6):451-7.

31.Isshiki N, Taira T, Kojima H, Shoji K. Recent modifications in thyroplasty type I. Ann Otol Rhinol Laryngol. 1989 Oct;98(10):777-9.

32.Hess M. M., Fleischer S. Curr Opin Otolaryngol Head & Neck Surg 2016, 24:505-509

33.Payr E. Plastik am schildknorpel zur behebung der folgen einseitiger stimmbandlähmung. Dtsch Med Wochenschr. 1915; 43:1265-1270

34.Montgomery® Thyroplasty Implant System: Instructions for Use. Boston Medical Products, Shrewbury,MA,USA; MK-THYCAT-C; 05-2016

35.Young VN, Zullo TG, Rosen CA. Analysis of laryngeal framework surgery: 10-year follow-up to a national survey. Laryngoscope. 2010 Aug;120(8):1602-8. doi: 10.1002/lary.21004.

36.Almohizea MI, Prasad VM, Fakhoury R, Bihin B, Remacle M. Using peak direct subglottic pressure level as an objective measure during medialization thyroplasty: a prospective study. Eur Arch Otorhinolaryngol. 2016 Sep;273(9):2607-11. doi: 10.1007/s00405-016-4059-5. Epub 2016 Apr 30.

37.Zapater E, García-Lliberós A, López I, Moreno R, Basterra J. A new device to improve the location of a Montgomery thyroplasty prosthesis. Laryngoscope. 2014 Jul;124(7):1659-62. doi: 10.1002/lary.24545. Epub 2014 Jan 28.

38.Laccourreye O, Benkhatar H, Ménard M. Lack of adverse events after medialization laryngoplasty with the montgomery thyroplasty implant in patients with unilateral laryngeal nerve paralysis. Ann Otol Rhinol Laryngol. 2012 Nov;121(11):701-7.

39.Matar N, Remacle M, Bachy V, Lawson G, Giovanni A, Lejoly-Devuyst V, Legou T. Objective measurement of real time subglottic pressure during medialization thyroplasty: a feasibility study. Eur Arch Otorhinolaryngol. 2012 Apr;269(4):1171-5. doi: 10.1007/s00405-011-1867-5. Epub 2011 Dec 11.

40.Hartl DM, Hans S, Crevier-Buchman L, Vaissière J, Brasnu DF. Long-term acoustic comparison of thyroplasty versus autologous fat injection. Ann Otol Rhinol Laryngol. 2009 Dec;118(12):827-32.

41.Ayala MA, Patterson MB, Bach KK. Late displacement of a Montgomery thyroplasty implant following endotracheal intubation. Ann Otol Rhinol Laryngol. 2007 Apr;116(4):262-4.

42.Laccourreye O, El Sharkawy L, Holsinger FC, Hans S, Ménard M, Brasnu D. Thyroplasty type I with Montgomery implant among native French language speakers with unilateral laryngeal nerve paralysis. Laryngoscope. 2005 Aug;115(8):1411-7.

43.Borel S, Crevier-Buchman L, Tessier C, Hans S, Laccourreye O, Brasnu D. [Quality of life before and after thyroplasty for vocal fold paralysis]. Rev Laryngol Otol Rhinol (Bord). 2004;125(5):287-90. French.

44.Cesari U, Faggioli C, Testa D, Vecchio O, Galli V. Montgomery thyroplasty. Case report focusing on endoscopic and functional findings. Acta Otorhinolaryngol Ital. 2004 Aug;24(4):226-33.
Nouwen J, Hans S, De Mones E, Brasnu D, Crevier-Buchman L, Laccourreye O. Thyroplasty type I without arytenoid adduction in patients with unilateral laryngeal nerve paralysis: the montgomery implant versus the Gore-Tex implant. Acta Otolaryngol. 2004 Aug;124(6):732-8.

45.Michel F, Hans S, Crevier-Buchman L, Brasnu D, Menard M, Laccourreye O. [Montgomery thyroplasty implant under local anesthesia for unilateral laryngeal paralysis]. Ann Otolaryngol Chir Cervicofac. 2003 Nov;120(5):259-67. French.

46.Laccourreye O, Papon JF, Ménard M, Crevier-Buchman L, Brasnu D, Hans S. [Treatment of recurrent unilateral paralysis with thyroplasty with Montgomery implant]. Ann Chir. 2001 Oct;126(8):768-71. French.

47.Peretti G, Provenzano L, Piazza C, Giudice M, Antonelli AR. [Functional results after type I thyroplasty with the Montgomery's prosthesis]. Acta Otorhinolaryngol Ital. 2001 Jun;21(3):156-62. Italian.

48.McLean-Muse A, Montgomery WW, Hillman RE, Varvares M, Bunting G, Doyle P, Eng J. Montgomery Thyroplasty Implant for vocal fold immobility: phonatory outcomes. Ann Otol Rhinol Laryngol. 2000 Apr;109(4):393-400.

49.Gliklich RE, Glovsky RM, Montgomery WW. Validation of a voice outcome survey for unilateral vocal cord paralysis. Otolaryngol Head Neck Surg. 1999 Feb;120(2):153-8.

50.Montgomery WW, Blaugrund SM, Varvares MA. Thyroplasty: a new approach. Ann Otol Rhinol Laryngol. 1993 Aug;102(8 Pt 1):571-9.

51.Desuter G, Henrard S, Boucquey D, Van Boven M, Gardiner Q, Remacle M. Learning curve of medialization thyroplasty using a Montgomery™ implant. Eur Arch Otorhinolaryngol. 2015 Feb;272(2):385-90. doi: 10.1007/s00405-014-3292-z.

52.Storck C, Lüthi M, Honegger F, Unteregger F. Surgical Impact of the Montgomery Implant System on Arytenoid Cartilage and the Paralyzed Vocal Fold. J Voice. 2018 Aug 29. pii: S0892-1997(18)30232-7. doi: 10.1016/j.jvoice.2018.07.019. [Epub ahead of print]

CHAPTER 2:

Voice outcome indicators for unilateral vocal fold paralysis surgery: a review of the literature

Abstract

Introduction

There is no consensus on which voice outcome indicators (VOI) should be used to compare the merits of the various surgical treatments for unilateral vocal fold paralysis (UVFP). Authors performed a literature review to identify which VOIs are most frequently used and most relevant, in terms of significant change in pre- and post-operative measurements, in order to assess UVFP surgical treatments.

Method

A Medline/Pubmed literature review was performed and the most frequently used VOIs were identified using a Pareto diagram. For these most frequently used VOI's the number of studies that showed a statistically significant change in pre and post-operative results were compared to the total number of studies found, this portion was expressed in percent. This percentage was defined as the "percentage of significance" and used to assess changes of each VOI.

Results

Eleven VOIs were identified using the Pareto analysis. These were, in decreasing order of frequency of citation: Maximum Phonation Time (MPT), Jitter, Shimmer, Video-stroboscopic examination, Noise to Harmonic Ratio (NHR/HNR), Mean Air Flow (MeAF), Fundamental Frequency (F0), "Infrequent Perceptional Scales", GRBAS scale, Mean Subglottic Pressure (MSGP). MPT, MeAF, factor G of GRBAS-I, Jitter, shimmer and VHI-30 had respective "percentage of significance" of 90%, 86%, 85%, 74%, 68% and 64% respectively.

Conclusion

The results indicate that MPT, MeAF and GRBAS-I, represent the top-three most frequently used and the most relevant VOIs in terms of "percentage of significance". VHI showed a relatively low rate of use and low "percentage of significance". The role of Jitter and Shimmer remains unclear. Finally, MSGP and the F0 appear to be less relevant VOIs for the evaluation of UFVP surgical treatments in terms of significant change in pre- and post-operative measurements.

Introduction

Abduction in Unilateral Vocal Fold Paralysis (UFVP) causing dysphonia, dysphagia and "phonatory" dyspnea, represents a defined pathological entity for which many different surgical treatments have been proposed over the years. Although diverse in their approach these surgeries all primarily seek closure of the glottis during phonation. Unfortunately, there is no consensus on which voice outcome indicators (VOI)s should be used to compare the merits of these various treatments. If voice quality assessment is thought to be necessarily multidimensional, some authors have advocated, in the recent literature, the need for disease specific sets of VOIs. This paper is a Medline/Pubmed based review and evaluation of the literature focusing on VOIs that have been utilized for the assessment of UVFP surgical treatments.

The primary aim of this review was to determine the frequency of use of every VOI that has been utilized to assess patient's voice, after surgical treatment for UVFP, using a Pareto diagram. Having determined the most frequently used VOI's according to the Pareto diagram, the secondary aim of this review was to report their pre- and post-intervention results. The ultimate goal of the review was to identify which VOIs are most frequently used and most relevant in terms of significant change in pre- and post-operative measurements when it comes to assess UVFP surgical treatments.

Methods

In October 2016, a systematic search was performed in Medline/Pubmed to identify articles published after 1990 on assessment of UVFP surgical treatments. Using the following Medical Subject Heading (MeSH) and Subheadings, “Vocal Cord Paralysis/Diagnosis” [MeSH] OR “Vocal Cord Paralysis/Surgery” [MeSH] OR “Vocal CordParalysis/Therapy” [MeSH], a total of 3052 articles were found. Two thousand two-hundred ninety-five articles (2295) were published after 1990. The first selection was based on the exclusion criteria. Seven hundred sixty articles (760) were selected after title reading. Abstracts of these 760 were reviewed. One hundred and fifty-six (156), of these articles were selected for extensive reading. Eventually, 72 of these 156 articles met the inclusions criteria and were analyzed [1-72].

Exclusion and Inclusions criteria are listed in table 1. Figure 1 shows the flowchart of articles selection.

Inclusion criteria	Exclusion criteria
	Meta-analysis
Studies published after 1990 referenced in the « PubMed » database	Studies published before 1990 referenced in the « PubMed » database
Unilateral vocal fold paralysis	Other pathologies than unilateral vocal fold paralysis
Intervention (medialization thyroplasty, injection, arytenoid adduction, reinnervation)	No intervention or unspecified intervention
Voice outcome indicator before and after surgery	Post-surgery outcomes non available or reported in correlation
Studies on human living subjects	Outcomes in dead subjects
	Studies about surgical complications
	Case studies
	Animal studies

Table 1: Inclusion criteria are listed on the right column. Exclusion criteria are listed on the left column.

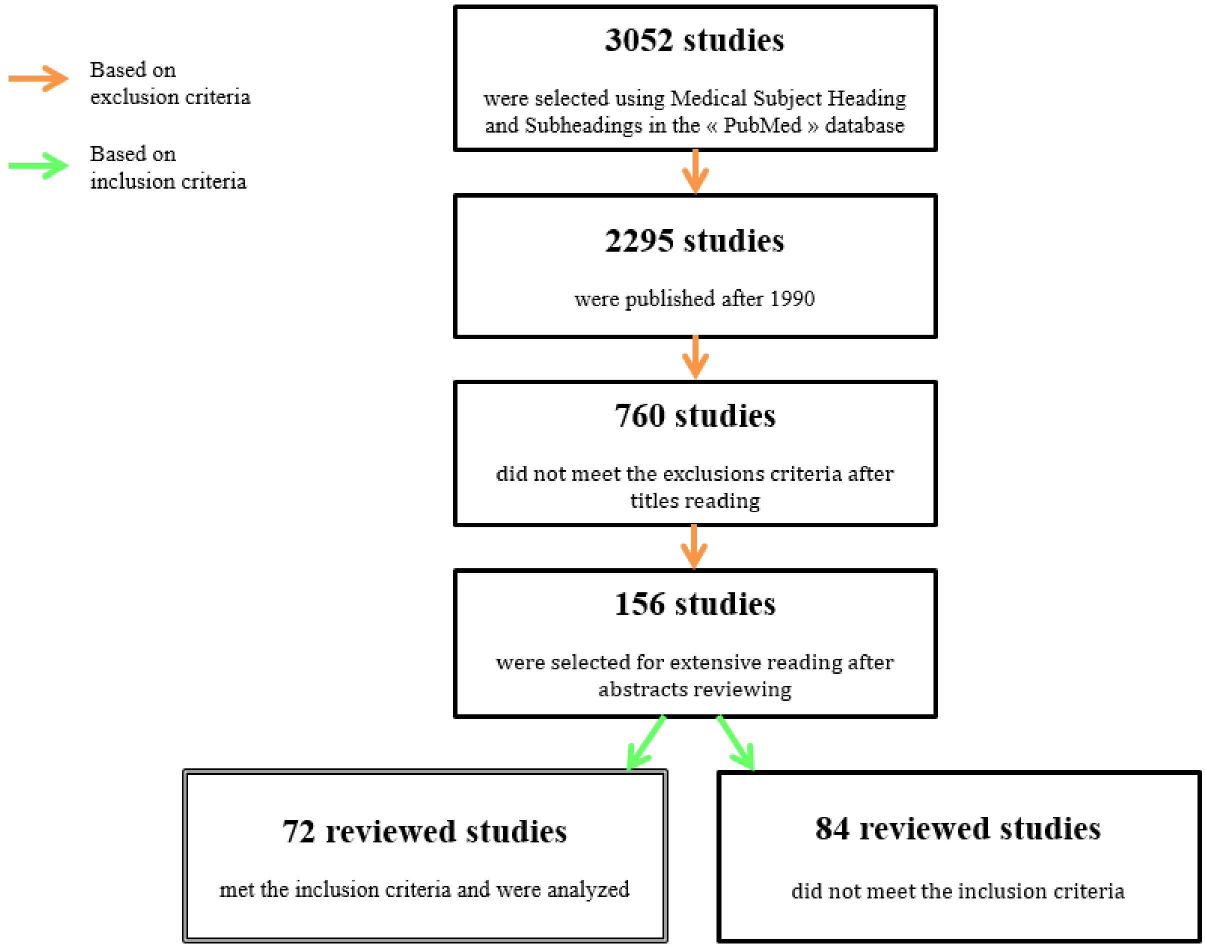


Figure 1: Flowchart of articles selection

An extensive data bank was set up. Type of study, type of surgical intervention(s), type of VOI used and their values, along with the time interval from the intervention date to the moment of assessment, were collected. The total frequency of use of each VOI was classified in descending order. A Pareto diagram that combines bars showing individual values by descending order and a line graph showing the cumulative percentage of data was drawn. Using the Pareto diagram, the most frequently used VOIs, accounting for 80% of the total VOIs, were identified. Once the most frequently used VOIs had been identified their pre- and post-intervention mean values were compared.

Two choices regarding VOI grouping were made by the authors. (a) The number of citations of Noise to Harmonic Ratio and Harmonic to Noise Ratio (NHR and HNR) VOIs were merged. Authors postulate that NHR and HNR represented the same VOI differing only by a software setting swopping the numerator and denominator of the same ratio.

(b)Inversely, the number of citations of VHI-30 and VHI-10 were not merged. Authors postulated that they represented two different -although similar- VOI's that were based on different validation studies in different languages.

Concerning the GRBAS-I score, only the general score (G) will be considered.

The pre- and post-intervention mean values of the VOIs selected using the Pareto diagram were compared. One post-intervention VOI result was considered for each surgical technique and each time-interval of post-intervention assessment. The same pre-intervention data were used in case of studies comparing (1) multiple techniques and (2) post-intervention at multiple time points. This explains why post-intervention data were more numerous than pre-intervention data.

Boxplot graphs were used to display pre-and post- intervention means. Line graphs were preferred to boxplot graphs when no clear post-operative trends in the voice outcome could be found.

Finally, for these most frequently used VOI's the number of studies that showed a statistically significant change in pre and post-operative results (≤0.005) were compared to the total number of studies found, this portion was expressed in percent. This percentage was defined as the "percentage of significance" and used to assess changes of each VOI.

Results

Fifty-three (73,6 %) out of 72 studies were prospective. Some of these 72 studies evaluated more than one type of procedure. In total 107 procedures were reported. Some articles did compare the outcomes of combined procedures. Surgeries of UVFP that were reported were respectively, Medialization or type 1 thyroplasty (ML) (56,1%), Arytenoid adduction (AA), usually combined with ML (18,7%), Injection Laryngoplasty (IL) (17,8%), Larynx Reinnervation (LR) (6,5%) and Arytenoidopexy (AP),usually combined with ML (0.9%).

The most reported interval for post-operative voice outcome analysis was six months (60 articles) whereas one month (50 articles), three months (49 articles) and one year (48 articles) intervals were also commonly reported. Table 2 shows the details of VOI frequency of citation in descending order with their cumulative percentage. Figure 2 displays the frequency of VOIs use and the 80% cumulative percentage cut-off point within a Pareto Diagram.

		Frequency	Percent	Cumulative Percent
Valid	MPT	45	13,6	13,6
	Jitter	33	9,9	23,5
	Shimmer	32	9,6	33,1
	Videostroboscopy	30	9,0	42,2
	NHR	27	8,1	50,3
	Mean Air Flow	22	6,6	56,9
	Fundamental Frequency	22	6,6	63,6
	Home Made Perceptual Scales	17	5,1	68,7
	GRBAS-I	16	4,8	73,5
	Mean Subglottic Pressure	10	3,0	76,5
	VHI-30	9	2,7	79,2
	Intensity	8	2,4	81,6
	Glottal Flow Rate	6	1,8	83,4
	NNE	6	1,8	85,2
	CAPE-V	4	1,2	86,4
	VHI-10	3	,9	87,3
	V-RQOL	3	,9	88,3
	Laryngeal Airway Resistance	3	,9	89,2
	Pitch Range	3	,9	90,1
	Frequency Range	3	,9	91,0
	Pitch Perturbation Quotient	3	,9	91,9
	Amplitude Perturbation Quotient	3	,9	92,8
	Phrase Grouping	2	,6	93,4
	Word per Minute	2	,6	94,0
	Maximum Intensity Range	2	,6	94,6
	Sound Pressure Level	2	,6	95,2
	Standard Deviation of F0	2	,6	95,8
	Phonetogram	2	,6	96,4
	Vocal Performance Questionnaire Score	1	,3	96,7
	NHP	1	,3	97,0
	Voice Symptoms Scale	1	,3	97,3
	Voice Outcomes Survey	1	,3	97,6
	SR-36	1	,3	97,9
	Forced Vital Capacity	1	,3	98,2
	Intra-Abdominal Pressure	1	,3	98,5
	Peak Expiratory Flow	1	,3	98,8
	Forced Expiratory Volume in 1 sec	1	,3	99,1
	Peak Inspiratory Flow	1	,3	99,4
	Volume O2 Maximum	1	,3	99,7
	S/Z Ratio	1	,3	100,0
	Total	332	100,0	

Table 2 displays the frequency of use of the different VOIs utilized in the literature, their overall percentage of use and the cumulative percentage of all VOIs.

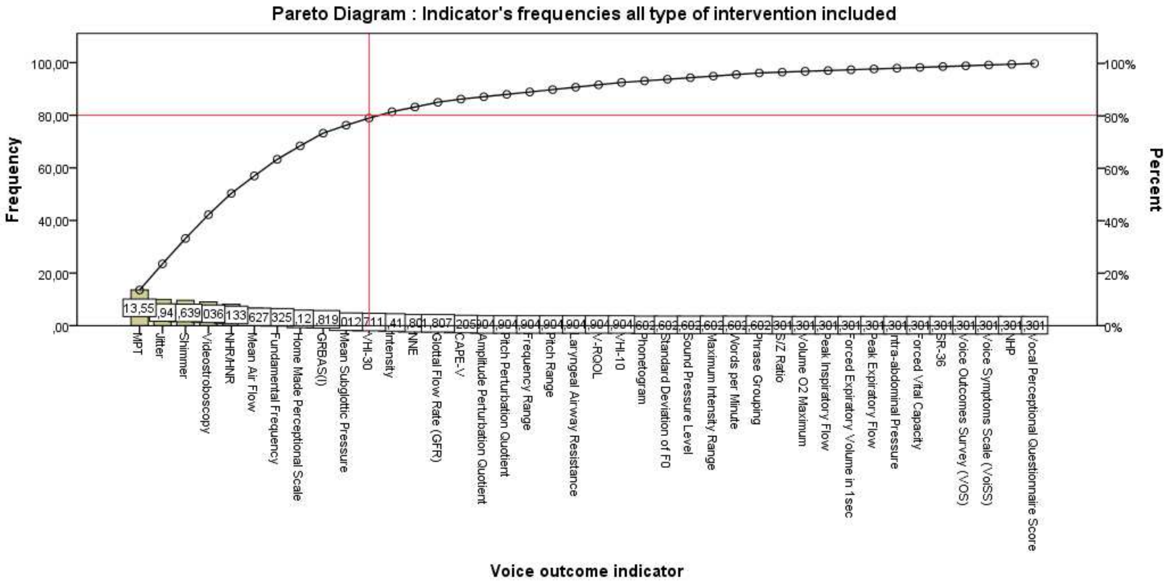


Figure 2 showing the Pareto diagram of all the VOIs that were listed

Eleven VOIs accounted for 80% of all reported VOIs, when it comes to assessment of voice after Surgery for UVFP. These were, in decreasing order of frequency of citation: Maximum Phonation Time (MPT), Jitter, Shimmer, Video-stroboscopic examination, Noise to Harmonic Ratio (NHR/HNR), Mean Air Flow (MeAF), Fundamental Frequency (F0), “Infrequent Perceptional Scales”, GRBAS scale, Mean Subglottic Pressure (MSGP) and the original Jacobson’s Voice Handicap Index (VHI-30)[73].

All the voice perceptional scales that were found in the literature whether validated or not, and used by only one team were grouped together in VOI “infrequent Perceptional Scales”. By definition, such scales could not be compared. Likewise, video-stroboscopic examinations results could not be compared due to the lack of protocol standardization. Accordingly, the pre-and post-intervention results of the remaining 9 VOI’s were analyzed.

Voice outcome indicators	n Pré	Pré *(M, SD)*	n Post	Post *(M, SD)*	n Delta	Delta *(M, SD)*
MPT (sec)	52	5.69 (1.78)	66	12.41 (3.51)	66	6.57 (3.3)
Mean Air Flow (ml/sec)	28	460 (185.21)	31	224.28 (59.84)	31	261.93 (175.56)
GRBAS-I (factor G)	13	2.27 (0.67)	18	0.9 (0.38)	18	1.46 (0.5)
HNR (dB)	10	8.8 (1.83)	15	11.6 (2.08)	15	4.1 (0.9)
Jitter (%)	35	5.17 (3.29)	46	1.76 (0.8)	46	3.27 (2.88)
Shimmer (%)	31	11.22 (4.82)	39	5.11 (2.07)	39	5.66 (4.11)
VHI-30	14	76.36 (13.87)	16	30.86 (11.21)	16	48.91 (20.44)
NHR (dB)	15	0.27 (0.02)	20	0.17 (0.14)	20	0.1 (0.15)
Mean Subglottic Pressure (cm H2O)	11	9.58 (3.93)	14	8.8 (4.5)	14	2.77 (2.63)
F0 (Hz)	24	172.74 (38.49)	36	166.93 (28.12)	36	25.33 (26.99)

Table 3: displays for each VOI; number of pre-op data, means of pre-intervention mean values; number of post-op data, means of post-interventions mean values, number of pre-post data delta available.

Table 3 shows means of pre-intervention values compared to means of post-interventions values for each VOI, at every given post-operative time-point. Table 4 shows the percentage of studies showing “P-values ≤ 0.05” versus studies with “P-values > 0.05 and no P-values available”, for each VOI. For this table, only the first post-operative assessment was considered, no matter how many post-operative assessments were provided by the study. This percentage was defined as the percentage of significance.

Voice outcome indicators	P-values ≤0.05	% significance
MPT (sec)	47/52 (0 NS ; 5 NA)	90.38
Mean Air Flow (ml/sec)	24/28 (2 NS ; 2 NA)	85.71
GRBAS-I (factor G)	11/13 (0 NS ; 2 NA)	84.61
HNR (dB)	8/10 (0 NS ; 2 NA)	80
Jitter (%)	26/35 (5 NS ; 4 NA)	74.29
Shimmer (%)	21/31 (6 NS ; 4 NA)	67.74
VHI-30	9/14 (2 NS ; 3 NA)	64.29
NHR (dB)	7/15 (5 NS ; 3 NA)	46.67
Mean Subglottic Pressure (cm H2O)	5/11 (3 NS ; 3 NA)	45.45
F0 (Hz)	8/24 (6 NS ; 10 NA)	33.33

Table 4: shows, for each VOI the proportion of studies showing significant results ($p \leq 0.005$) between pre-operative and the first post-operative assessments. (NS: not significant, NA: not available). The last column translates this proportion into a “percentage of significance”.

In 7 out of the 9 VOIs we found that a high percentage of the studies showed a significant difference in the pre-and post- measurements. The pre-and post-intervention means of these 7 studies are displayed in Figure 3. Figure 4 displays the pre- and post-interventions means of the remaining two VOIs, MSGP and the F0. Here no clear post-operative trends in the voice outcome could be found.

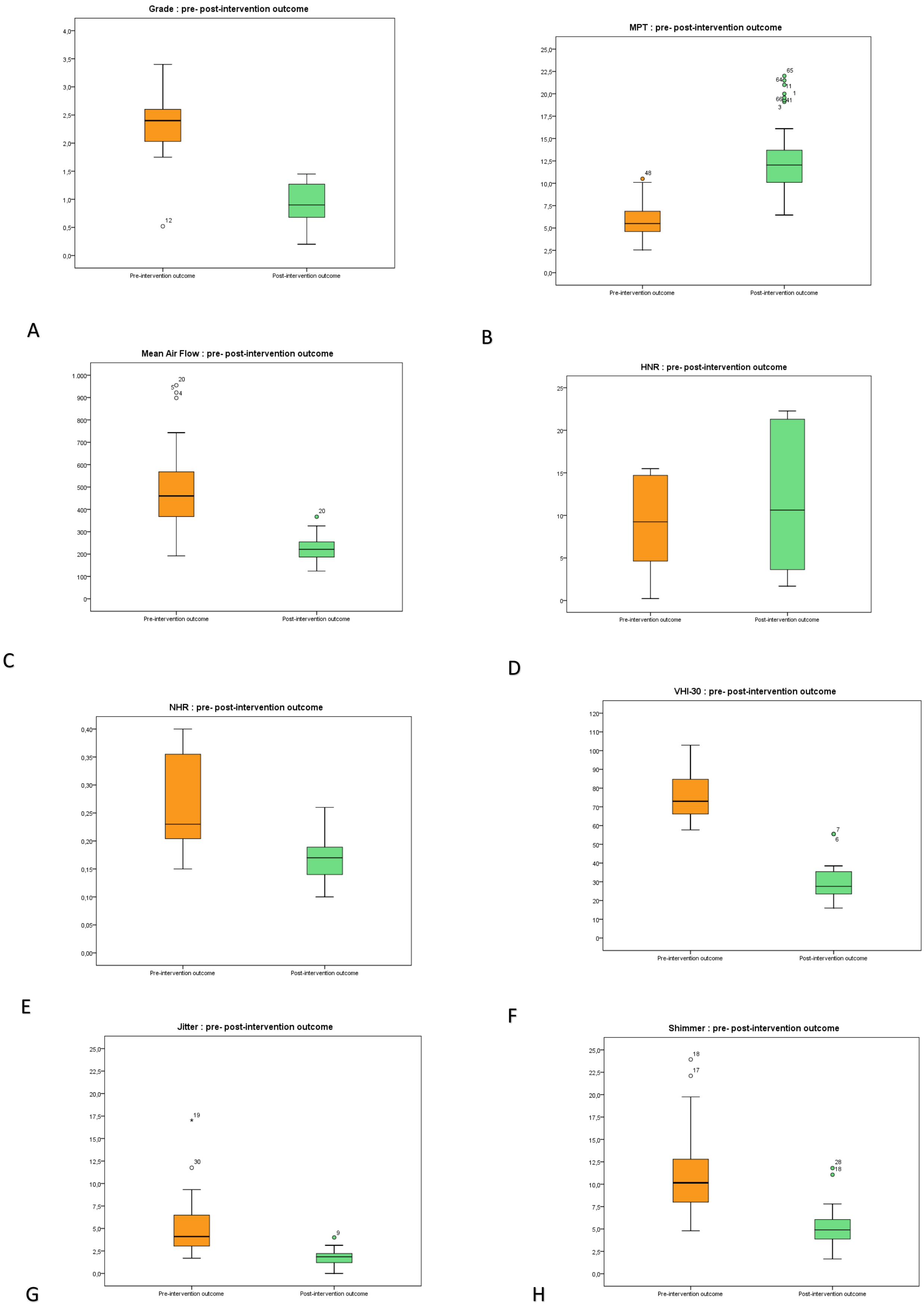
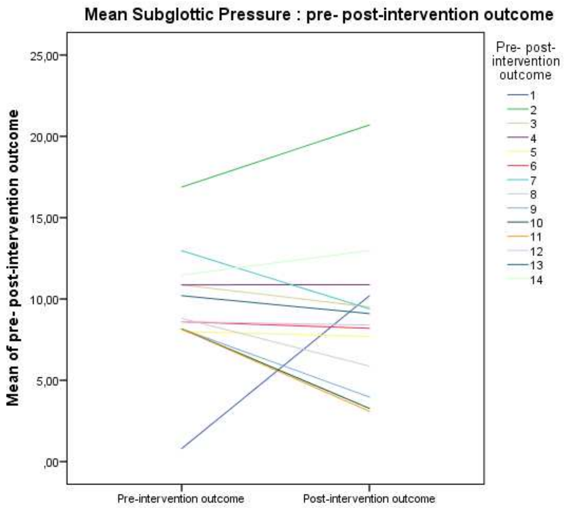


Figure 3: Pre- and post- interventions results of G score of GRBAS-I (A), MPT (B), MeAF (C), HNR (D), NHR (E), VHI-30 (F), Jitter (G) and Shimmer (H).

A



B

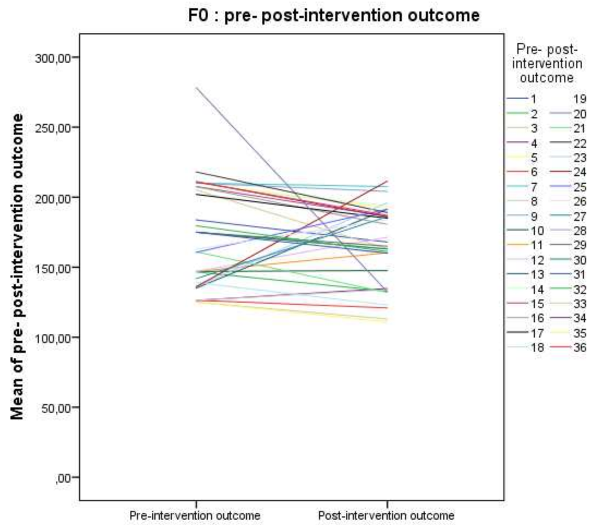


Figure 4: Pre- and post-interventions results of MSGP (A) and F0 (B).

Discussion

This study is a literature review performed to reveal the most frequently cited VOIs used for UVFP surgical treatment assessment. Using the Pareto technique eleven VOIs were found to account for 80% of the total number of indicators cited. Although, the frequency of use of these VOIs may indirectly reflect their accessibility and/or facility to measure, it does not mean per se, that these VOIs are the most appropriate or accurate for the specific purpose of UVFP surgical treatments assessment. Nevertheless, if one could propose a standardized set of VOIs, its implementation could be made easier if they are already frequently used by surgeons.Very recently, Siu et al, performed a systematic review of the literature comparing outcomes of interventions for unilateral vocal fold paralysis. They concluded that "*lack of standardization in outcome measures and differences in reporting outcome data make generalizability between studies difficult*" [74]. Hypothetically, an ideal standardized set of VOIs should be significant as well as accessible.

A notable effort has been made by the European Laryngological Society to standardize the description of vocal fold motion impairment as well as to propose a basic protocol for functional assessment of all voice pathologies, especially for investigating the efficacy of treatments [75, 76]. No data is available about the use of such standardizations of protocols. A survey performed in 2010 among U.S. board certified otolaryngologists conducted by Young et al., reported that only 50% of respondents performing medialization thyroplasties report collecting pre-operative voice recordings [77]. This suggests an underuse of pre- and post-intervention voice assessment, which is probably not only restricted to the US.

In an attempt to simplify but also make the voice assessment more accurate and significant, some authors looked at tailoring the voice assessment to the disease that is under scrutiny. Dastolfo et al. followed this strategy and demonstrated that pre- and postoperative changes in aerodynamic measurements were shown to be very significant in UVFP treatment evaluations. They specifically advocate Airflow in the "all-voiced sentence" as a routine voice laboratory measure for UVFP patients [78].

Of the 9 VOIs that were selected using the Pareto analysis, 3 VOIs have a "percentage of significance" of more than 80%, Table 4. Maximum Phonation Time (MPT) appears to be the most used and the second most significant VOI in terms of pre- and post-operative change. Its use for UVFP treatment assessment has been frequently advocated since an initial article by Lundy et al, published in 2004, stated that "*the intra-operative measure of MPT appears to be an adequate predictor of the postoperative* -thyroplasty-*outcome"* [79]. Determination of MPT is easy to perform and does not require specific equipment. There are, however, still some recording conditions and patient collaboration issues concerning the MPT. Likewise, MPT has been reported as less sensitive than MeAF to characterize laryngeal dysfunction. [80]

GRBAS-I general score (G), for grade of dysphonia, represents a widely used perceptional scale. Overall voice quality is scored from 0 to 3 by listener. Inter- as well as intra-rater reliability is satisfactory [79] and there should be no obstacle to its widespread use. Nevertheless, the GRBAS-I scale has its drawbacks. It has been recently demonstrated that the GRABAS evaluation should be blind [81] and that a particular attention should be paid to task design when it comes to perceptional analysis [82].

MeAF represents a more complex VOI than the previous ones. The MeAF is a similar VOI to Airflow in the “all-voiced sentence”, which was shown by Dastolfo’s team to be very significant in measuring the pre-post UVFP surgical treatment. Access to this VOI can be an issue considering the need of a pneumotachograph to be able to measure it, it is therefore somewhat reassuring to find the MeAF in our short list. Phonatory Quotient (PQ), a ratio between Vital Capacity and MPT that correlates with MeAF, could represent a valid surrogate.

Jitter and Shimmer are respectively ranked at fifth and sixth place in terms “percentage of significance” (Table 4). They are usually provided systematically by most voice laboratory software tools available on the market. This may explain their frequency of use, even though, their respective usefulness is questionable. As a matter of fact, Shimmer has a “percentage of significance” of only 68% and Jitter of 74%. Also, Jitter is calculated with the f0, which is in itself a VOI with low significance. VHI-30 ranking is low in terms of frequency of use and significance ratio. Merging of the VHI-30 and VHI-10 wouldn’t have changed these results significantly. Mean subglottic pressure and the Fundamental Frequency do not show clear outcome tendencies after UVFP treatment and thus, despite being widely reported, don’t seem to have much added value.

The limits of this review must certainly be underscored. (1) Firstly, this review has been done using exclusively the Pubmed research tool. Nevertheless, we believe that the majority of the articles published on the subject, have been included although some publications might have not been considered. The sole published review on the specific topic of VOIs to assess UVFP treatments –all-together- is the recently published article by Siu et al. mentioned above.

Secondly, ML interventions are over-represented in comparison to IL interventions. This does not reflect the reality of practice. The main reason of this discrepancy lies in the selection and inclusion criteria of the studies that favored ML interventions. Many publications concerning IL did not exclusively deal with UFVP patients and did not systematically present pre-and post-op results data.

Thirdly, the extensive databank – more than 150 excel sheets- that has been created, may have been subject to coding errors or bias.

Fourthly, raw data of these numerous studies could not be collected, limiting the validity of our conclusions. The presented outcome results are means of means. Likewise, the percentage of significance represents a ratio between studies showing statistical differences and studies showing no statistical differences or no statistical data at all. Furthermore, the fact that authors are more likely to publish significant results rather than non-significant results represents a clear bias.

Finally, this study may overlook VOIs that might be very relevant but not widely reported in the literature. Also, a statistical difference in pre- and postoperative VOI may not necessarily correspond to a clinically relevant change for the patient and the surgeon and for many VOIs there is still some uncertainty as to what the normal value and a clinically significant difference should be.

Conclusion

The goal of this review was to cross match frequency of use and relevance in terms of significant change in pre- and post-operative measurements of VOIs used in the evaluation of treatment of UVFP treatment. The results indicate that MPT, MeAF and GRBAS-I, represent the top-three VOIs in terms of significance within the most frequently used VOI's. The VHI showed a relatively low rate of use and low "percentage of significance". The role of the Jitter and Shimmer remains unclear. Finally, MSGP and the F0 appear to be less relevant VOIs for the evaluation of UFVP surgical treatments in terms of significant change in pre- and post-operative measurements.

Compliance with ethical standards

- The authors declare that they have no conflict of interest
- This article does not contain any studies with human or animals performed by anu of the authors
- Informed consent collection is not applicable to this study

REFERENCES

1. Abdel-Aziz, M. F., El-Hak, N. G., & Carding, P. N. (1998). Thyroplasty for functional rehabilitation of the incompetent larynx. *The Journal of Laryngology & Otology*, *112*(12), 1172-1175.

2. Adams, S. G., Irish, J. C., Durkin, L. C., Wong, D. L., & Brown, D. H. (1996). Evaluation of vocal function in unilateral vocal fold paralysis following thyroplastic surgery. *The Journal of otolaryngology*, *25*(3), 165-170.

3. Alghonaim, Y., Roskies, M., Kost, K., & Young, J. (2013). Evaluating the timing of injection laryngoplasty for vocal fold paralysis in an attempt to avoid future type 1 thyroplasty. *Journal of Otolaryngology-Head & Neck Surgery*, *42*(1), 1.

4. Almeida, A. A. F. D., Fernandes, L. R., Azevedo, E. H. M., Pinheiro, R. S. D. A., & Lopes, L. W. (2015, April). Characteristics of voice and personality of patients with vocal fold immobility. In *CoDAS* (Vol. 27, No. 2, pp. 178-185). Sociedade Brasileira de Fonoaudiologia.

5. Asik, M. B., Karasimav, O., Birkent, H., Merati, A. L., Gerek, M., & Yildiz, Y. (2015). Airway and Respiration Parameters Improve Following Vocal Fold Medialization A Prospective Study. *Annals of Otology, Rhinology & Laryngology*, *124*(12), 972-977.

6. Bielamowicz, S., Berke, G. S., & Gerratt, B. R. (1995). A comparison of type I thyroplasty and arytenoid adduction. *Journal of Voice*, *9*(4), 466-472.

7. Billante, C. R., Clary, J., Childs, P., & Netterville, J. L. (2002). Voice gains following thyroplasty may improve over time1. *Clinical Otolaryngology & Allied Sciences*, *27*(2), 89-94.

8. Borel, S., Crevier-Buchman, L., Tessier, C., Hans, S., Laccourreye, O., & Brasnu, D. (2003). [Quality of life before and after thyroplasty for vocal fold paralysis]. *Revue de laryngologie-otologie-rhinologie*, *125*(5), 287-290.

9. Bryant, N. J., Gracco, L. C., Sasaki, C. T., & Vining, E. (1996). MRI evaluation of vocal fold paralysis before and after type I thyroplasty. *The Laryngoscope*, *106*(11), 1386-1392.

10. Cantillo-Baños, E., Jurado-Ramos, A., Gutiérrez-Jódas, J., & Ariza-Vargas, L. (2013). Vocal fold insufficiency: medialization laryngoplasty vs calcium hydroxylapatite microspheres (Radiesse Voice®). *Acta oto-laryngologica*, *133*(3), 270-275.

11. Choi, H. S., Chung, S. M., Lim, J. Y., & Kim, H. S. (2008). Increasing the closed quotient improves voice quality after type I thyroplasty in patients with unilateral vocal cord paralysis: analysis using SPEAD program. *Journal of Voice*, *22*(6), 751-755.

12. Chowdhury, K., Saha, S., Saha, V. P., Pal, S., & Chatterjee, I. (2013). Pre and post operative voice analysis after medialization thyroplasty in cases of unilateral vocal fold paralysis. *Indian Journal of Otolaryngology and Head & Neck Surgery*, *65*(4), 354-357.

13. Chhetri, D. K., Gerratt, B. R., Kreiman, J., & Berke, G. S. (1999). Combined arytenoid adduction and laryngeal reinnervation in the treatment of vocal fold paralysis. *The Laryngoscope*, *109*(12), 1928-1936.

14. Dastolfo, C., Gartner-Schmidt, J., Yu, L., Carnes, O., & Gillespie, A. I. (2015). Aerodynamic Outcomes of Four Common Voice Disorders: Moving Toward Disorder-Specific Assessment. *Journal of Voice*, *30*(3), 301-307.

15. Desuter G, Henrard S, Boucquey D, Van Boven M, Gardiner Q, Remacle M. Learning curve of medialization thyroplasty using a Montgomery™ implant. Eur Arch Otorhinolaryngol. 2015 Feb;272(2):385-90.

16. Devos, M., Schultz, P., Guilleré, F., & Debry, C. (2010). Thyroplasty for unilateral vocal fold paralysis using an adjustable implant in porous titanium. *European annals of otorhinolaryngology, head and neck diseases*, *127*(6), 204-212.

17. Elnashar, I., El-Anwar, M., Amer, H., & Quriba, A. (2015). Voice Outcome after Gore-Tex Medialization Thyroplasty. *International archives of otorhinolaryngology*, *19*(3), 248-254.

18. Gliklich, R. E., Glovsky, R. M., & Montgomery, W.M. (1999). Validation of a voice outcome survey for unilateral vocal cord paralysis. *Otolaryngology--Head and Neck Surgery*, *120*(2), 153-158.

19. Gray, S. D., Barkmeier, J., Jones, D., Titze, I., & Druker, D. (1992). Vocal evaluation of thyroplastic surgery in the treatment of unilateral vocal fold paralysis. *The Laryngoscope*, *102*(4), 415-421.

20. Guerrero, J., Cobeta, I., García-Díaz, J. D., Vegas, A., Montojo, J., Lorenzo, F., & Mate, A. (1997). [Surgery of the laryngeal framework: type I thyroplasty]. *Acta otorrinolaringologica espanola*, *49*(1), 45-49.

21. Hajioff, D., Rattenbury, H., Carrie, S., Carding, P., & Wilson, J. (2000). The effect of Isshiki type 1 thyroplasty on quality of life and vocal performance. *Clinical Otolaryngology & Allied Sciences*, *25*(5), 418-422.

22. Harries, M. L., & Morrison, M. (1995). Short-term results of laryngeal framework surgery--thyroplasty type 1: A pilot study. *The Journal of otolaryngology*, *24*(5), 281-287.Hassan, MM., Yumoto, E., Sanuki, T., Kumai, Y., Kodama, N., Baraka, MA., Wahba, H., Hafez, NG., & El-Adawy, AA. (2014). Arytenoid adduction with nerve-muscle pedicle transfer vs arytenoid adduction with and without type i thyroplasty in paralytic dysphonia. *JAMA Otolaryngology–Head & Neck Surgery*, *140*(9), 833-839.

23. Havas, T. E., & Priestley, K. J. (2003). Autologous fat injection laryngoplasty for unilateral vocal fold paralysis. *ANZ journal of surgery*, *73*(11), 938-943.

24. Hogikyan, N. D., Wodchis, W. P., Terrell, J. E., Bradford, C. R., & Esclamado, R. M. (2000). Voice-related quality of life (V-RQOL) following type I thyroplasty for unilateral vocal fold paralysis. *Journal of Voice, 14*(3), 378-386.

25. Jang, J. Y., Lee, G., Ahn, J., & Son, Y. I. (2015). Early voice rehabilitation with injection laryngoplasty in patients with unilateral vocal cord palsy after thyroidectomy. *European Archives of Oto-Rhino-Laryngology*, *272*(12), 3745-3750.

26. Konomi, U., Watanabe, Y., & Komazawa, D. (2014). Application of pitch range evaluation subsequent to arytenoid adduction and thyroplasty. *Journal of Voice*, *28*(3), 394-e5.

27. Kraus, D. H., Orlikoff, R. F., Rizk, S. S., & Rosenberg, D. B. (1999). Arytenoid adduction as an adjunct to type I thyroplasty for unilateral vocal cord paralysis. *Head & neck*, *21*(1), 52-59.

28. Laccourreye, O., El Sharkawy, L., Holsinger, F. C., Hans, S., Ménard, M., & Brasnu, D. (2005). Thyroplasty type I with Montgomery implant among native French language speakers with unilateral laryngeal nerve paralysis. *The Laryngoscope*, *115*(8), 1411-1417.

29. Leder, S. B., & Sasaki, C. T. (1994). Long-term changes in vocal quality following isshiki thyroplasty type I. *The Laryngoscope*, *104*(3), 275-277.

30. Lee, W. T., Milstein, C., Hicks, D., Akst, L. M., & Esclamado, R. M. (2007). Results of ansa to recurrent laryngeal nerve reinnervation. *Otolaryngology--Head and Neck Surgery*, *136*(3), 450-454.

31. Li, A. J., Johns, M. M., Jackson-Menaldi, C., Dailey, S., Heman-Ackah, Y., Merati, A., & Rubin, A. D. (2011). Glottic closure patterns: type I thyroplasty versus type I thyroplasty with arytenoid adduction. *Journal of Voice*, *25*(3), 259-264.

32. Lorenz, R. R., Esclamado, R. M., Teker, A. M., Strome, M., Scharpf, J., Hicks, D., ... & Lee, W. T. (2008). Ansa cervicalis-to-recurrent laryngeal nerve anastomosis for unilateral vocal fold paralysis: experience of a single institution. *Annals of Otology, Rhinology & Laryngology*, *117*(1), 40-45.

33. Lu, F. L., Casiano, R. R., Lundy, D. S., & Xue, J. W. (1996). Longitudinal evaluation of vocal function after thyroplasty type I in the treatment of unilateral vocal paralysis. *The Laryngoscope*, *106*(5), 573-577.

34. Lu, F. L., Lundy, D. S., Casiano, R. R., & Xue, J. W. (1998). Vocal evaluation of thyroplasty type I in the treatment of nonparalytic glottic incompetence. *Annals of Otology, Rhinology & Laryngology*, *107*(2), 113-119.

35. Lundy, D. S., Casiano, R. R., M cClinton, M. E., & Xue, J. W. (2003). Early results of transcutaneous injection laryngoplasty with micronized acellular dermis versus type-I thyroplasty for glottic incompetence dysphonia due to unilateral vocal fold paralysis. *Journal of Voice*, *17*(4), 589-595.

36. Lundy, D. S., Casiano, R. R., & Xue, J. W. (2004). Can maximum phonation time predict voice outcome after thyroplasty type I?. *The Laryngoscope*, *114*(8), 1447-1454.

37. Lundy, D. S., Casiano, R. R., Xue, J. W., & Lu, F. L. (2000). Thyroplasty type I: short-versus long-term results. *Otolaryngology--Head and Neck Surgery*,*122*(4), 533-536.

38. Mahieu, H., Norbart, T. H., & Snel, F. (1995). Laryngeal framework surgery for voice improvement. *Revue de laryngologie-otologie-rhinologie*, *117*(3), 189-197.

39. Malik, A., Ramalingam, W. V. B. S., Nilakantan, A., Nair, S., Ramesh, A. V., & Raj, P. (2014). Comparison of the use of silastic with titanium prefabricated implant in type I thyroplasty. *Brazilian journal of otorhinolaryngology*, *80*(2), 156-160.

40. Manfredi, C., & Peretti, G. (2006). A new insight into postsurgical objective voice quality evaluation: application to thyroplastic medialization. *Biomedical Engineering, IEEE Transactions on*, *53*(3), 442-451.

41. Matar, N., Remacle, M., Bachy, V., Lawson, G., Giovanni, A., Lejoly-Devuyst, V., & Legou, T. (2012). Objective measurement of real time subglottic pressure during medialization thyroplasty: a feasibility study. *European Archives of Oto-Rhino-Laryngology*, *269*(4), 1171-1175.

42. McLean-Muse, A., Montgomery, W. W., Bunting, G., Hillman, R. E., Doyle, P., Varvares, M., & Eng, J. (2000). Montgomery® Thyroplasty Implant for vocal fold immobility: phonatory outcomes. *Annals of Otology, Rhinology & Laryngology*,*109*(4), 393-400.

43. Mohammed, H., Masterson, L., Gendy, S., & Nassif, R. (2015). Outpatient based injection laryngoplasty for the management of unilateral vocal fold paralysis-clinical outcomes from a UK centre. *Clinical Otolaryngology*.

44. Morgan, J. E., Zraick, R. I., Griffin, A. W., Bowen, T. L., & Johnson, F. L. (2007). Injection versus medialization laryngoplasty for the treatment of unilateral vocal fold paralysis. *The Laryngoscope*, *117*(11), 2068-2074.

45. Mortensen, M., Carroll, L., & Woo, P. (2009). Arytenoid adduction with medialization laryngoplasty versus injection or medialization laryngoplasty: the role of the arytenoidopexy. *The Laryngoscope*, *119*(4), 827-831.

46. Murata, T., Yasuoka, Y., Shimada, T., Shino, M., Iida, H., Takahashi, K., & Furuya, N. (2011). A new and less invasive procedure for arytenoid adduction surgery. *The Laryngoscope*, *121*(6), 1274-1280.

47. Nouwen, J., Hans, S., De Mones, E., Brasnu, D., Crevier-Buchman, L., & Laccourreye, O. (2004). Thyroplasty type I without arytenoid adduction in patients with unilateral laryngeal nerve paralysis: the Montgomery implant versus the Gore-Tex implant. *Acta oto-laryngologica*, *124*(6), 732-738.

48. Omori, K., Slavit, D. H., Kacker, A., & Blaugrund, S. M. (1996). Quantitative criteria for predicting thyroplasty type I outcome. *The Laryngoscope*, *106*(6), 689-693.

49. Paniello, R. C., Edgar, J. D., Kallogjeri, D., & Piccirillo, J. F. (2011). Medialization versus reinnervation for unilateral vocal fold paralysis: a multicenter randomized clinical trial. *The Laryngoscope*, *121*(10), 2172-2179.

50. Parker, N. P., Barbu, A. M., Hillman, R. E., Zeitels, S. M., & Burns, J. A. (2015). Revision Transcervical Medialization Laryngoplasty for Unilateral Vocal Fold Paralysis. *Otolaryngology--Head and Neck Surgery*, 0194599815585091.

51. Peretti, G., Provenzano, L., Piazza, G., Giudice, M., & Antonelli, A. R. (2001). Risultati funzionali dopo tiroplastica di I tipo con protesi di Montgomery. *Acta Otorhinolaryngol Ital*, *21*, 156-61.

52. Prendes, B. L., Yung, K. C., Likhterov, I., Schneider, S. L., Al-Jurf, S. A., & Courey, M. S. (2012). Long-term effects of injection laryngoplasty with a temporary agent on voice quality and vocal fold position. *The Laryngoscope*,*122*(10), 2227-2233.

53. Ryu, I. S., Nam, S. Y., Han, M. W., Choi, S. H., Kim, S. Y., & Roh, J. L. (2012). Long-term voice outcomes after thyroplasty for unilateral vocal fold paralysis. *Archives of Otolaryngology–Head & Neck Surgery*, *138*(4), 347-351.

54. Sakai, N., Nishizawa, N., Matsushima, J. I., Kurihara, H., Kokubun, T., Koichi, K. I., ... & Inuyama, Y. (1996). Thyroplasty type I with ceramic shim. *Artificial organs*, *20*(8), 951-954.

55. Sasaki, C. T., Leder, S. B., Petcu, L., & Friedman, C. D. (1990). Longitudinal voice quality changes following Isshiki thyroplasty type I : the Yale experience.*The Laryngoscope*, *100*(8), 849-852.

56. Schwarz, K., Cielo, C. A., Steffen, N., Becker, J., & Jotz, G. P. (2011). Voice and laryngeal configuration of men with unilateral vocal fold paralysis before and after medialization. *Journal of Voice*, *25*(5), 611-618.

57. Shin, J. E., Nam, S. Y., Yoo, S. J., & Kim, S. Y. (2002). Analysis of voice and quantitative measurement of glottal gap after thyroplasty type I in the treatment of unilateral vocal paralysis. *Journal of Voice*, *16*(1), 136-142.

58. Smith, M. E., & Houtz, D. R. (2015). Outcomes of Laryngeal Reinnervation for Unilateral Vocal Fold Paralysis in Children Associations With Age and Time Since Injury. *Annals of Otology, Rhinology & Laryngology*, 0003489415615364.

59. Sonoda, S., Kataoka, H., & Inoue, T. (2005). Traction of lateral cricoarytenoid muscle for unilateral vocal fold paralysis: comparison with Isshiki's original technique of arytenoid adduction. *Annals of Otology, Rhinology & Laryngology*, *114*(2), 132-138.

60. Sridhara, S. R., Ashok, K. G., Raghunathan, M., & Mann, S. B. S. (2003). To study voice quality before and after thyroplasty type 1 in patients with symptomatic unilateral vocal cord paralysis. *American journal of otolaryngology*, *24*(6), 361-365.

61. Stuut, M., Gi, R. E. T. P., & Dikkers, F. G. (2014). Change of Voice Handicap Index after treatment of benign laryngeal disorders. *European Archives of Oto-Rhino-Laryngology*, *271*(5), 1157-1162.

62. Suehiro, A., Hirano, S., Kishimoto, Y., Tanaka, S., & Ford, C. N. (2009). Comparative study of vocal outcomes with silicone versus Gore-Tex thyroplasty. *The Annals of otology, rhinology, and laryngology*, *118*(6), 405-408.

63. Thompson, D. M., Maragos, N. E., & Edwards, B. W. (1995). The study of vocal fold vibratory patterns in patients with unilateral vocal fold paralysis before and after type I thyroplasty with or without arytenoid adduction. *The Laryngoscope*, *105*(5), 481-486.

64. Tokashiki, R., Hiramatsu, H., Shinada, E., Motohashi, R., Nomoto, M., Toyomura, F., & Suzuki, M. (2012). Analysis of pitch range after arytenoid adduction by fenestration approach combined with type I thyroplasty for unilateral vocal fold paralysis. *Journal of Voice*, *26*(6), 792-796.

65. Tokashiki, R., Hiramatsu, H., Tsukahara, K., Kanebayashi, H., Nakamura, M., Motohashi, R., Yamada, T., & Suzuki, M. (2007). A "fenestration approach" for arytenoid adduction through the thyroid ala combined with type I thyroplasty. *The Laryngoscope*, *117*(10), 1882-1887.

66. Tucker, H. M. (1999). Long-term preservation of voice improvement following surgical medialization and reinnervation for unilateral vocal fold paralysis. *Journal of Voice*, *13*(2), 251-256.

67. Umeno, H., Chitose, S., Sato, K., & Nakashima, T. (2009). Comparative study of framework surgery and fat injection laryngoplasty. *The Journal of Laryngology & Otology*, *123*(S31), 35-41.

68. Umeno, H., Chitose, S. I., Sato, K., & Nakashima, T. (2008). Efficacy of additional injection laryngoplasty after framework surgery. *Annals of Otology, Rhinology & Laryngology*, *117*(1), 5-10.

69. Umeno, H., Chitose, S. I., Sato, K., Ueda, Y., & Nakashima, T. (2012). Long-term postoperative vocal function after thyroplasty type I and fat injection laryngoplasty. *Annals of Otology, Rhinology & Laryngology*, *121*(3), 185-191.

70. Vinson, K. N., Zraick, R. I., & Ragland, F. J. (2010). Injection versus medialization laryngoplasty for the treatment of unilateral vocal fold paralysis.*The Laryngoscope*, *120*(9), 1802-1807.

71. Wen, M. H., Cheng, P. W., Liao, L. J., Chou, H. W., & Wang, C. T. (2013). Treatment outcomes of injection laryngoplasty using cross-linked porcine collagen and hyaluronic acid. *Otolaryngology--Head and Neck Surgery*, 0194599813508082.

72. Zur, K. B., & Carroll, L. M. (2015). Recurrent laryngeal nerve reinnervation in children: Acoustic and endoscopic characteristics pre-intervention and post-intervention. A comparison of treatment options. *The Laryngoscope*, *125*(S11), S1-S15.

73. Jacobson B.H,, Johnson A., GrywalskiC., Silbergeit A., Jocobson G., Benninger M.S;, Newman C.W., (1997)The Voice Handicap Index (VHI) : development and validation. Am J Speech Lang Pathol 6:66-70.

74. Siu J, Tam S, Fung K. A comparison of outcomes in interventions for unilateral vocal fold paralysis: A systematic review. Laryngoscope. 2016 Jul;126(7):1616-24.

75. Dejonckere PH, Bradley P, Clemente P, Cornut G, Crevier-Buchman L, FriedrichG, Van De Heyning P, Remacle M, Woisard V; Committee on Phoniatrics of theEuropean Laryngological Society (ELS).. A basic protocol for functional assessment of voice pathology, especially for investigating the efficacy of (phonosurgical) treatments and evaluating new assessment techniques. Guideline elaborated by the Committee on Phoniatrics of the European Laryngological Society (ELS). Eur Arch Otorhinolaryngol. 2001 Feb;258(2):77-82.

76. Rosen CA, Mau T, Remacle M, Hess M, Eckel HE, Young VN, Hantzakos A, Yung KC, Dikkers FG. Nomenclature proposal to describe vocal fold motion impairment. Eur Arch Otorhinolaryngol. 2016 Aug; 273(8):1995-9.

77. Young VN, Zullo TG, Rosen CA. Analysis of laryngeal framework surgery: 10-year follow-up to a national survey. Laryngoscope. 2010 Aug;120(8):1602-8.

78. Dastolfo C, Gartner-Schmidt J, Yu L, Carnes O, Gillespie AI. Aerodynamic Outcomes of Four Common Voice Disorders: Moving Toward Disorder-Specific Assessment. J Voice. 2016 May;30(3):301-7.

79. Lundy DS, Casiano RR, Xue JW. Can maximum phonation time predict voice outcome after thyroplasty type I? Laryngoscope. 2004 Aug;114(8):1447-54.

80. Woo P, Casper J, Colton R, Brewer D, Aerodynamic and Stroboscopic findings before and after microlaryngeal surgery. J Voice. 1994 Jun; 8(2):186-94.

81. Webb AL, Carding PN, Deary IJ, MacKenzie K, Steen N, Wilson JA. The reliability of three perceptual evaluation scales for dysphonia. Eur Arch Otorhinolaryngol. 2004 Sep;261(8):429-34.

82. Ghio A, Revis J, Merienne S, Giovanni A, Top-down mechanisms in dysphonia perception: the need for blind tests. J Voice. 2013 Jul; 27(4):481-5

CHAPTER 3:

Voice outcome indicators for unilateral vocal fold paralysis surgery: a survey among surgeons

Abstract:

Introduction

Standardization of voice outcomes indicators (VOIs) is an important issue when it comes to evaluating and comparing surgical treatments for Unilateral Vocal Fold Paralysis (UVFP). In a recent review, 11 VOIs were found to represent 80% of the VOIs cited in the literature. A survey was launched among the European laryngologists to acquire surgeons' opinions on the above mentioned preselected VOIs.

Method

The electronic survey took place between November and December 2016. Three general questions were asked about surgeon's practice setting(s) and experience. The eleven next questions concerned (a) surgeon's VOIs preference and (b) their estimates of post-operative target values, they would consider to be satisfactory.

Results

The response rate was 16% (50 surveys). The majority of responders worked in tertiary hospitals (50%), had 15 years of experience with UVFP surgeries and performed on average 20 UVFP-related procedures a year. The VOIs that were favored by the responding surgeons were, in decreasing order of importance, Voice handicap Index (VHI-30), Maximum Phonation Time (MPT), GRBAS-I, Mean Airflow Rate (MeAF), Jitter and Shimmer. There was an excellent consensus on post-operative VOI target values between survey's results and the literature data, except for three VOIs that showed somewhat divergent tendencies (absolute VHI-30, Jitter and Shimmer).

Conclusions

Three VOIs are favored by surgeons: VHI-30, MPT and GRBAS-I. Jitter and Shimmer, although very frequently reported and statistically valid in the literature, come last concerning surgeon's choice as VOI for UVFP treatment assessment.

Introduction

Standardization of voice outcomes indicators (VOIs) is an important issue when it comes to evaluating and eventually comparing surgical treatments for Unilateral Vocal Fold Paralysis (UVFP) [1]. More than 15 years ago, the European Laryngological Society (ELS) published a basic protocol for functional assessment of voice pathology, in order to be able to evaluate, compare and investigate effectivity of phonosurgical treatments [2]. Our recently performed review of the literature looking at VOIs used for the assessment of UVFP surgical treatments, showed that this protocol was not systematically used [3]. The same review showed that Maximum Phonation Time (MPT), GRBAS-I perceptional scale and Mean Airflow Rate (MeAF) were most frequently used and were most effective in terms of statistically significant improvement after surgery. Jitter, Shimmer and Voice Handicap Index (VHI-30) had an intermediary position whereas Fundamental Frequency (F0) and Mean Sub-glottic Pressure (MSGP) showed the least significant improvement.

These VOIs were found to be the most frequently used according to recent literature, but how these findings relate to daily treatment of UVFP remains unclear. In order to relate these literature review findings to common practice among laryngologists treating UVFP, a survey was launched among ELS members. The aim of the survey was (a) to acquire surgeons' opinions on the above mentioned preselected VOIs (b) to reveal any other VOIs that may be commonly used but overlooked by the literature review.

Methods

The survey was performed with the “Monkey Survey Platform” internet software.

All active members of the ELS of whom an e-mail address was available were addressed.

The link to the survey along with a general introduction was send by e-mail to the 310 ELS members on the November 2016. A second round of e-mails took place 15 days later on November 2016.

Collection of surveys was closed on December 2016, one month after the first round of e-mails, 15 days after the second round of e-mails.

After a written introduction about the aim of the survey and the identity of the authors, three general questions were asked. These were: (a) the number of years of practice regarding surgical treatment of UVFP, (b) the average number of these interventions performed by year and (c) the type of setting(s) the surgeon was working in (tertiary hospital, secondary hospital and private practice). The two first questions were open numeral questions whereas the last one offered *scroll-down option* of answers. This set of questions allowed for surveys filled in by non-surgeon to be disregarded and gave some socio-professional data as well as the degree of experience of the responder. The next eleven questions related to the VOIs. Table 1 lists the 11 questions of the survey. For the survey to be valid, all questions had to be answered.

Question	Answering modality
1.In which order would you classify these voice parameter indicators, from the most important to the least important?	The 6 VOIs had to be listed in order of decreasing importance.
2. Which indicators are considered by you as a must for UVFP assessment?	One to six VOIs could be selected
3. What post intervention time point(s) do you consider the most relevant for voice outcome measurement?	Options: 1, 2, 3, 9, 12 months one or more answers possible
4. What relative percentage improvement of the VHI-30 score would you consider a satisfactory post-intervention result?	Options: 25%, 50%, 75%, one choice allowed
5. What absolute numeral improvement of the VHI-30 would you consider a satisfactory post-intervention result?	Options: scores of 20, 40 or 60, one choice allowed
6. What according to you is the threshold under which the Jitter should go down post-intervention to be satisfactory?	Options: 2.5%, 5%, 7.5%, one choice allowed
7. What according to you is the threshold under which the Shimmer should go under post-intervention to be satisfactory?	Options: 2.5%, 5%, 7.5%, one choice allowed
8. What do you consider a satisfactory score for G (grade) post-intervention?	Options: scores of 0, 1, 2, one choice allowed
9. What according to you can be considered as a satisfactory increase of MPT post-intervention?	Options: 5sec., 7 sec., 10 sec., one choice allowed
10. What threshold should the MPT exceed post-intervention to be satisfactory?	Options: 10 sec., 12 sec., 14 sec., one choice allowed
11. Which MeAF post-intervention would you consider as satisfactory?	Options: 200 ml/sec., 250 ml/sec., 300ml/sec., one choice allowed

Table 1: Questions and answering modalities of the survey

The Voice Outcomes Indicators (VOI)

In our recent literature review [3], 11 VOIs accounted for 80% of the most cited VOIs for UVFP surgical treatments assessments. These were: Maximum Phonation Time (MPT), Jitter, Shimmer, Video-stroboscopy, Noise to Harmonic Ratio and Harmonic to Noise Ratio (NRH/HNR), Mean Airflow Rate (MeAF), Fundamental frequency (F0), GRBAS-I, Mean Subglottic Pressure (MSGP), Voice Handicap Index -30 (VHI-30) and the group of "infrequent perceptual scale".

Of these 11 VOIs, five were not selected for the survey for the following reasons: (a) infrequent perceptual scales are by definition specific to each center and/or not validated, (b) video-stroboscopy has no universally accepted protocol for standardization, even though it was considered by authors as "a must have" of the laryngologist's facilities when it comes to UVFP treatment (c) the NHR/HNR, the MSG and the F0 were not considered for the survey because they showed an overall "percentage of significance" of less than 50% .

Finally, the following six VOIs were selected for the survey and submitted for the surgeon's evaluation: VHI-30, Jitter, Shimmer, GRBAS-I, MPT and MeAF. Surgeons were also asked to suggest alternative VOI's within the free-text section.

For each of these 6 VOIs, three options of answers were possible. Each answer corresponded to a post-operative value of VOI, surgeons would personally consider as most satisfactory to them.

The questions were designed such that the mean post-operative value obtained by the literature review corresponded to the middle option. For each question, a higher and a lower value proposition was arbitrarily proposed. Ideally, these upper and lower propositions would correspond to the P25 and P75 of the literature's mean value result. As the literature review was not a meta-analysis, these data were not available.

The fact that the middle value corresponded to the literature data was not disclosed to the survey participants.

The aim of this method was to assess the degree of consensus, among surgeons, relative to the average post-operative VOI value found in the literature. Accordingly, questions showing a large dispersion of answers will be the reflection of a low consensus on the post-operative VOI value suggested by the literature. Inversely, questions showing a concentration of answers on the middle proposition will reflect a reasonable agreement of the responding surgeons on the post-operative value suggested by the literature review.

Regarding the answers to question 1 of table 1; in order to aggregate the results of VOI's classification for the entire group of responders, a global score was ascribed to each VOI based on the following formula: for each responder 6 points were ascribed to the highest ranking VOI, 5 for the second highest and so on with the lowest ranking VOI receiving 1 point. Ranking points were then multiplied by the respective percentage of responders assigning a particular rank to a VOI, and added up to obtain a global score, divided by 100.

For instance, the **global ranking score** of the VHI-30 is: 42(%)X6 + 30(%)X5 + 14(%)X4 + 8(%)X3 +4(%)X2 + 2(%)X1 = 492/100 = **4,92**

Results

After the first round of 310 E-mails, 160 "laryngologists" opened the e-mail of which 46 completed the survey. After a, non-selective, second round of 310 E-mails, 146 laryngologists opened the E-mail and another 16 more surveys were collected. Double submission was electronically not possible.

In total, 62 of the 310 ELS members responded. This represents a response rate of 20%. Of the 62 responders, 10 (16%) were not complete and were excluded. Two surveys were filled out by other professionals than surgeons and were subsequently also excluded. Therefore, the results represent the outcome of 50 surveys. Forty of these surveys were collected after the first round of e-mails and 10 after the second round.

Fifty percent of responders worked in a tertiary university hospital; 12% in a secondary hospital and 18% exclusively in a private practice. Six percent had a combined tertiary/private practice and 4% a combined secondary/private practice. Figure 1 shows surgical experience in years of experience of UVFP surgery.

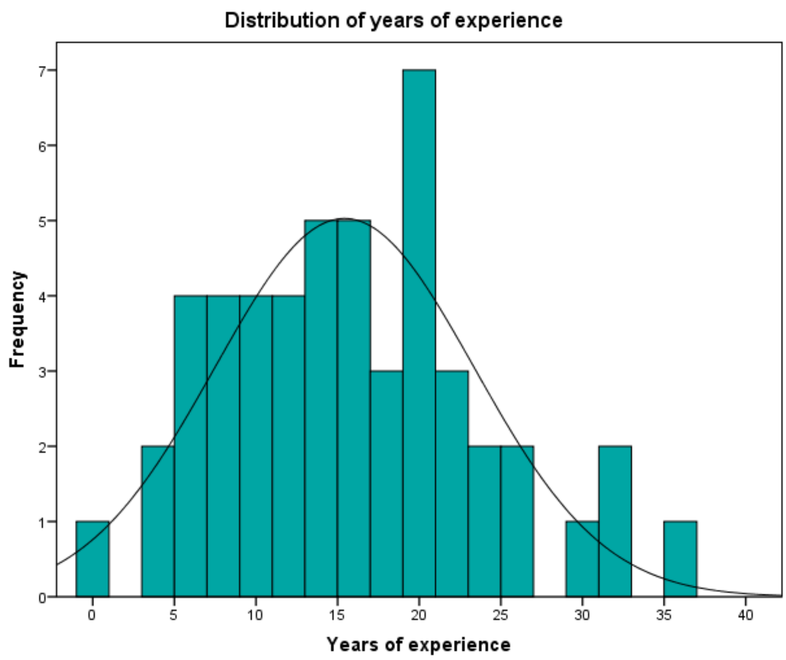


Figure 1 displays experience of answering surgeons in terms of years of UVFP surgical treatments practice.

Figure 2 displays the global ranking score of each VOIs (Question 1 of table 1). The VOIs that were favored by the responding surgeon were, in decreasing order of importance, VHI-30, MPT, GRBAS-I, MeAF, Jitter and Shimmer.

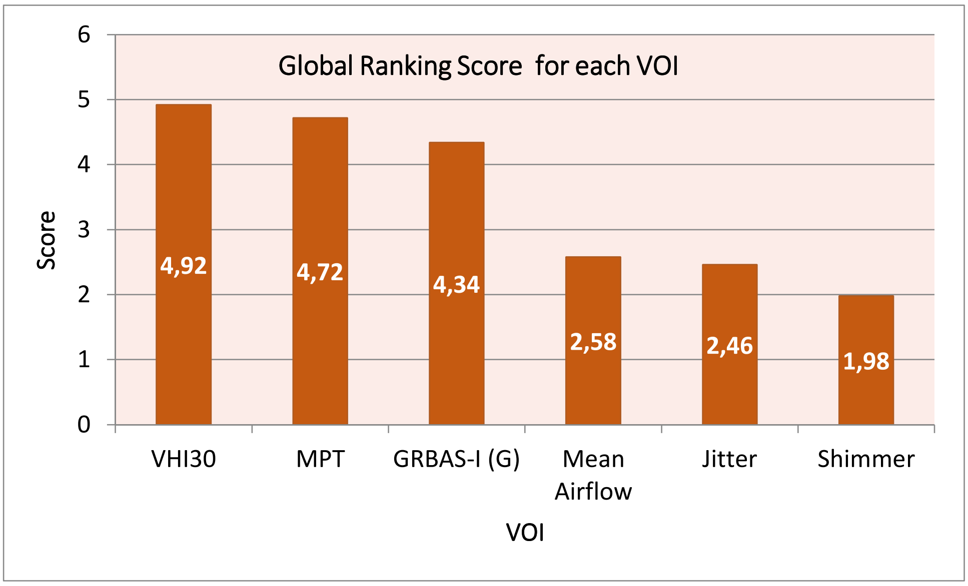


Figure 2 shows the global ranking score of each VOIs according to surgeon's preference

Regarding the answers to question 2 of table 1, both VHI-30 and the MPT are considered as “a must” by 33,1% of surveyed laryngologists. The GBRAS scale is considered “a must” by 20,8% while for MeAF, Jitter and Shimmer the score was 5,6%, 4% and 2,4% respectively.

Regarding the answers to question 3 of table 1, thirty-eight percent of the surgeons advocate a post-operative voice assessment at 3 months, 16% at one month, 12% at 6 months and 2% at 12 months. Multiple post-operative voice assessments are favored by some responders who suggested post-operative assessments both at 3 and 12 months for 12% and 1 and 6 months for 8% of the surgeons.

Table 2 summarizes the answers to questions four to eleven of Table 1.

Regarding the answers to question 4 of Table1, 60% of the surgeons would be satisfied with a relative improvement of 50% of the VHI-30.

Regarding the answers to question 5 of Table 1, the improvement of the absolute value of the VHI-30 generates more divergences with 48% of surgeons that would be satisfied with an increment of 40 points, while 38% would consider an increment of 20 points of VHI-30 sufficient.

Regarding the answers to question 6 and 7 of Table 1, the satisfactory value of Jitter and Shimmer would be 5% for 54% of the surgeons. These questions generated numerous negative free comments and 34% of the answering surgeons declared that they hardly pay attention to these VOIs. More than 30% of surgeons considered a reduction of 2,5% of Jitter as a satisfactory post-operative result. Similarly, 30% of surgeons considered a reduction of 2.5% of Shimmer as satisfactory.

Regarding the answers to question 8 of table 1, a post-operative general score (G) of the GRBAS-I of 1 was considered as satisfactory by 78% of the surgeons. 16% scored a 0 and 6 % scored a 2 as satisfactory.

Regarding the answers to questions 9 and 10 of Table1, a post-operative MPT improvement of 5, 7 and 10 seconds would be a satisfactory increase for respectively 28%, 58% and 14% of the respondents. A post-operative threshold value of 12 seconds would be considered a satisfactory result by 56% of the surgeons. Twenty-two percent would accept a threshold of 10 sec and the same percentage of responders would accept a threshold value of 14 sec.

Finally, regarding the answers to question 11 of table 1, sixty percent of the surgeons would be satisfied with a post-operative MeAF of 250ml/sec. Twenty-four percent would be satisfied with a MeAF of 200ml/sec whereas 16% would expect a MeAF of 300 ml/sec.

Twenty-two percent of the surgeons wrote a free comment concerning the MeAF. The majority of the comments indicated that, despite the fact that they valued the VOI, they were not using it as a routine VOI.

No other VOI besides ones proposed in the survey were spontaneously advocated by the survey participants.

Questions		Answers		
What relative percentage improvement of the VHI-30 would you consider as a satisfactory post-operative result?	Answers options	25%	50%	75%
	%age of answers	14%	66%	20%
What absolute numeral improvement in VHI-30 would you consider as a satisfactory post-operative result?	Answers options	↘20 pts	↘40 pts	↘60 pts
	%age of answers	38%	48%	14%
What according to you is the threshold under which the Jitter should go down post-intervention to be satisfactory?	Answers options	2.5%	5%	7.5%
	%age of answers	30%	54%	16%
What according to you is the threshold under which the Shimmer should go under post-intervention to be satisfactory?	Answers options	2.5%	5%	7.5%
	%age of answers	30%	54%	16%
What do you consider a satisfactory score for G (grade) post-intervention?	Answers options	0	1	2
	%age of answers	16%	78%	6%
What, according to you, can be considered as a satisfactory increase of MPT post-intervention?	Answers options	↗5sec	↗7sec	↗10sec
	%age of answers	28%	58%	14%
What threshold should the MPT exceed post-intervention to be satisfactory?	Answers options	10sec	12sec	14sec
	%age of answers	22%	56%	22%
Which MeAF post-intervention would you consider as satisfactory?	Answers options	200ml/sec	250ml/sec	300ml/sec
	%age of answers	24%	60%	16%

Table 2 summarizes the answers to questions four to eleven of Table 1.

Discussion

This survey represents, to our knowledge, the first survey interviewing surgeons on their opinions concerning relevance of VOIs in assessment of surgical treatments for UVFP.

The results of the survey show that VHI is highly valued by the surgical community. In fact, it was found to be the most important VOI in their opinion. This is in contrast with the literature review that ranked VHI-30 in 11th position in terms of utilization and 7th position in terms of "percentage of significance" (64% of the studies utilizing the VHI-30 as a VOI showed significant post-op results). Surprisingly, a certain consensus exists among surgeons about the relative increase the VHI should show post-operatively, whereas no real consensus could be found regarding its numeral post-operative improvement. Surgeons indeed show a tendency to target somewhat lower than VHI-30 difference in absolute value indicated by the literature.

MPT and general score (G) of the GRBAS-I scale represent the two next VOIs favored by surgeons. The survey revealed a good consensus among surgeons for MPT (absolute and relative increase) and an excellent one for G of GRBAS-I regarding the desired post-operative values as revealed by the literature review.

The MeAF seems to have a special status for surgeons. They acknowledge its value and importance, but, at the same time, confess its little use. Did this group of surgeons read the recent literature advocating the use of a disease-specific set of indicators including the MeAF [4] or do they have the sense that another aero-dynamic indicator would be necessary when it comes to UVFP assessment? This survey cannot answer this question. A couple of responders mentioned that they were using the Phonatory Quotient (PQ =Vital Capacity divided by the MPT) instead. The PQ is known to be directly correlated to the MeAF and thus might be considered of a surrogate of it [2]. A reasonable consensus exists among surgeons to consider the 250ml/sec as a satisfactory post-operative value. This is in accordance with the data obtained and observed in the literature.

According to the survey results, Jitter and Shimmer are not preferred by the surgeons. It is not clear what the reason is. These indicators could have a low predictability for the surgeons, concerning the intended voice improvement, especially if they have limited experience in interpreting the measures. Moreover, surgeons may feel that these indicators correspond less to clinical factors such as perceptive dysphonia and voice fatigue than other VOIs. Finally, there is no wide consensus on the satisfactory post-operative value these VOIs should have. Surgeons, as a group, seem to hesitate between

2.5% and 5%. The fact that more than 10% of surgeons chose the 7.5% supports the idea that there is a lack of knowledge of these acoustic parameters.

Several limits and bias of this survey have to be underscored. The survey participation rate was of 16% of the ELS members gathering also physicians that are not involved, at all, in voice surgery. This represents a sample of 50 laryngologists practicing UVFP surgeries on a regular base. This participation rate was the lower limit that was foreseen by authors to declare the survey valid.

Authors were well aware of a possible bias due to the design of the answer options in this survey. The questions were designed such that the mean post-operative value obtained by the literature review corresponded to the middle option. For each question, a higher and a lower value proposition was arbitrarily proposed. This design may give a tendency to favor the middle option, and thus, favor the consensus. This bias is called "the central tendency bias" [5]. Results should be interpreted accordingly. The bias favoring consensual answers, gives an extra weight to answers that were not so consensual, such as answers on the numeral improvement of VHI-30, the Jitter and the Shimmer.

Video-stroboscopy, while being largely used as a post-surgery outcome indicator, was not included in the survey. This was a deliberate choice as there is no universally accepted protocol for standardization. The number of VOIs was limited. They were however selected by a previously done literature review and no voice outcome indicators were claimed to have been omitted by the survey responders. Options of responses were limited and could only be overruled by free comments. These were abundantly used for the questions relative to the Jitter and the Shimmer. Finally, all questions had to be answered before taking the next one. Two of the responders indicated that they had rather skipped some questions, had it been possible.

CONCLUSION

Based on this survey, three VOIs are favored by surgeons: VHI-30, MPT and GRBAS-I.

Although strongly valued by surgeons, there is no clear consensus about the post-operative difference of VHI-30 absolute value that should be targeted. There is a discrepancy between the high value that surgeons appear to attribute to the VHI-30 as UVFP treatment VOI and its rather moderate percentage of significance revealed by the literature review.

The Jitter and the Shimmer, although very frequently reported and statistically valid in the literature come last in surgeon's choice as VOI for UVFP treatment assessment. Furthermore, many surgeons expect post-operative values of Shimmer that are higher than those found within the literature. Further studies should investigate this discrepancy to better ascertain the value of these acoustic parameters as voice outcome measures after phonosurgery generally and surgical treatment of UVFP specifically along with surgeon's knowledge about acoustics parameters.

MeAF seems to be valued by surgeons but is not used as much as surgeons would like. The access to a pneumotachograph could be an explanation for its under-use.

No other VOI besides ones proposed in the survey were spontaneously advocated by the survey participants.

Finally, expected VOI's results after surgical treatment for UVFP that were chosen by a majority of surgeons were generally in accordance with the data provided by the literature review.

Compliance with ethical standards

- The authors declare that they have no conflict of interest
- This article does not contain any studies with human or animals performed by anu of the authors
- Informed consent collection is not applicable to this study

References

1. Siu J, Tam S, Fung K. A comparison of outcomes in interventions for unilateral vocal fold paralysis: A systematic review. Laryngoscope. 2016 Jul;126(7):1616-24
2. Dejonckere PH, Bradley P, Clemente P, Cornut G, Crevier-Buchman L, Friedrich G, Van De Heyning P, Remacle M, Woisard V; Committee on Phoniatrics of the European Laryngological Society (ELS).. A basic protocol for functional assessment of voice pathology, especially for investigating the efficacy of (phonosurgical) treatments and evaluating new assessment techniques. Guideline elaborated by the Committee on Phoniatrics of the European Laryngological Society (ELS). Eur Arch Otorhinolaryngol. 2001 Feb;258(2):77-82.
3. Desuter G, Dedry M, Schaar B, van Lith-Bijl J, van Benthem PP, Sjögren EV. Voice outcome indicators for unilateral vocal fold paralysis surgery: a review of the literature. Eur Arch Otorhinolaryngol. 2017 Dec 20. doi:10.1007/s00405-017-4844-9. [Epub ahead of print] PubMed PMID: 29264655.
4. Dastolfo C, Gartner-Schmidt J, Yu L, Carnes O, Gillespie AI. Aerodynamic Outcomes of Four Common Voice Disorders: Moving Toward Disorder-Specific Assessment. J Voice. 2016 May;30(3):301-7.
5. Klos, Alexander. (2012). Central Tendency Bias and Self-Reported Risk Attitudes. SSRN Electronic Journal. . 10.2139/ssrn.2050899.

CHAPTER 4:

Very long term voice handicap index voice outcomes after Montgomery thyroplasty: a cross-sectional study.

Abstract:

Objective

The aim of this multi-centric cross-sectional study was to examine the permanency of Montgomery Thyroplasty (MTIS) results from a patient's perspective.

Design

The study consisted of collecting Voice Handicap Index (VHI-30) questionnaires from patients who had been previously been operated with MTIS between 2 and 12 years before. Very long term (>2 years) post-operative data were compared to the previously acquired pre-operative and early post-operative VHI results. Influence of factors such as age, gender, size/side of the prosthesis, and length follow-up were also analyzed.

Setting

Multi-centric study involving three tertiary European voice centers.

Participants

Forty-nine Unilateral Vocal Fold Paralysis (UVFP) patients, treated by MTIS, were included in the study .

Main Outcome Measures

The Voice Handicap Index-30 score.

Results & Conclusions

The median VHI was significantly different over time-points (Friedman's test p<0.001), with a significant difference between pre-operative and early post-operative time point (median VHI: 70 vs 21, respectively; p<0.001) and between pre-operative and very-long-term post-operative time-point (median VHI: 70 vs 16, respectively; p<0.001). The median VHI did not differ for the early and very-long -term post-op time-point (median VHI: 21 vs 16; p=0.470).

Age differences, gender differences and size/side differences of the prosthesis, centers where surgery took place and length of the follow-up showed no significant influence.

MT (medialization thyroplasty) overall and MTIS in particular, should be considered as a possible standard of care for UVFP when permanency of voice results is sought.

Introduction

Unilateral Vocal Fold Paralysis (UVFP) in abduction is responsible for breathy voice, phonatory dyspnea and, in some cases, dysphagia. Many treatments have been advocated in the past for this debilitating condition. Besides voice therapy, four different surgical procedures have been proposed as treatment for UVFP: the medialization thyroplasty (MT), the injection laryngoplasty (IL), the arytenoid adduction or pexy (AA) and the laryngeal reinnervation (LR). These techniques can be combined. All four of these interventions have shown satisfactory short and long term post-operative results.

Unfortunately, the difference between short -or early- and long term post-operative results regarding UVFP surgery is not clearly defined. A recent literature review revealed that the term “short-term” is used up to 14 months after surgery while the term “long-term” is already used 12 months after surgery, creating some semantic confusion [1]. For more clarity, we defined very long term results, as results that were obtained, at least, 2 years after surgery.

All the surgical techniques mentioned above have their advantages and limitations. Among them MT presents a relatively low technical challenge. This is even more true for MT using the Montgomery Thyroplasty Implant System (MTIS) for which a short learning curve has been shown [2]. MT is also reputed to be a one-time procedure assuring long terms results. So much so that many authors consider MT as the gold standard for permanent treatment of UVFP. Concerns remain, however, about the permanency of the results of MT due to possible vocal fold atrophy over time [3, 4].

Only four studies address the very long term results of MT as defined by this study. None of these studies investigate MT performed with the MTIS. One of these studies is a case series of 5 patients [5], two look at voice results in terms of acoustics and aerodynamics parameters [6,7], the last study looks at the voice results in terms of Voice-Related Quality of Life parameter [8]. This last study concluded that “Patients that were more distant from surgery had lower V-QROL scores than those who had more recently been treated”. In other words, the only very long term study investigating voice results from a patient’s perspective demonstrates a fading of voice results in terms of voice-related quality of life in the course of time.

In order to assess very long term voice results for patients undergoing a MT with the MTIS, we launched a multi-centric cross sectional study collecting Voice Handicap Index questionnaires (VHI-30) from patients operated at least two years before. These very long term post-operative data were compared to the previously acquired pre-operative and the short term post-operative VHI results.

Influence of factors such as age, gender, size/side of the prosthesis, and length follow-up were also analyzed.

Material and Method

The study protocol has been approved by the Ethical Committees of all participating institutions.

Patients, from 3 different treatment centers practicing the MTIS and meeting the inclusion criteria, were included.

To be included in the protocol, patients had to have undergone a MTIS -with no associated procedure- for a UVFP, at least 2 years before inclusion. The UVFP had to be of neurogenic origin as defined by the ELS guidelines [9]. There was no length of time limit for the follow-up. Patients had to be aged between 18 years and 80 years at the time of the MTIS. All patient's files had to include a pre-op VHI-30 questionnaire and an early post-op VHI-30 that had been performed less than 12 months before and less than 14 months after the MTIS respectively. Fourteen months was chosen as this was found to be the cut-off between short and long term post-op according to the literature. In case of multiple post-operative early VHI-30 assessments, the earliest data were considered for the study. The VHI-30 must have been validated and published for the language of use.

A careful electronic medical record (EMR) review excluded deceased patients and patients that had to undergo further voice surgeries after the MTIS.

This study is a cross-sectional, survey based, multi-centric study filed on NIH's ClinicalTrials.gov under the number NCT02969993 (first received November 18th 2016).

The study consisted of collecting Voice Handicap Index (VHI-30) questionnaires from patients who had been previously been operated with MTIS at least 2 years before.

The questionnaires were obtained in two different ways. In case of center 1 and 3, VHI-30 questionnaires were sent out by mail accompanied by an introduction letter and an informed consent that had to be returned. The patient certified having filled in the VHI-30 personally, with no assistance whatsoever. Furthermore, patients were asked to disclose possible further voice surgeries or new disease or condition that could affect their voice quality. It was also possible for relatives to communicate about the death of the patient by returning the mail.

In case of center 2, patients were invited by phone, to come to the hospital to fill in the VHI-30 along with an informed consent. Questions about possible further voice related surgeries or conditions that could affect their voice quality were checked by phone. Patients were isolated alone in a room in order to personally fill in the VHI-30 questionnaire.

Dead patients reported by relatives and patients presenting post MTIS surgeries or diseases/ conditions that would affect voice quality were excluded and not considered for the study.

All 3 centers entered their data in one Excel data bank and included: anonymized identification of the patient, date of birth, gender, side and size of the prosthesis, date of the MTIS procedure, date and value of pre-operative VHI-30, date and value of early post-operative VHI-30 and date and value of very long term post-operative VHI-30. Inclusion and exclusion data were also checked for each center.

Once data was obtained, very long term (>2 years) post-operative data were compared to the previously acquired pre-operative and early post-operative VHI results. Influence of factors: age, gender, size/side of the prosthesis, center where surgery has been performed and length of VHI-30 follow-up were also analyzed.

Continuous variables were summarized using medians, interquartile ranges and ranges. To analyze the evolution of VHI in time (repeated measurements: pre-operative, early and very-long-term post-operative), Friedman's rank sum test, a non-parametric alternative to the parametric test one-way repeated measures ANOVA, was used. A pairwise comparison using Nemenyi multiple comparison test was then applied to identify significant differences between time period groups. Variables associated with the decrease in VHI over time were assessed using random effects-expectation maximization (RE-EM) tree, a mixed effects model for longitudinal data, to take into account repeated measurements. Time period and patient identifier were inserted as random effects to take into account repeated measures for each patient. The center was assessed as a fixed effect in the model because of the low number of categories (3 centers).

Results

Eighty-two (82) patients were considered for the study, as they had undergone a thyroplasty using MTIS for UVFP, as a sole procedure, that had been performed at least two years earlier. The number of deceased patients according to the data available in their EMR were 13, 1 and 0 for center 1, 2 and 3 respectively. In none of the cases the cause of death was related to the MTIS. The EMR review revealed one patient that underwent a complimentary injection laryngoplasty (IL) after MTIS because of unsatisfactory voice result. This additional procedure was performed within 2 years postoperatively. Therefore, in total 15 of the initial 82 patients were excluded from the study.

The 67 remaining patients were asked to participate in the study. The VHI-30 score along with an accompanying letter and an informed consent form, to be returned, were sent to 33 patients from center 1 and 16 patients from center 3. Eighteen patients from center 2 were invited by phone to fill in the VHI-30 questionnaire at the hospital.

The overall response rate was 78% (81% for center 1, 89% for center 2 and 56% for center 3).

Relatives informed authors of the death of 2 patients from center 1. Moreover, one patient from center 1 informed authors about the occurrence of a voice impairing disease (the recurrence of metastatic thyroid papillary carcinoma for which he was treated with external radiotherapy). These patients were categorized as non-responders and excluded from the study. Finally 49 patients were included in the study (24 from center 1, 16 from center 2 and 9 from center 3).

Table 1 shows the patients characteristics of the cohort.

	Median [P25; P75] (min-max) or n (%)
Age at time of surgery, years	52.9 [42.3; 61.8] (16.3 – 74.5)
Females	34 (69.4)
Prosthesis	
Side : left	32 (65.3)
Size	9 [8; 10] (6 – 12)
Size : large*	34 (69.4)
Center	
Center 1	24 (49.0)
Center 2	16 (32.6)
Center 3	9 (18.4)
Time between date pre-op VHI and date surgery, in months	3 [1; 3] (0 – 12)
Time between date early post-op VHI and date surgery, in months	1 [1; 2] (0 – 14)
Time between date very long term post-op VHI and date surgery, in months	55 [42; 66] (24 - 142)

* ≥10 for males and ≥9 for females

Table 1: Patients characteristics at the time of MTIS (n=49)

The median time between the pre-operative VHI-30 and the procedure was 3 months. The median latency for early post-operative VHI-30 was 1 month (0-14 months) and the median latency for very-long-term post-operative VHI-30 was 55 months or 4,5 years (2-11,8 years).

The median [P_{25}; P_{75}] VHI score was 70 (59; 84] before the MTIS. It decreased to 21 [9; 37] and 16 [9; 30] in the early and very long term post-operative period respectively. The median VHI was significantly different over the 3 time points (Friedman's test $p<0.001$) with a significant difference between pre-op and early post-op (median VHI: 70 vs 21, respectively; $p<0.001$) and between pre-op and very-long-term post-op time points (median VHI: 70 vs 16, respectively; $p<0.001$). The median VHI did not differ significantly between early and very-long-term post-op time points (median VHI: 21 vs 16; $p=0.470$).

Figure 1 displays the linear graph (a) and boxplots (b) showing the evolution of VHI-30 scores over time in all patients.

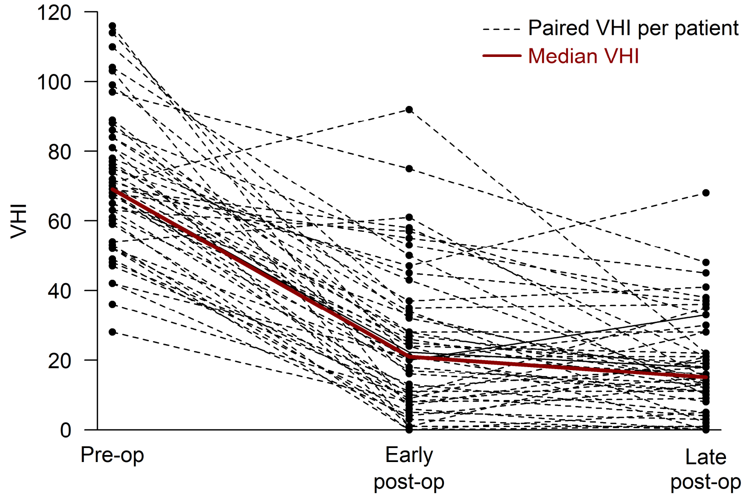
The cohort was grouped by their latency period, i.e. the period between the MTIS and the moment the very long term post-operative VHI-30 was scored. Two types of grouping were performed. The first grouping compared three latencies in years (from 2 to 4 years, from 4 to 8, longer than 8 years). The second grouping compared three latencies in months offering three comparable groups in terms of number of months (<40 months, 40 - 59 months and ≥ 60 months of latency).

Tables 2 shows the difference in VHI-30 between different time-points for the three different groups of latencies calculated with both grouping techniques. Results indicate no statistical difference of VHI-30 between early and very long term post-operative assessment up to 8 years and more of follow-up. This indicates a strong stability of voice results over time.

Four variables possibly influencing these results were analysed through the RE-EM tree technique. Results for age differences, gender differences and size/side differences of the prosthesis are displayed in Figure 2. None of these variables showed a significant effect on previously mentioned results.

A possible "centre" effect was also statistically ruled-out. Figure 3 displays a boxplots comparing VHI-30 results by centers.

A



B

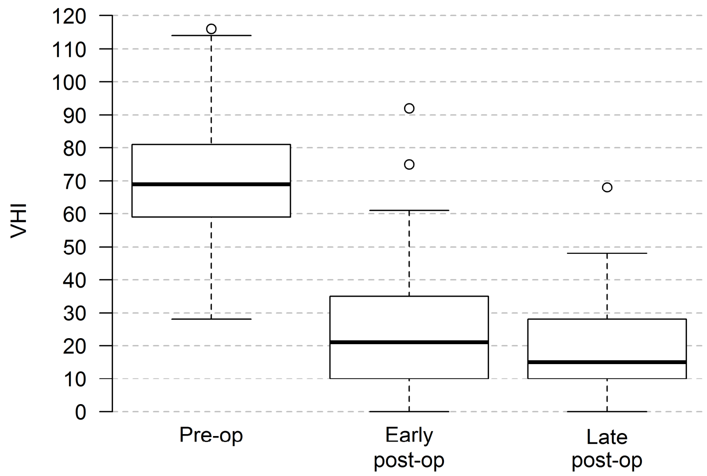


Figure 1: Linear graph (a) and boxplot (B) showing the evolution of VHI-30 scores over time in all patients

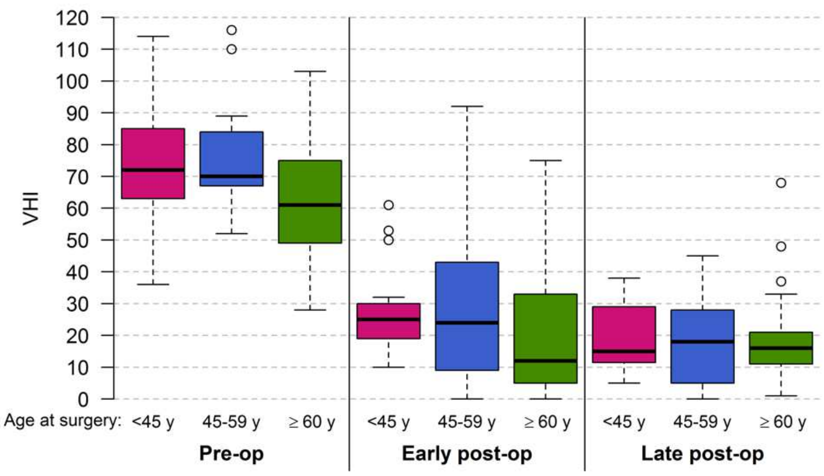
A

	Latency time <48 months (4yrs) (n=19)	48-95 months (4-8yrs) (n=22)	≥96 months (8yrs) (n=8)	p-value
VHI, median [P_{25}; P_{75}] (min; max)				
Pre-op	69.0 [56.5; 82.0] (42.0; 110.0)	66.0 [52.3; 81.0] (28.0; 116.0)	72.0 [68.0; 78.0] (61.0; 84.0)	0.724
Early post-op	24.0 [9.0; 50.0] (0.0; 92.0)	17.0 [8.3; 27.5] (1.0; 57.0)	26.0 [20.8; 30.3] (17.0; 55.0)	0.232
Late post-op	20.0 [11.0; 27.5] (1.0; 68.0)	12.5 [4.8; 20.3] (0.0; 37.0)	23.5 [16.8; 32.8] (8.0; 45.0)	0.101
Difference pre-op and early post-op	-35.0 [-60.0; -23.0] (-102.0; 21.0)	-44.0 [-57.8; -38.3] (-110.0; -6.0)	-48.0 [-51.8; -43.8] (-56.0; -13.0)	0.565
Difference pre-op and very long term post-op	-49.0 [-62.0; -41.0] (-82.0; -3.0)	-53.0 [-78.5; -36.5] (-116.0; -1.0)	-52.0 [-55.3; -43.8] (-58.0; -23.0)	0.791
Difference early and very long term post-op	-5.0 [-23.5; 3.0] (-70.0; 21.0)	-4.0 [-14.0; 4.5] (-40.0; 25.0)	-5.0 [-9.3; 1.0] (-13.0; 10.0)	0.959

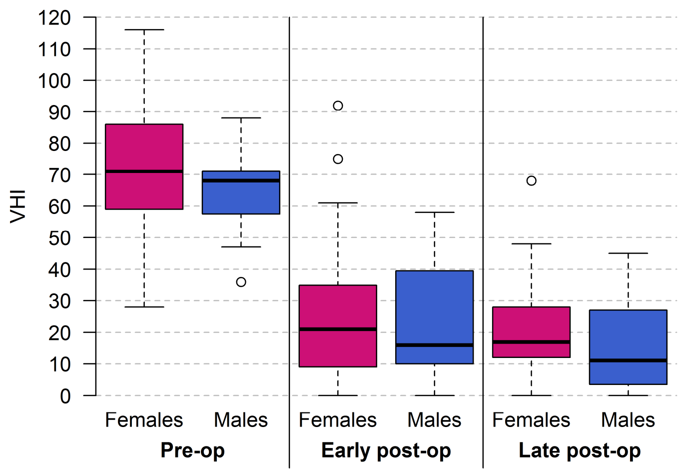
B

	<40 months (n=15)	Latency time 40-59 months (n=21)	≥60 months (n=17)	p-value
VHI, median [P_{25}; P_{75}] (min; max)				
Pre-op	68.5 [53.5; 74.8] (42.0; 103.0)	71.0 [58.0; 82.3] (28.0; 116.0)	68.0 [61.0; 81.0] (49.0; 114.0)	0.850
Early post-op	22.5 [11.8; 54.3] (1.0; 92.0)	14.0 [7.5; 33.5] (0.0; 75.0)	25.0 [20.0; 32.0] (3.0; 57.0)	0.329
Late post-op	21.0 [15.8; 24.8] (5.0; 68.0)	12.0 [0.0; 15.8] (4.8; 48.0)	19.0 [12.0; 30.0] (0.0; 45.0)	0.089
Difference pre-op and early post-op	-32.5 [-54.0; -18.5] (-102.0; 21.0)	-47.5 [-60.0; -34.3] (-110.0; -20.0)	-47.0 [-51.0; -40.0] (-94.0; -6.0)	0.246
Difference pre-op and very long term post-op	-45.5 [-51.5; -35.8] (-82.0; -3.0)	-56.5 [-68.8; -43.3] (-116.0; -1.0)	-53.0 [-56.0; -43.0] (-84.0; -23.0)	0.279
Difference early and very long term post-op	-3.5 [-20.5; 13.0] (-70.0; 21.0)	-5.5 [-15.5; 2.0] (-40.0; 25.0)	-4.0 [-13.0; 0.0] (-32.0; 19.0)	0.981

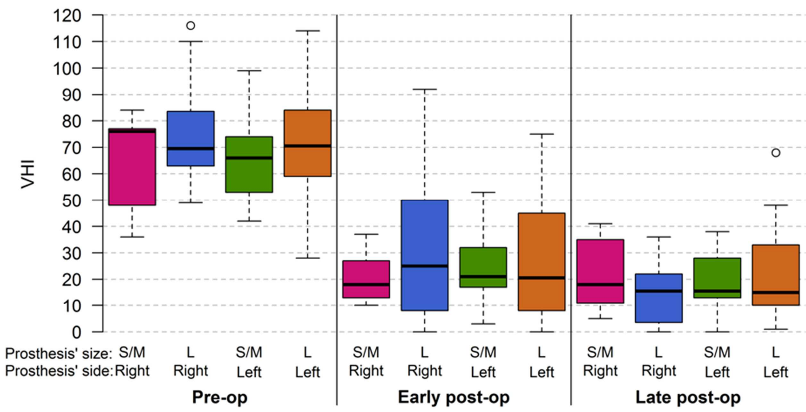
Table 2: VHI decrease according to the time since the surgery (N=49). Latency times in years (A). latency times in months (B)



A: results by age of the patient at the age of MTIS



B: results by gender



C: results by size of prosthesis

Figure 2: Boxplots comparing pre-operative, early post-operative and late post-operative VH1-30 results for various variable grouping of the cohort. (A) age of patients at the time of MTIS, (B) gender of patients, (C) small and medium (S/M), or large (L)Montgomery prosthesis used. A large prosthesis is defined as being ≥ size 9 for female patients and ≥ size 10 for male patients.

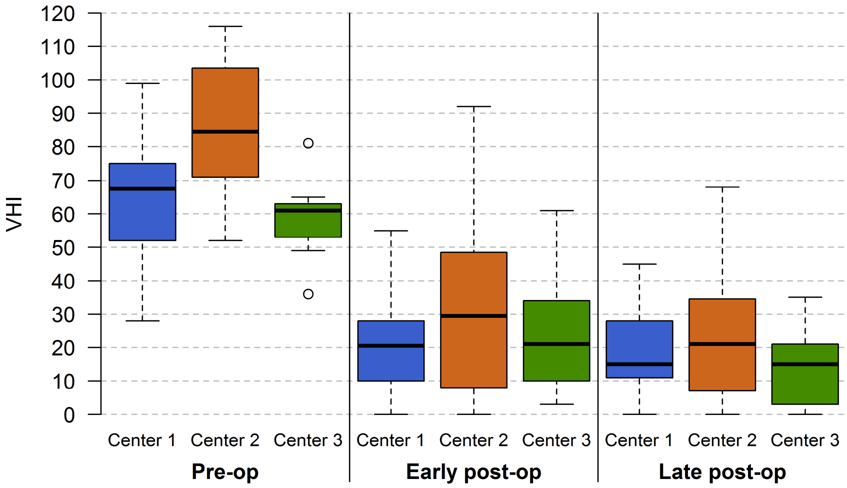


Figure 3: Boxplots comparing pre-operative, early post-operative and late post-operative VH1-30 results by center.

Discussion

Unilateral Vocal Fold Paralysis (UVFP) has been defined in a consensus paper by Rosen et al. as unilateral vocal fold immobility of neurogenic origin [9]. MT is considered by a majority of authors as a “permanent” treatment of UVFP. There is a lack of data that supports this and Siu et al. postulated a progressive fading of MT’s results due to a possible continued vocal fold atrophy along the years after in-depth review of the literature [4]. Moreover, Hogikyan’s (et al.) results seem to support this hypothesis in terms of Voice-related Quality of Life. [8].

The results of this study, however, strongly support the hypothesis that from the patient’s perspective, MT, in this case performed with the MTIS, offers a stable voice improvement over the years. MTIS results did not deteriorate over time and were independent of patient’s age and gender, prosthesis size and side. The postulated effect of muscle atrophy does not appear to be an issue. Whether this remarkably stable benefit can be called *permanent* remains a rather semantic debate.

This is the largest study assessing the very long term voice results of MTIS from the patient’s perspective. Ryu et al. conducted a retrospective study on 40 patients operated for MT with self-carved silicone implants in 2012 [7]. The long-term follow-up was done using acoustic (Jitter, Shimmer) and aerodynamic measures (Mean Airflow Rate and Maximum Phonation Time). Their results were similar, showing stable early and very long term (up to 5 years) post-operative results. They concluded their study by suggesting the launch of further very long term studies on other implants and other voice outcome indicators.

Although the VHI-30 is largely recognized as a valid self-evaluation tool [10], correlation between the subjective VHI-30 and objective acoustic and aerodynamic measures is poor [11-13]. Therefore this patient-centered approach represents a different very long-term assessment method. Considering Ryu’s results and the results in this study, a five-year permanency of MT results has now been established using two different research methods (cross-sectional versus retrospective), two different voice assessment approaches (VHI-30 versus acoustic and aerodynamic measures) and with two different types of implants (MTIS and self-carved silicone). Furthermore, this study demonstrates that variables such as age of the patient at the time of surgery, gender and prosthesis characteristics (size and side) do not influence this permanency of results.

The permanency of MT results is of particular interest when it comes to cost minimization analysis and treatment decision making. A recent Canadian study by Tam et al. [14] compared the costs of MTIS versus repeated injection laryngoplasty (IL) with hydroxyapatite. They concluded that, for a similar early (<2 years) effectiveness, IL will offer a cost saving of 596 CA$. However the hydroxyapatite has a lifespan on average of 18 months [15], and with the MT’s results now showing evidence of 5 years permanency, the cost/benefit analysis could switch in favor of MT, especially for patients having a longer life expectancy than 2 years. Further prospective studies should focus on life expectancy of the patients as a surgical decision making determinant.

Some bias and limitations of our study should be taken into consideration. In order to gather enough patients meeting the inclusion criteria, a multi-centric approach was chosen. The way the VHI-30 questionnaires were collected differed for one center. Center 2 invited patients by phone rather than by mail. Center 2's VHI-30 were also filled in within the clinic setting rather than at patients' homes. This modification of data collection was considered more appropriate to the cultural and sociological background of this particular group of patients. Authors acknowledge a possible data collection bias although no statistical differences in very long-term VHI-30 assessments were noted between centers.

Furthermore, although the MTIS procedure is known as an easily reproducible step-wise surgical approach, operative variances in techniques and variations in operative experience between centers might have influenced results. However, one complimentary injection laryngoplasty for unsatisfactory post-MTIS voice result out of 50 surgeries (2%), represents a lower failure rate than the MT failure rates that are published in the literature [16,17]. Therefore we believe that technical variability did not have a large impact on our results.

Finally, as centers 1 and 2 had a response rate above the 80%, and center 3 a response rate of 56%, this difference could also represent a possible bias. We don't have much rationale for this difference of responder's rate except for the fact that some of this center's patients had been operated by a surgeon who left the institution. Some patients of center 3 might have been less motivated by a request for participation signed by an unknown surgeon. Nevertheless, despite this caveat, the overall response rate (78%) was 10% higher that the response rate of Hogikyan et al. (68%)[8] and was thus considered valid for interpretation.

Conclusions

This study shows that MT performed with the MTIS offers permanency of voice improvement from the patient's perspective. Age, gender, side of procedure and size of MTIS implants does not influence very long term results in terms of VHI-30. Therefore, MT overall and MTIS in particular, should be considered as a possible standard of care for UVFP when permanency of voice results is sought.

References

1.Desuter G, Dedry M, Schaar B, van Lith-Bijl JT, van Benthem PP, Sjögren EV. Voice outcome for unilateral vocal fold paralysis surgery: a review of the literature. Eur Arch Otolaryngolol. 2018 In press

2.Desuter G, Henrard S, Boucquey D, Van Boven M, Gardiner Q, Remacle M. Learning curve of medialization thyroplasty using a Montgomery™ implant. Eur Arch Otorhinolaryngol. 2015 Feb;272(2):385-90.

3.Lundy DS, Casiano RR, Xue JW, Lu FL. Thyroplasty type I: short- versus long-term results. Otolaryngol Head Neck Surg. 2000 Apr;122(4):533-6.

4. Siu J, Tam S, Fung K. A comparison of outcomes in interventions for unilateral vocal fold paralysis: A systematic review. Laryngoscope. 2016 Jul;126(7):1616-24.

5.Leder SB, Sasaki CT. Long-term changes in vocal quality following Isshiki thyroplasty type I. Laryngoscope. 1994 Mar;104(3 Pt 1):275-7.

6.Umeno H, Chitose S, Sato K, Ueda Y, Nakashima T. Long-term postoperative vocal function after thyroplasty type I and fat injection laryngoplasty. Ann OtolRhinol Laryngol. 2012 Mar;121(3):185-91.

7. Ryu IS, Nam SY, Han MW, Choi SH, Kim SY, Roh JL. Long-term voice outcomes after thyroplasty for unilateral vocal fold paralysis. Arch Otolaryngol Head Neck Surg. 2012 Apr;138(4):347-51.

8. Hogikyan ND, Wodchis WP, Terrell JE, Bradford CR, Esclamado RM. Voice-related quality of life (V-RQOL) following type I thyroplasty for unilateral vocal fold paralysis. J Voice. 2000 Sep;14(3):378-86.

9.Rosen CA, Mau T, Remacle M, Hess M, Eckel HE, Young VN, Hantzakos A, Yung KC, Dikkers FG. Nomenclature proposal to describe vocal fold motion impairment. Eur Arch Otorhinolaryngol. 2016 Aug;273(8):1995-9.

10. Jacobson B.H,, Johnson A., GrywalskiC., Silbergeit A., Jocobson G., Benninger M.S;, Newman C.W., (1997)The Voice Handicap Index (VHI) : development and validation. Am J Speech Lang Pathol 6:66-70.

11.Woisard V, Bodin S, Yardeni E, Puech M. The voice handicap index: correlation between subjective patient response and quantitative assessment of voice. J Voice. 2007 Sep;21(5):623-31.

12. Wheeler KM, Collins SP, Sapienza CM. The relationship between VHI scores and specific acoustic measures of mildly disordered voice production. J Voice. 2006 Jun;20(2):308-17.

13. Dastolfo C, Gartner-Schmidt J, Yu L, Carnes O, Gillespie AI. Aerodynamic Outcomes of Four Common Voice Disorders: Moving Toward Disorder-Specific Assessment. J Voice. 2016 May;30(3):301-7.

14. Tam S, Sun H, Sarma S, Siu J, Fung K, Sowerby L. Medialization thyroplasty versus injection laryngoplasty: a cost minimization analysis. J Otolaryngol Head Neck Surg. 2017 Feb 20;46(1):14.

15. Shen T, Damrose EJ, Morzaria S. A meta-analysis of voice outcome comparing calcium hydroxylapatite injection laryngoplasty to silicone thyroplasty. Otolaryngol Head Neck Surg. 2013 Feb;148(2):197-208.

16. Rosen CA. Complications of phonosurgery:results of a national survey. Laryngoscope1998;108(11):1697-1703

17. Young VN, Zullo TG, Rosen CA. Analysis of laryngeal frameworksurgery: 10-year follow-up to a national survey. Laryngoscope. 2010;120(8):1602-8

CHAPTER 5:

The *Larynx Ruler* to measure height and profile of vocal folds: a proof of concept.

Abstract:

Introduction:

Glottic leakage during phonation is a direct consequence of unilateral vocal fold paralysis. This air leakage can be in the horizontal plane as well as in the vertical plane. Presently there is no easily applicable medical device allowing noninvasive, office-based measurement of the relative vertical position of the vocal folds. The Larynx Ruler (LR) is a laser-based measuring device that could meet the previously stated need, using a flexible endoscope. This study represents a proof of concept regarding the use of the LR in assessing vocal fold relative positions in the vertical plane.

Material and methods:

One fresh male human cadaver larynx, free of neurologic and anatomic disease, was explored with the LR system through the operative channel of a flexible gastroenterology video-endoscope. The tip of the video-endoscope was located in the laryngeal vestibule. The right crico-arytenoid joint was posteriorly disarticulated. Tilting of the vocal fold (VF) was obtained by pulling or pushing the arytenoid cartilage with a mosquito forceps fixed to the stump of the previously sectioned superior tip of the posterior crico-arytenoid muscle allowing anterior and posterior tilting of the arytenoid cartilage in order to induce an elevation or a depression of the VF process. .Ten “push” and ten “pull” sessions were performed. The distance from the tip of the video-endoscope to each illuminated pixel of the laser beam was recorded. The level difference between the left and right VF’s was measured for each recording.

Results:

Data provided by the LR were consistently in accordance with the movements applied on the vocal folds. The accuracy of 0.2 mm of the LR is compatible with the envisioned applications for the human larynx.

Conclusions:

The LR system represents a feasible technique to evaluate respective vertical position of vocal folds in the human larynx. Technical limitations were identified that will require improvements before experimental use on human.

Level of Evidence: NA

Key words: laryngoscopy, laser, measurement device, unilateral vocal fold paralysis

Introduction

During phonation, the closed vocal folds (VF) offer resistance to the air expelled by the lungs during expiration. Their vibro-elastic properties allow to interrupt the air flow that eventually will lead to vibration of the vocal folds and creation of sound.

The VF are located in the midpart of the thyroid cartilage. Their common anterior insertion is fixed at the anterior commissure. Their posterior anchoring corresponds to the vocal process of each arytenoid cartilage and is mobile in the three dimensions. The position of the vocal process is determined by the balanced contraction of all intrinsic laryngeal muscles under the neurological control of the vagal nerve and its terminal branches. Under normal conditions, the position of both vocal processes will be located at equal distance from any reference point located at the midline of the larynx.

In case of innervation unbalance of the larynx, for example in unilateral vocal fold paralysis (UVFP) the above-mentioned symmetry will be disrupted and may result in incomplete glottic closure during phonation leading to leakage of air at the level of the glottis. This innervation unbalance of the larynx will not only lead to a closure defect in the horizontal or axial plane but possibly also, in the vertical or coronal plane. This is why determination of the exact three-dimensional position of the posterior part of the VF is key when it comes to pre-operative planning of UVFP treatment.

As a matter of fact, the best treatment strategy to obtain optimal voice outcome after UVFP treatment is still debated. Most discussions concentrate on addressing posterior leakage. For instance, some authors advocate a systematic arytenoid adduction strategy, while others deny any use to it at all (1-6). The truth is that no evidence exists and the question remains unanswered (7-8).

Determination of the VF exact three-dimensional position before and after treatment could help to answer the above-mentioned question. Three-dimensional CT imaging has shown its value in tackling this problem but requires patient irradiation and delayed image processing. Presently there is no device allowing, real-time, harm free and office-based quantification of vocal fold vertical relative position. Industry is developing 3D video-endoscopic imaging but quantification of exact VF position remains impossible.

The Larynx Ruler (LR) is a laser based, endoscopically guided, measuring device that could meet the previously stated needs.

The primary purpose of this study is to see whether the LR technology could measure relative VF height (or level) differences, between the right and the left VF, measured from the tip of the endoscope.

Material and methods

The Laryngeal Ruler (LR) Device.

The LR device consists of a laser probe based on a miniaturized pattern projector placed in the instrument channel of the endoscope (Olympus GIF-100, Hamburg, Germany). It has a diameter of 2.7mm (Figure 1) and projects a line used as reference for analysis.

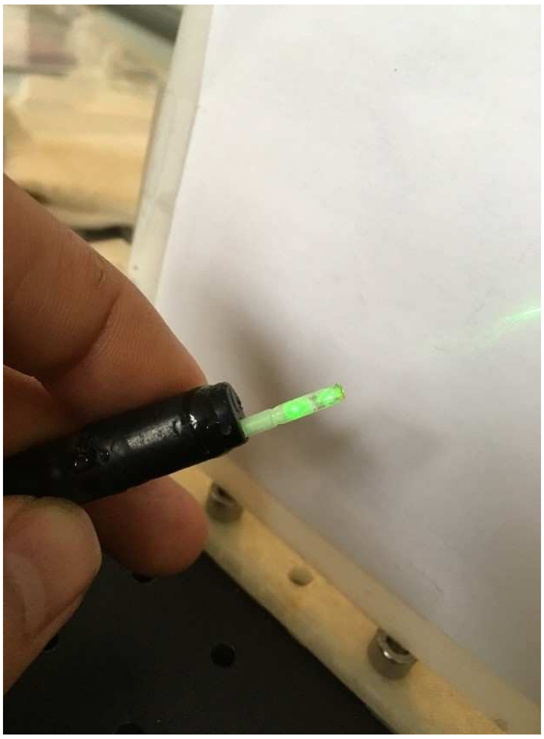


Figure 1: Laser probe placed in the instrument channel of the endoscope.

Principle of 3D reconstruction:

The LR is based on the structured light technology. A known pattern is projected and its image is analyzed to recover the 3D position of the points of interest (Figure 2). The projector P projects a laser line towards a point A on a surface, the camera C acquires the image. Depth (z) is then easily calculated as, α is the angle of projection measured using the pixel position of the point A as detailed in , β is known by calibration.9.It is the angle of projection of the line in the camera coordinates, and the distance d (between camera and projector) is the baseline known by calibration. 10.It can be easily shown that:

$$z = \frac{d}{\tan(\alpha) - tan(\beta)}$$

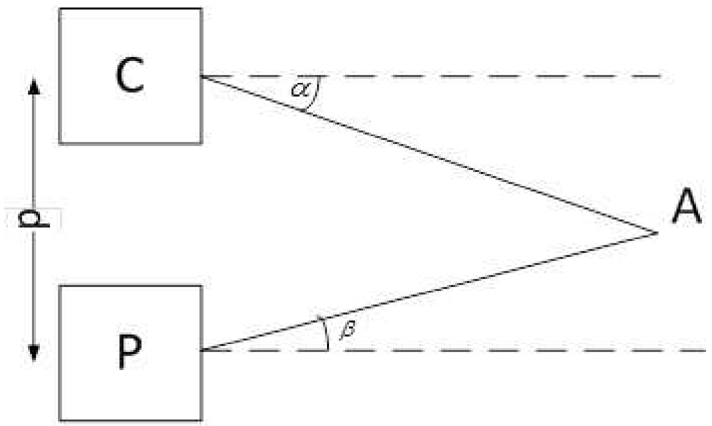


Figure 2: The point A is found by triangulation knowing the baseline d and the angles α and β.

In this example, the system is brought back to a 2D system, but it can be generalized to a 3D system. More information about structured light 3D reconstruction can be found in. 9.

Projection principle:

The projection is based on a diffracted laser beam using a diffractive optical element (DOE). DOE's are commercially available (e.g. Holoeye, Berlin, Germany) and are engraved to project a pattern (in this case, a simple line) as a focused laser beam pass through it (Figure 3). The pattern used is a single line, placed perpendicularly to the epipolar plane. It enables a direct measurement of every point of the line.

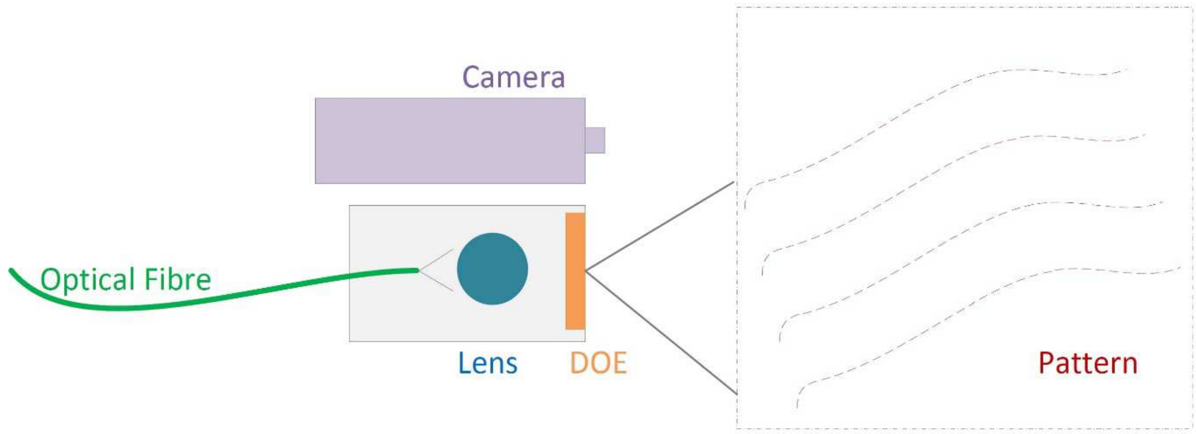


Figure 3: The system is composed of an optical fiber to transmit the beam, a lens to focus it and a diffractive optical element (DOE) to generate the pattern. The pattern is then analyzed using the camera of the endoscope.

This principle was already used by several authors have both developed a device based on two laser dots that provide a mean for estimating depth of the region of interest. 11.12.13. However, in this solution, the measurements are based on approximations. If the region of interest is not flat, it could lead to relatively important errors. Neitsch et al have proposed a smart solution based on a matrix of points (instead of two points).14. The main limitation here is that measurements are possible only where points are projected (or detectable). The laser source has a maximum power of 20mW at a wavelength of 532nm.

With regard to safety, the power density is lower than a conference laser pointer as the beam is used for a complete line whereas a laser pointer is focused on a single point. The power density is of 16 W/m^2 with a total power lower than 1mW. LR is thus harm-free for the patient.

The accuracy of this technology has been demonstrated elsewhere (9).

In a nutshell, the accuracy can be calculated by:

$$\delta z = \frac{\delta p_x z^2}{d f_x}$$

Where:

- δz is the accuracy (in m);
- δp_x is the accuracy of the line detection (in pixel);
- z is the working depth (in m);
- d is the baseline (distance between the camera and the projector, in m);
- f_x is the focal length of the camera (in pixels) .

Measuring process

The probe is kept in place by friction, the diameter of the device being the same as the channel diameter. The user places the device in the instrument channel and calibrates it before performing the endoscopy. The user checks the calibration (a ruler is used as reference) before and after performing the endoscopy.

To proceed with the measurement, the following steps were followed:

1. The endoscopist places the endoscope in a way the line is placed where the measurement must be made. The image is then freeze.
2. An external dedicated computer acquires the image and processes it to compute the data.
3. The user may picks-up the points of interest for exact measurements.
4. Data is displayed instantaneously on the endoscopic image and the profile in a dedicated window.

Homemade dedicated software using the Open CV library is used to compute the complete profile based on the equations mentioned here above. The system is calibrated prior any use to take the lens distortion and the tolerances of assembly into account. The processing time is below 50ms.

The generated profile is required to provide the user the ability to select exactly the relevant points of interests. In addition to that, the points of interests are shown on both the endoscopic image and the 3D profile to make sure the distances are relevant. Therefore, the user is able to select visually the points of interest by considering the anatomical structures on the endoscopic image itself.

However, the position of the tip of the endoscope (specially a possible angle-view) related to the larynx must be understood by the user to properly understand the generated profiles. The distance of the endoscope to the larynx has no influence as the profile is generated in 3D (it simply moves the profile along depth).

Height measurements at each pixel points of the laser-illuminated structures open the field of three-dimensional assessment of the larynx.

Proof of concept measurements

The study protocol was approved by the University of Louvain Institutional Ethical Committee under the number 2017/18JAN/028. The anatomical material was harvested according to Institutional Ethical Committee regulations.

One fresh unfrozen human male larynx was used for assessment of VF heights. According to patient medical file examination and anatomical inspection, the larynx was declared free of disease.

The specimen was examined with the LR system through the operative channel of a gastroenterology video-endoscope (Olympus GIF-100, Hamburg, Germany). The tip of the video-endoscope was positioned in the laryngeal vestibule. Experimental setting is detailed in Figure 4.

The right crico-arytenoid joint of the larynx was posteriorly disarticulated allowing anterior and posterior tilting of the arytenoid cartilage in order to create an elevation or a depression of the VF process. Tilting of the VF was obtained by pulling or pushing the arytenoid cartilage with a mosquito forceps fixed to the stump of the previously sectioned superior tip of the posterior crico-arytenoid muscle. The experimentally induced “push-and-pull” motions were compared at a given time with VF distances measured from the tip of the endoscope provided the LR technology. Ten “push” and ten “pull” sessions were performed. The distance from the tip of the video-endoscope to each illuminated pixel of the laser beam was recorded and plotted on a diagram (Figure 5). The level difference between the left and right VF’s was measured for each recording.

A vocal fold profile, showing the surface of the laser illuminated VF, was realized during each measurement. Profile characteristics that were scrutinized were: (a) ease of finding the medial edge pixel of VFs; (b) seamless surface profile of the VF and (c) identification of Morgani’s ventricles gap.

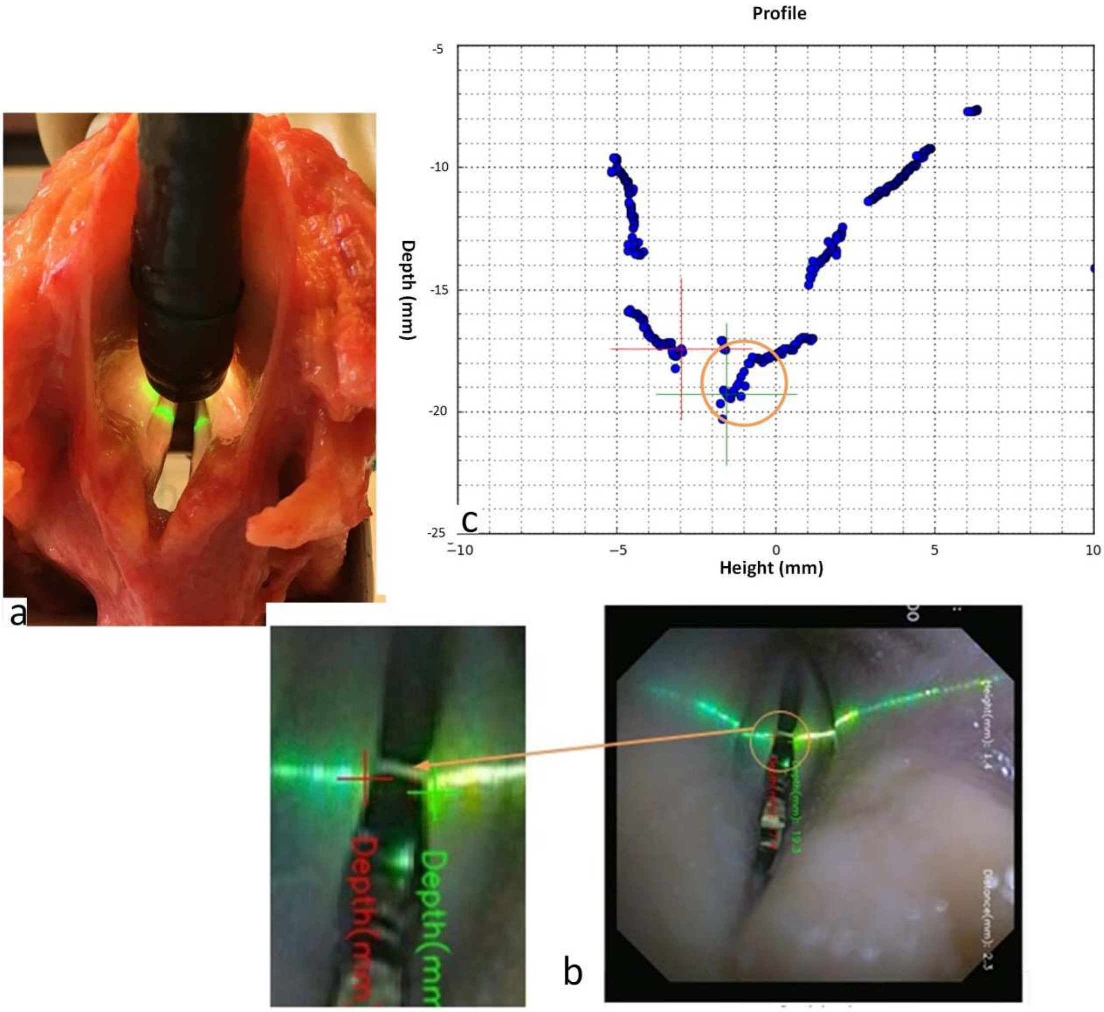


Figure 4: (a) Study setting showing the operative video-gastroscope introduced into the larynx vestibule with the laser beam "scanning" both vocal folds. (b) Endoscopic image of the laser beam "scanning" the glottis and the larynx vestibule; a zoomed image shows the respective positions of VF medial edges were VF height was measured from the tip of the video-endoscope (crosses represents medial free edges (green=right, red=left); note the fortuitous presence of a secretion between the vocal folds at the level of the laser beam) (c) LR screen capture showing the section profile by plotting heights measured from the tip of the video-endoscope, of every pixel that is illuminated along the laser beam.

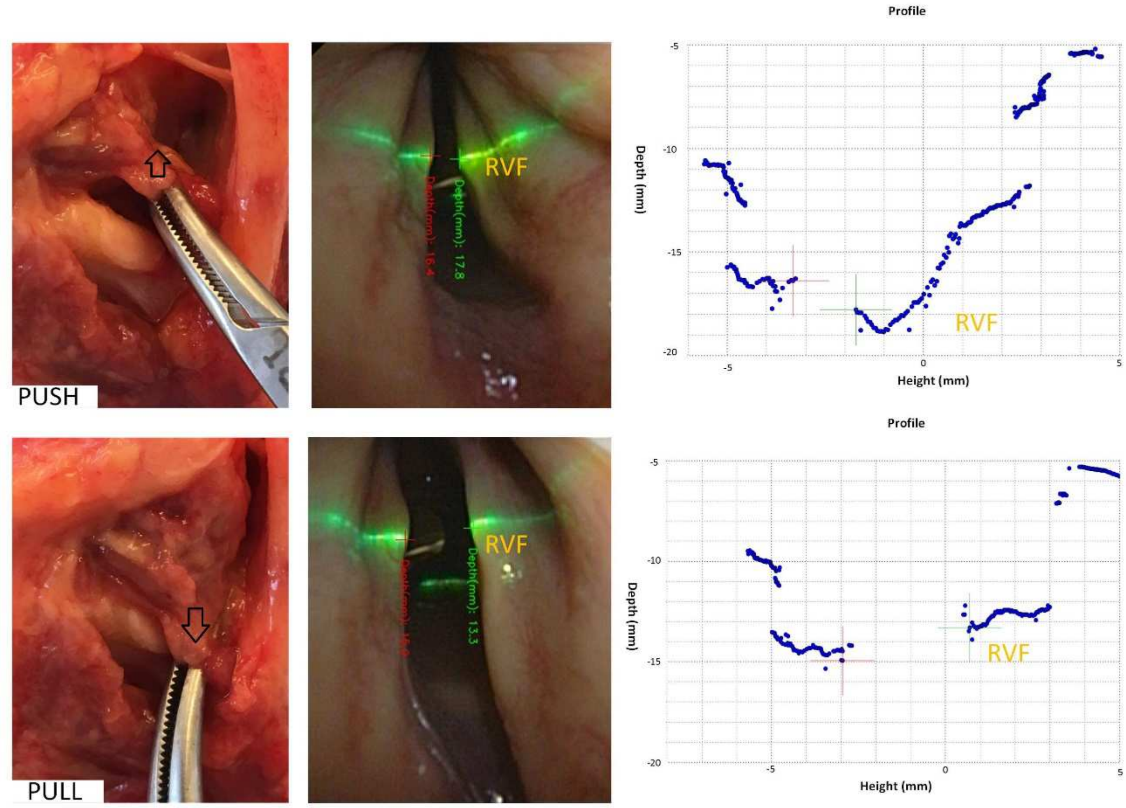


Figure 5: shows from left to right; simultaneous images of (1) The arytenoid motion applied on the specimen by a mosquito forceps on the posterior crico-arytenoid muscle stump. The *push motion* opens the crico-arytenoid joint and glides the arytenoid cartilage down internally on the cricoid cartilage. This lowers the VF. The *pull motion* glides the arytenoid posteriorly on the cricoid crest. This elevates the VF (2) The endoscopic image obtained with the LR video-endoscope showing the laser beam position (3) the corresponding screen capture provided by the LR. Note the difference of heights between VFs visualized and quantified on the screen capture images. These differences are not clearly visible on 2D endoscopic images.

Result

The results are shown in table 1. There was a perfect correlation between the relative position of the VFs (above or below the contralateral control side) and the relative heights measured by the LR technology. In other words, using the LR, it was possible to detect and quantify the difference in VF heights, measured from the tip of the video-endoscope, induced by manipulating the arytenoid cartilage. The force applied on the arytenoid cartilage was different for each session; therefore, the value of the height difference was variable. Likewise, the position of the tip of the endoscope was not completely fixed thus the absolute value of the VF height was different for each measurement.

Sessions	PUSH of the Right Arytenoid			PULL of the Right Arytenoid		
	Left VF height (mm)	Right VF height (mm)	Relative position of mobilized (right) VF (mm)	Left VF height (mm)	Right VF height (mm)	Relative position of mobilized (right) VF (mm)
1	17.6	19.5	1.9 mm Below	14.8	12.7	2.1 mm Above
2	14.5	16.2	1.7 mm Below	14.2	12.9	1.3 mm Above
3	15.9	16.8	0.9 mm Below	15.9	12.8	3.1 mm Above
4	18.6	21.7	3.1 mm Below	12.4	10.4	2.0 mm Above
5	20.0	22.5	2.5 mm Below	19.1	16.5	2.6 mm Above
6	18.4	20.2	1.8 mm Below	16.7	14.8	1.9 mm Above
7	16.4	17.8	1.4 mm Below	15.0	13.3	1.7 mm Above
8	19.6	21.4	1.8 mm Below	16.8	14.0	2.8 mm Above
9	11.3	16.5	5.2 mm Below	13.6	12.2	1.4 mm Above
10	15.0	17.9	2.9 mm Below	15.0	13.2	1.8 mm Above

Table 1: Table indicating, for each session, VF heights from the tip of the video-endoscope and the relative position of the mobilized VF.

The profiles were measured during the endoscopy and were available for post checking after the endoscopy.

A profile (or shape) of the surface of the VF at the level of the LR laser beam was always obtainable. This profile offers a visualization of a virtual coronal section of the VF at the level of LR's laser beam (Figure 6).

VF heights could be measured in all the evaluated positions. In 4 of the 20 screen captures, a seamless profile was not obtainable. These profiles were discontinuous and did not allow a clear profiling of glottic surface. Despite these caveats, Morgani's ventricles depths were always visible and quantifiable. No tissue damage was observed.

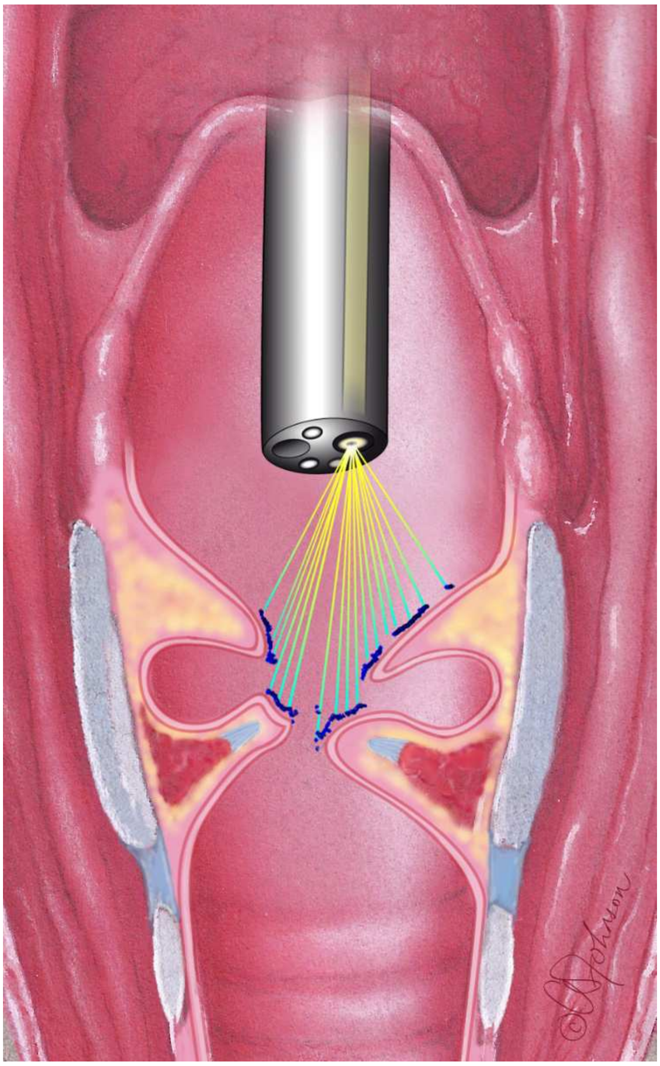


Figure 6: Drawing figuring the relationship between the scanning laser beam and the "profile" offered by the LR data interpretations

Discussion:

Our results show that use of the LR is technically feasible in a human larynx. A perfect correlation of VF height differences between left and right vocal folds and imposed VF motions was found. Qualitative analysis showed that a VF profile was obtainable in all of the push-pull sessions. The aim of this *proof-of-concept* was not to assess the accuracy of the LR but rather to assess its possible utility in the laryngology field in general and in UVFP management in particular.

Nevertheless, in the case of our experiment in the larynx, with a distance between the LR and the VF of approximately 2 cm, the accuracy is about 0.2 mm which is compatible with the foreseen clinical applications of LR. Indeed, none of our height differences were less than 0.9 mm.

At present, there is considerable interest concerning the topic of three–dimensional positioning of the vocal fold for which MRI and CT studies in patients have been performed as well as laryngoscopic high-speed camera imaging in animal models 15.MRI has a lower resolution and CT scanner necessitates radiation exposure and post-acquisition software based interpretation 16.17.18.19.20.Both these imaging techniques are costly and do not allow for the examination of patients under physiological conditions. The high-speed camera does not have the disadvantage of irradiation but requires two simultaneously introduced endoscopes and 2 high-speed cameras. Furthermore, it also requires post-recording analysis, so it does not yield real-time readings. Compared to prior articles using the same technology, apart from application using a flexible endoscope, it is the first experiment with a continuous line and it enables a fine analysis of the vocal fold with the generated profile. 11.12.13.14.

Profiling of the explored surfaces can be realized using multiplication of the acquired measures. As shown in Figure 6, profiling of VF surface could possibly reflect and quantify the degree of TA atrophy in cases of UVFP. Some of these profiles were discontinuous and tedious to read. Technical refinements and adaptations that are specific to the larynx anatomy should be done in order to offer clinically useful profiles.

Despite these encouraging results many challenges still have to be overcome before the LR use in patients. The endoscope that was used is a gastroscope (11mm of diameter) which is too large for intranasal use. A device with a maximum diameter of 1.9 mm should be developed to allow its use through the operative channel of ENT flexible video-endoscope. Specific software for vocal fold analysis and interpretation should be developed to improve the profile representations and height measurement in a more reliable way.

In our study models, the vocal processes were always easily visualized. However, in clinical UVFP situations, the vocal process on the paralyzed side, can be difficult to visualize due to the anterior tilt of the arytenoid cartilage. Hypothetically, this hurdle could be overcome by the development of software that would (a) measure various VF free edge points that can be effectively visualized, (b) draw a line through these points, (c) calculate the VF free edge slope, and eventually (d) extrapolate the invisible VF depth based on the contralateral VF length.

Conclusion

Innovative technology is not so frequent in the field of laryngology. This *proof of concept* could signify a new breakthrough. Study's results allow authors to achieve their goal of demonstrating potential utility of the device. With the LR technology, a tool is acquired that allows a reliable, real-time, three-dimensional position determination of the vocal folds, free of harm for the patient and instantaneously performed within an office setting. Therefore, it contributes to pre-operative planning of laryngeal surgery as well as the post-operative follow-up. The LR technology deserves further clinical testing, even though several technical improvements are still required.

References

1.Daniero JJ, Garrett CG, Francis DO. Framework Surgery for Treatment of Unilateral Vocal Fold Paralysis. Curr Otorhinolaryngol Rep. 2014 Ju1;2(2):119-130. PubMed PMID: 24883239; PubMed Central PMCID: PMC4036824.

2.Hess MM, Fleischer S. Laryngeal framework surgery: current strategies. CurrOpin Otolaryngol Head Neck Surg. 2016 Dec;24(6):505-509. PubMed PMID: 27585082.

3. Li AJ, Johns MM, Jackson-Menaldi C, Dailey S, Heman-Ackah Y, Merati A, Rubin AD. Glottic closure patterns: type I thyroplasty versus type I thyroplasty with arytenoid adduction. J Voice. 2011 May;25(3):259-64. doi:10.1016/j.jvoice.2009.11.001. PubMed PMID: 20335002.

4. Mortensen M, Carroll L, Woo P. Arytenoid adduction with medialization laryngoplasty versus injection or medialization laryngoplasty: the role of the arytenoidopexy. Laryngoscope. 2009 Apr;119(4):827-31. doi: 10.1002/lary.20171.PubMed PMID: 19263407.

5.Woo P. Arytenoid adduction and medialization laryngoplasty. Otolaryngol Clin North Am. 2000 Aug;33(4):817-40. PubMed PMID: 10918663.

6.Benninger MS, Manzoor N, Ruda JM. Short- and long-term outcomes after silastic medicalization laryngoplasty: are arytenoid procedures needed? J Voice. 2015 Mar;29(2):236-40. doi: 10.1016/j.jvoice.2014.07.008. PubMed PMID: 25510165.

7.Siu J, Tam S, Fung K. A comparison of outcomes in interventions for unilateral vocal fold paralysis: A systematic review. Laryngoscope. 2016 Jul;126(7):1616-24.doi:10.1002/lary.25739. Review. PubMed PMID: 26485674.

8. Chester MW, Stewart MG. Arytenoid adduction combined with medicalization thyroplasty: an evidence-based review. Otolaryngol Head Neck Surg. 2003 Oct;129(4):305-10. Review. PubMed PMID: 14574281.

9. Mertens, B., & Delchambre, A. (2016). 3D reconstruction: Why should the accuracy always be presented in the pixel unit? *Image and Vision Computing*, *48*, 57-60.

10. Geng, J., 2011. Structured-light 3d surface imaging: A tutorial*. Advances in Optics and Photonics* 3 (2), 128-160.11.

11. Herzon GD, Zealear DL. New laser ruler instrument for making measurements through an endoscope. Otolaryngol Head Neck Surg. 1997 Jun;116(6 Pt 1):689-92.PubMed PMID: 9215386.

12.Kuo CF, Wang HW, Hsiao SW et al. (2014) Development of laryngeal video stroboscope with laser marking module for dynamic glottis measurement. Comput Med Imaging Graph 38:34-41

13.Schade G, Hess M, Rassow B. [Possibility for endolaryngeal morphometric measurements with a new laser light method]. HNO. 2002 Aug;50(8):753-5. German.

14.Neitsch M, Horn IS, Hofer M, Dietz A, Fischer M. Integrated Multipoint-Laser Endoscopic Airway Measurements by Transoral Approach. Biomed Res Int. 2016;2016:6838697. doi: 10.1155/2016/6838697. Epub 2016 Feb 15.

15. Vahabzadeh-Hagh AM, Zhang Z, Chhetri DK. Quantitative Evaluation of the In Vivo Vocal Fold Medial Surface Shape. J Voice. 2017 Jan 12. Pii S0892-1997(16)30320-4. doi: 10.1016/j.jvoice.2016.12.004. [Epub ahead of print. PubMed PMID: 28089390.

16. Vachha BA, Ginat DT, Mallur P, Cunnane M, Moonis G. "Finding a Voice": ImagingFeatures after Phonosurgical Procedures for Vocal Fold Paralysis. AJNR Am J Neuroradiol. 2016 Sep;37(9):1574-80. doi: 10.3174/ajnr.A4781. Review.

17. Burdumy M, Traser L, Burk F, Richter B, Echternach M, Korvink JG, Hennig J, Zaitsev M. One-second MRI of a three-dimensional vocal tract to measure dynamic articulator modifications. J Magn Reson Imaging. 2016 Dec 9. doi:10.1002/jmri.25561. [Epub ahead of print] PubMed PMID: 27943448

18. Vorik A, Unteregger F, Zwicky S, Schiwowa J, Potthast S, Storck C. Three-dimensional Imaging of High-resolution Computer Tomography of Singers'Larynges-A Pilot Study. J Voice. 2016 Jul 11. pii: S0892-1997(16)30044-3. doi:10.1016/j.jvoice.2016.03.011. [Epub ahead of print] PubMed PMID: 27427164.

19. Storck C, Juergens P, Fischer C, Wolfensberger M, Honegger F, Sorantin E,Friedrich G, Gugatschka M. Biomechanics of the cricoarytenoid joint:three-dimensional imaging and vector analysis. J Voice. 2011 Jul;25(4):406-10.doi: 10.1016/j.jvoice.2010.03.005. PubMed PMID: 20579841.

20. Hiramatsu H, Tokashiki R, Kitamura M, Motohashi R, Tsukahara K, Suzuki M. New approach to diagnose arytenoid dislocation and subluxation using three-dimensional computed tomography. Eur Arch Otorhinolaryngol. 2010 Dec;267(12):1893-903. doi: 10.1007/s00405-010-1300-5. PubMed PMID: 20549225.

Acknowledgments

Authors are thankful to C. Behets-Wydemans, B. Caelen and M. van de Woestijne from the department of Anatomy and Morphology of the University of Louvain and F. van Immerseel, J Aarents and J. den Boeft from the department of Anatomy and Embryology at the Leiden University Medical Center for their assistance.

CHAPTER 6:

« Shape of thyroid cartilage influences outcome of Montgomery medialization thyroplasty. a gender issue.”

Abstract

Objective:

This study aimed to determine whether the shape of the thyroid cartilage and/or the gender influence voice outcomes after Montgomery thyroplasty (MTIS).

Methods:

A retrospective cohort study was performed on 20 consecutive patients that underwent MTIS. Voice outcome variables were the relative decrease in VHI (%) and the absolute increase in MPT (sec.). Material variables were the angle between the thyroid cartilage laminae (α-angle), the size of the prosthesis and a combination of both (the α-ratio). Continuous variables were analyzed using medians, and were compared between groups using the Mann-Whitney test. Factors associated with the outcome variables were assesses by multivariable linear regression. A Pearson coefficient was calculated between material variables.

Results:

The absolute increase in MPT between the pre and post-op period was significantly different between males and females, with a median absolute increase of 11.0 se. for males and of 1.3 sec. for females ($p<0.001$). A strong inverse correlation between the α-ratio and the absolute increase in MPT is observed in all patients, with a Pearson's correlation coefficient $R=-0.769$ ($p<0.001$). No factors were significantly associated with the relative VHI decrease in univariable or multivariable analyses. A better Pearson coefficient between the α-angle and the prosthesis size was found for females (0.8 vs 0.71).

Conclusion:

The MTIS is a good thyroplasty modality for male patients but inadequate design of MTIS female implants leads to poor MPT outcomes. This represents a gender issue that needs to be further studied and eventually tackled.

Introduction

Unilateral vocal fold paralysis (UVFP) causes insufficient glottis closure resulting in hoarseness as well as swallowing problems. If spontaneous recovery or compensation does not occur, treatment may be sought.

Medialization thyroplasty represents a recognized efficient treatment. It is considered as a standard treatment when long lasting improvement is required (1, 2). Different types of techniques and materials have been proposed over the years. Amongst these, the technique and material named Montgomery Thyroplasty Implant System (MTIS) has gained interest for its facility of use and its short learning curve (3, 4).

The MTIS was designed to be a simplified implant technique. It provides a step-by-step surgical approach along with pre-molded soft silicone implants in six sizes; the range of sizes differing for male and female patients (5). Voice results reported in the literature using the MTIS are comparable to those achieved with other techniques, so it appears that MTIS simplification is justified (6, 7).

Opponents of the MTIS, argue that only 6 sizes of implants per gender could never be sufficient to match the variability in shape of individual larynges.

The primary aim of our research was to assess MTIS results retrospectively and investigate whether (a) the shape of the larynx represented by the angle between the two laminae of the thyroid cartilage (the α-angle), (b) the size of the Montgomery prosthesis or (c) a combination of both (the α-ratio) correlate with subjective and/or objective voice outcomes.

Shape of the larynx being a gender-related feature, the secondary aim of our research was to analyze MTIS voice outcome for gender differences.

Material and Methods

Study design, patient selection and intervention

The study protocol was approved by the Ethics Committee of Saint-Luc university hospital (number 2014/20MAI/256).

A retrospective study was performed on a cohort of 20 consecutive patients presenting a UVFP as defined by Rosen *et al.* (8) between May 2011 and November 2014. Each patient presented a UVFP with a large glottis gap at video-stroboscopic examination. No patient presented other features potentially affecting the quality of their voice except smoking habit before surgery. All patients were then treated with MTIS, with a minimum time period of 6 months between the initial diagnostic of UVFP and the surgery. Surgeries were performed according to the technique described by W. Montgomery and colleagues in 1993 (5). All MTIS were performed under light intravenous sedation and cutaneous local anesthesia with per-operative voice feedback as sole outcome control.

The routine clinical pathway of MTIS patients included a postoperative CT scan of the larynx without injection of contrast material performed one month after the surgery in order to assess implant positioning and stability. The prosthesis was considered well positioned if: a) 90% or more of the intra-laryngeal portion of the Montgomery prosthesis lay inside the inner perichondrium plane of the thyroid cartilage; b) the antero-posterior plane of the prosthesis did not differ of 10° or more with the orientation of the opposite vocal fold; and c) the implant was not located in the Morgani's ventricle or the subglottic area

Finally, patients who presented a major health-event, such as a procedure-related complications, a new oncologic development or a new pulmonary disease, between pre and post voice assessment were excluded from the analysis.

Outcome measures and material variables

Subjective and objective voice outcomes

Before surgery and one month after surgery patients were asked to fill in a Voice Handicap Index Questionnaire (VHI) and maximum phonation time was measured (MPT).

The VHI-30 questionnaire was used. This is a 30-item self-administered questionnaire that allows patients to describe their voice state as well as the effects of their voice on their lives (a higher score implying a higher voice disorder impact on the patient's life). A validated native language VHI-30 questionnaire was used and filled in by patients without any guidance (9, 10). We chose the relative decrease in VHI as outcome in order to underscore the self-perceived improvement regardless of the pre-op baseline.

The objective assessment of a patient voice improvement was evaluated by the absolute increase in MPT in seconds before and after the surgery. The MPT measurement was performed according to the European Laryngological Society guidelines, recording the longest attempt of three trials of /a/ phonations at comfortable pitch and loudness (11).

Material variables

Three material variables were defined: α-angle, the size of the prosthesis and α-ratio.

The α-angle is the angle between the laminae of the thyroid cartilage and represents the shape of the larynx. The α-angle was determined according to a CT-scan reading protocol which was applied to each post-operative CT-scan. As shown in Figure 1, after optimal positioning of slice location on sagittal reformat through the axial oblique long axis of the Montgomery prosthesis, the angle between the posterior borders and the anterior midline points of the thyroid is electronically calculated using the angle calculation option of the post-processing software.

For females the available sizes of prosthesis are 6,7,8,9,10,11; for males: 8,9,10,11,12,13. All female prosthesis have the same length but vary according to size in depth. The male prosthesis are 2mm longer and 2mm thicker than the female prosthesis but vary similarly in depth. The depth dimensions of the overlapping female and male sizes 8 to 11 are identical per gender.

The α-ratio is the α-angle (in degrees) divided by the size of the prosthesis (6-13) and represents the relationship, or congruence, between the shape of the larynx and the size of the prosthesis.

(Figure 1).

Statistical analyses

Continuous variables were analyzed using medians [P_{25}; P_{75}], and were compared between groups using the Mann-Whitney test. Variables that were assessed in simple linear regression were the gender and the material variables (the size of the implant, the α-angle, and the α-ratio).

Factors associated with the outcome variables in simple linear regression were assessed by multivariable linear regression. A stepwise model was used to determine the final multivariable model by keeping only the contributing variables. The variance inflation factor was also used to avoid multicolinearity. Eventually, a simple Pearson's correlation coefficient was calculated between material variables, and between these variables and the outcomes variables.

All analysis were performed using R software Version 3.2.1 (Free software Foundation Inc., Boston, Massachusetts, USA). A p-value < 0.05 was considered statistically significant.

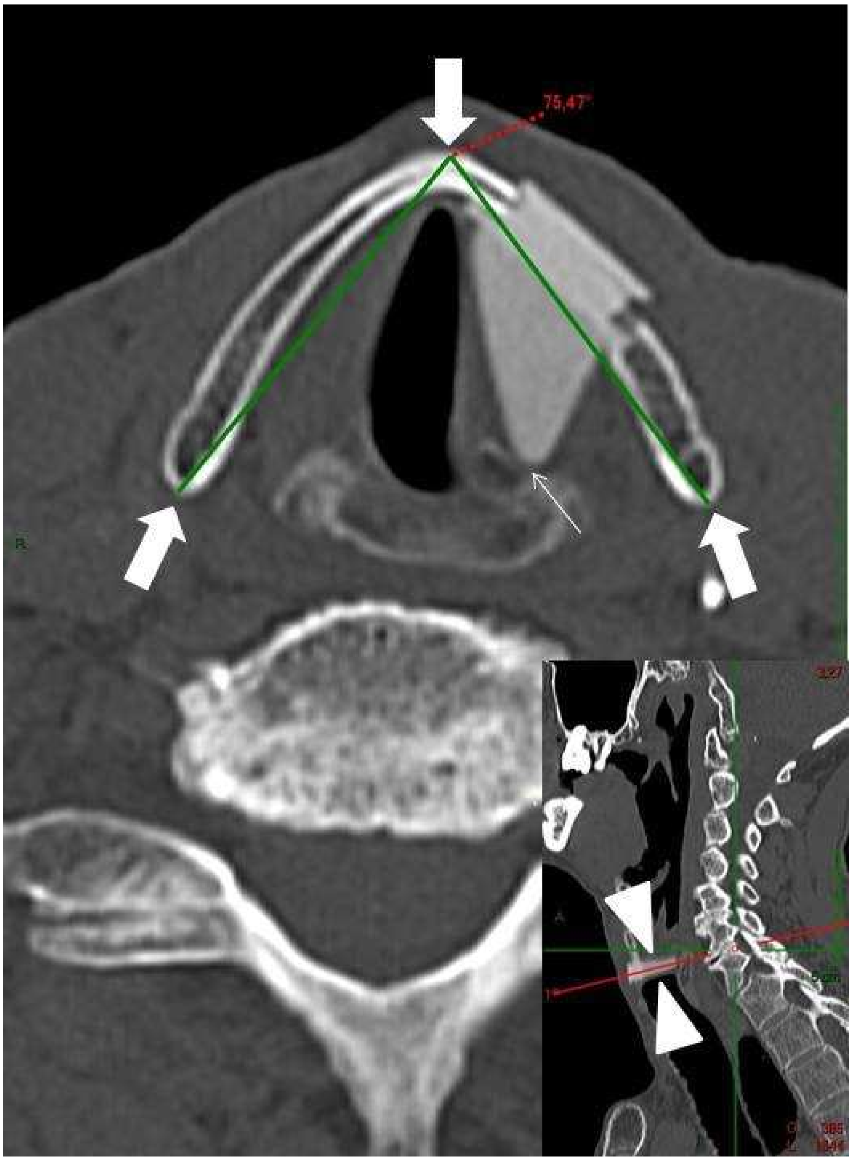


Figure 1: α-angle calculation. After optimal positioning of slice location on sagittal reformat through the axial oblique long axis of the prosthesis (arrowheads on right bottom insert), the angle between posterior borders and anterior midline points (arrows) of the thyroid cartilage is electronically calculated using the angle calculation option of the post-processing software. Observe close contact between prosthesis and the arytenoid cartilage (thin arrow)

Results

One male patient presented bone metastases and mandibular osteonecrosis within the timeframe between pre and post evaluation. This patient was excluded from the analyses. No complications, such as infection, bleeding, prosthetic extrusion or protrusion, were found. All in all, 19 patients were included in the analyses, 11 being females (57.9%, n=11/19). Etiology of UVFP was distributed as followed: lung neoplasm (6), post-thyroidectomy (5), post-mediastinoscopy (3), post-aortic surgery (2), post-skull base surgery (2) and idiopathic (1).

Table 1 shows results of the outcome and material variables and their differences between genders. At baseline, the median [P_{25}; P_{75}] VHI score and MPT were 52.0 [45.5; 69.0], and 5.0 [4.5; 6.0] seconds, respectively, with no significant differences between genders (Table 1). All three material variables were significantly different between genders, as demonstrated in Table 1.

Variables	Total (N=19) Median [P_{25}; P_{75}]	Males (n=8) Median [P_{25}; P_{75}]	Females (n=11) Median [P_{25}; P_{75}]	p-value
Baseline characteristics				
Age (years)	63.0 [52.5; 73.0]	72.0 [60.5; 75.3]	60.0 [45.5; 66.5]	0.173
Outcome measures				
VHI (/120)				
Before surgery	52.0 [45.5; 69.0]	49.5 [46.3; 70.8]	59.0 [45.0; 69.0]	0.836
After surgery	11.0 [7.5; 18.5]	11.0 [8.0; 13.8]	13.0 [6.5; 19.5]	0.868
Relative decrease (%)	76.6 [66.5; 88.4]	80.1 [72.2; 88.3]	73.9 [66.5; 89.3]	0.680
MPT (sec.)				
Before surgery	5.0 [4.2; 10.3]	5.0 [4.5; 6.0]	6.7 [4.2; 11.0]	0.508
After surgery	12.2 [7.7; 16.3]	19.5 [13.8; 22.0]	8.0 [6.9; 11.6]	0.005
Absolute increase (sec.)	3.2 [1.2; 9.5]	**11.0 [8.9; 17.0]**	**1.3 [-0.2; 2.9]**	**<0.001**
Material variables				
α-angle	68.0 [61.2; 77.2]	**62.5 [59.6; 66.8]**	**74.7 [67.2; 80.9]**	**0.021**
Size of the implant	9.0 [8.5; 10.0]	10.0 [9.0; 11.0]	9.0 [8.0; 9.0]	0.033
α-Ratio	8.2 [6.5; 8.7]	**6.2 [6.0; 6.9]**	**8.6 [8.4; 8.8]**	**<0.001**

VHI: Voice Handicap Index 30 score; MPT: maximum phonation time

Table 1: Characteristics of outcomes and material variables and differences between males and females (N=19)

The absolute increase in MPT between the pre and post-op period was significantly different between males and females, with a median [P_{25}; P_{75}] absolute increase of 11.0 sec. [8.9; 17.0] for males and of 1.3 sec. [-0.2; 2.9] for females (p<0.001) (Table 1). Finally, the relative VHI decrease between pre and post-operative measurements was not different between males and females (p=0.680), with a median [P_{25}; P_{75}] VHI relative decrease of 76.6 [66.5; 88.4] % for all patients (Table 1).

Factors associated with the absolute increase in MPT, in simple linear regression were the gender, the size of implant and the α-ratio (Table 2). In multivariable linear regression, the gender was significantly associated with this objective outcome, the absolute increase in MPT being higher in males than in females (β [95%CI] = 9.13 [5.00; 13.27], p<0.001). Size of the implant remained in the model although it was not a significant factor (p=0.104).

Variable	**Univariable analysis**		**Multivariable analysis**	
	β [95%CI]	**p-value**	**β [95%CI]**	**p-value**
Absolute increase in MPT (sec)				
Gender: males *vs* females	**10.90 [7.20; 14.60]**	**<0.001**	**9.13 [5.00; 13.27]**	**<0.001**
Alpha angle	-0.22 [-0.53; 0.10]	0.163	*Rejected by stepwise model*	
Size of the implant	3.15 [1.13; 5.16]	0.004	1.30 [-0.30; 2.89]	0.104
α-Ratio	-3.93 [-5.59; -2.26]	0.001	*Rejected by stepwise model*	
Relative VHI decrease (%)				
Gender: males *vs* females	6.66 [-16.13; 29.46]	0.546	*Rejected by stepwise model*	
α-Alpha	0.39 [-0.75; 1.52]	0.479	1.05 [-0.34; 2.44]	0.128
Size of the implant	6.70 [-1.50; 14.90]	0.103	*Rejected by stepwise model*	
α-Ratio	-3.23 [-12.07; 5.61]	0.451	-9.33 [-19.17; 2.51]	0.123

95%CI: 95% confidence interval; MPT: maximum phonation time in seconds; VHI: voice handicap index

Table 2: Variables associated with the absolute increase in MPT and the relative decrease in VHI between pre-op and post-op periods in linear regression (N=19)

In the Pearson's correlation a strong inverse correlation between the α-ratio and the absolute increase in MPT was observed with a Pearson's correlation coefficient of R=-0.769 (p<0.001) (figure 2). When splitting by gender, a significant correlation between the two variables was not observed anymore, with an R=-0.309 for females (p=0.355) and an R=-0.027 for males (0.949).

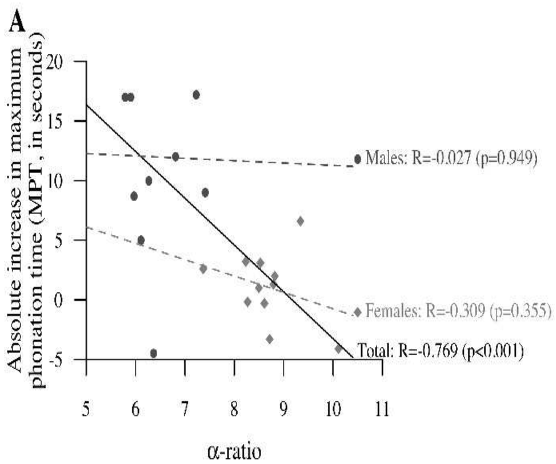


Figure 2: Graph showing correlation line and R^2 between the α-ratio and the absolute increase of MPT for the total cohort (continuous line) and by gender (dotted lines)

This confounding factor -the gender- explains why the α-ratio is highly associated with MPT increase in the univariable analysis (p=0.001) and is not anymore in the multivariable analysis when adjusting for gender through the stepwise model.

No factors were significantly associated with the relative VHI decrease in univariable or multivariable analyses.

Table 3 shows the correlation observed between material variables by gender, as measured by Pearson's correlation coefficient. A strong correlation is found between the size of the prosthesis that has been used and the α-angle. The Pearson's correlation coefficient appears to be higher for female than for male individuals.

	Size of the prosthesis	α-Ratio
Males		
Alpha angle	**0.71**	0.13
Size of the prosthesis		-0.61
Females		
Alpha angle	**0.80**	0.48
Size of the prosthesis		-0.15

Table 3: Pearson coefficient between material variables by gender

Discussion

Although the MTIS has gained interest for its facility of use and its short learning curve, it has been argued that the range of pre-molded silicone implants must be too small to match the variability in shape of individual larynges. Self-carved silicone bloc prostheses would therefore be more efficient. However, comparison between techniques of medialization thyroplasty is tedious due to the large variety of voice outcome indicators that have been used to assess UVFP surgical treatments in the past. In a recent systematic review comparing outcomes of interventions for UVFP, MPT and VHI appeared to be the most utilized and validated voice outcome measures (12). MPT is a common, easy to perform aerodynamic test that has been shown to be particularly useful in evaluating voice outcome after medialization thyroplasty (13). The VHI-30 developed by Jacobson in 1997 is of particular interest in cases of UVFP (14). Indeed, using the VHI, Benninger et al. showed that patients with vocal fold paralysis had the highest level of pretreatment disability among voice patients (9). In addition, Maertens et al. showed that gender and profession did not have a significant influence on the total VHI scores (15).

Three studies looking at the results of thyroplasties performed with self-carved silicone bloc, (i) as a sole procedure; (ii) using MPT and VHI as voice outcome variables and (iii) assessed within the same timeframe as in our study; are available in the recent English written literature (16-18).

Compared to the total sample absolute increase in MPT described in these three studies (see below), our male patients performed very well (11sec.) while our female patients performed poorly (1.3 sec.) In one of these studies the results were stratified per gender and showed slightly better absolute increase in MPT for females than for males (17). It should also be noted that, the higher the number of patients included in these studies the better the absolute increase in MPT is, raising the question of a possible longer learning curve of the self-carved silicone bloc technique compared to the MTIS (2.7 sec. for n=10 (16), 8.7 sec. for n=32 (17) and 14.2 sec. for n=78 (18)).

Gender differences were also not found in voice outcome results after injection laryngoplasty (19).

In their inaugural initial paper on MTIS outcomes, McLean-Muse et al. already noted a gender-related discrepancy, reporting an absolute MPT increase of 11 sec. for males and 5.6 sec. for females (6). Unfortunately, later reports on MTIS outcomes by Laccourreye's team did not stratify their results per gender (7, 20).

On the other hand, the relative decrease in VHI in our study was large and similar for both genders. This is in accordance with the findings of many publications that showed there was no correlation between VHI and voice laboratory measurements; with the notable exception of the Average Airflow rate in connected speech for UVFP (21-23). Two hypotheses can be postulated to explain this discrepancy between objective and subjective voice results after MTIS. One is that a MTIS is a “forgiving surgery”; a slight improvement of MPT causing an important degree of satisfaction, the second, is that patients simply may not value an increase in MPT as much as surgeons do.

Likewise, two hypotheses can be made to explain the post-operative absolute increase in MPT difference between genders: (a) the per-operative choice of implant size was for some reason systematically less appropriate for females than for males; b) there is a certain inadequacy between female larynx anatomy and the available choice of prosthesis size which is not present in males.

The first hypothesis is ruled out by a better Pearson coefficient between the α-angle and the size of the implant for the female population of the cohort (0.8 versus 0.71) (Table 3). In other words, the chosen prosthesis was comparatively slightly bigger for female than for males. Accordingly, the female “under-treatment” is not related to surgeon’s decisions.

The second hypothesis is supported by the inverse linear correlation between MPT improvement and α-ratio. All female patients of the cohort have a high α-ratio associated with disappointing voice outcomes in terms of MPT. In fact, females are doubly penalized when it comes to the α-ratio calculation. They present not only a higher numerator (α-angle) but also a lower denominator (size of implant) than males.

The fact that α-ratio - representing the relationship between larynx shape and prosthesis size - is deemed the underlying causal factor for poor MPT in this hypothesis but was not identified as a significant factor in the multivariable analysis is explained by the strong overlap between gender and larynx shape (alpha angle) in our cohort. Until puberty the laryngeal dimensions do not differ between genders but during puberty the male larynx follows a different developmental path under the influence of testosterone. Two of these anatomical changes are of particular interest: (a) the male larynx outgrows the female one in the antero-posterior dimension (b) the α-angle between the thyroid laminae decreases more in males than in females. Our study results, showing significant larger α-angles values in females, are in line with literature data (24, 25). As a matter of fact, all dimensions of the laryngeal framework are greater in males except for the thyroid angle (α) which is higher in females. This difference of angle between laminae can be measured in different ways. If the anterior commissure represents always the summit of the triangle, its sides can be determined whether using (a) the oblique line mark or (b) the posterior border of the laminae mark. The “oblique line” technique gives bigger figures (mean of 77° for males; mean of 91° for females) (26) and is mostly used in post-mortem anatomical studies (26-29).

Because the determination on the –sometime absent- oblique line can be tedious to identify on CT scan images (see the example of figure 1), we opted for the second measuring technique.

Ideally, this anatomical discrepancy between male and female larynxes should be compensated for by adjusting the implant design to these gender differences. However, female and male Montgomery implants hardly differ. The length of the intra-laryngeal portion of the implant is 2 mm longer in males (14 mm for males versus 12 mm for females), but the depth of female and male prosthesis are the same from size 8 (8 mm) to size 11 (11 mm). Moreover, the angle between the middle plate, embedding the prosthesis within the cartilage, and its free edge are similar for both genders.

If the larynx is seen as an isosceles triangle, the classical female larynx presents an open (obtuse) anterior angle and a shorter height. The obtuse anterior angle means that there is more distance to be covered by an implant between the thyroid lamina and the midline (Figure 3). Unfortunately, the MTIS implants set does not provide deeper implants for female. A too long implant could also possibly create a conflict with the homolateral arytenoid cartilage (Figure 1 thin arrow).

Intuitively it seems that female implants should be shorter and deeper to the midline. However, a definite recommendation for an ideal shape for female implants goes beyond our study's aim. Likewise, some readers could be tempted to infer a pre-operative planning strategy from our results. Indeed, by performing a rule of three with the calculated α determined on a pre-operative CT scan of the larynx, and seeking for a value of α-ratio of 8 and below, one could try to determine the smallest implant that would be needed to appropriately impact the MPT. It is adamant to remind these readers that the determination of a, CT based, pre-operative planning was not the aim of our study and would require further prospective studies in order to be validated.Finally, two weaknesses of the present study must be mentioned. The small size of the cohort and the use of only two outcome measurements, limit the confidence in the conclusions made from this study and call for further studies on the same topic.

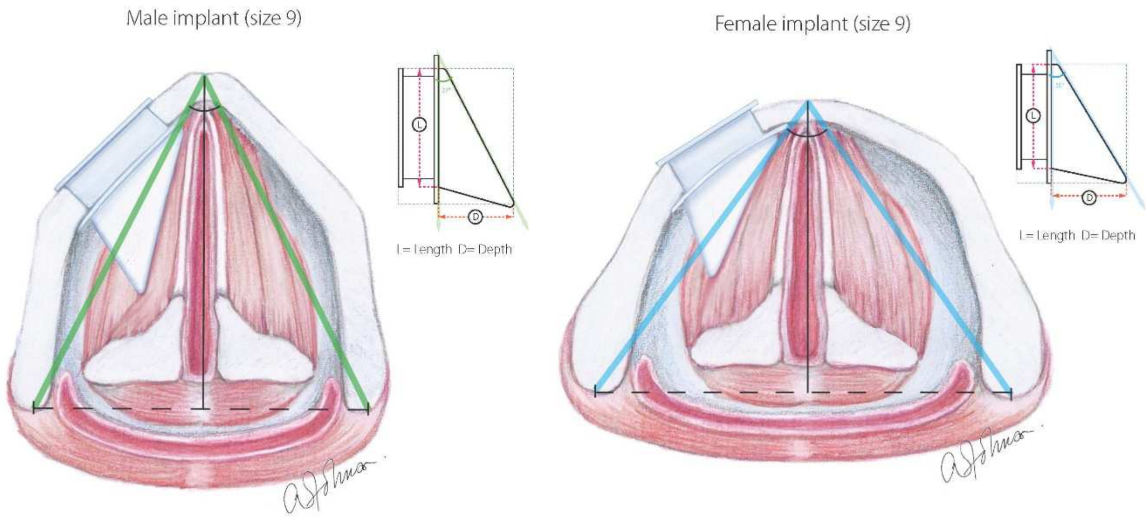


Figure 3: Male anatomy of the larynx, horizontal cut through the glottis plane (above), and Female larynx anatomy, horizontal cut through the glottis plane (below), both with a n°9 prosthesis inserted. Technical characteristics such as Length (L = 12mm for female, L=14mm for male), Depth (D= 9mm for both genders) and angle between middle plate and free edge of the prosthesis (27° for male and 30° for female) between the middle plate and the free edge are indicated aside for each prosthesis. Note the obtuse anterior angle and the shorter height of the female larynx in comparison with the male larynx, and the lower adductive potential of the female prosthesis.

Conclusion

This study is the first publication demonstrating a relationship between the shape of the larynx and voice outcome after MTIS. Excellent results were found for male patients. These results are comparable with those obtained by experienced surgeons carving silicone blocs. This supports the idea that 6 sizes of implants can match the results – whether objective or subjective- of custom-made, self-carved silicone implants.

On the other hand, poor voice outcome results were found for female patients in terms of absolute increase in MPT.

The inverse linear correlation between the α-ratio and the absolute increase in MPT supports the hypothesis of a female implant design that does not compensate gender-related anatomical differences.

Our findings show that the MTIS is a good thyroplasty modality for male patients but inadequate design of MTIS female implants leads to poor MPT outcomes. This represents a gender issue that needs to be further studied and eventually tackled.

References

1. Morgan JE, Zraick RI, Griffin AW, Bowen TL, Johnson FL. Injection versus medialization laryngoplasty for the treatment of unilateral vocal fold paralysis.Laryngoscope. 2007 Nov;117(11):2068-74.

2. Misono S, Merati AL. Evidence-based practice: evaluation and management of unilateral vocal fold paralysis. Otolaryngol Clin North Am. 2012 Oct;45(5):1083-108.

3. Young VN, Zullo TG, Rosen CA. Analysis of laryngeal framework surgery: 10-year follow-up to a national survey. Laryngoscope. 2010 Aug;120(8):1602-8.

4. Desuter G, Henrard S, Boucquey D, Van Boven M, Gardiner Q, Remacle M. Learning curve of medialization thyroplasty using a Montgomery™ implant. Eur Arch Otorhinolaryngol. 2015 Feb;272(2):385-90.

5. Montgomery WW, Blaugrund SM, Varvares MA. Thyroplasty: a new approach. Ann Otol Rhinol Laryngol. 1993 Aug;102(8 Pt 1):571-9.

6. McLean-Muse A, Montgomery WW, Hillman RE, Varvares M, Bunting G, Doyle P, Eng J. Montgomery Thyroplasty Implant for vocal fold immobility: phonatory outcomes. Ann Otol Rhinol Laryngol. 2000 Apr;109(4):393-400.

7. Nouwen J, Hans S, De Mones E, Brasnu D, Crevier-Buchman L, Laccourreye O. Thyroplasty type I without arytenoid adduction in patients with unilateral laryngeal nerve paralysis: the montgomery implant versus the Gore-Tex implant. Acta Otolaryngol. 2004 Aug;124(6):732-8.

8. Rosen CA, Mau T, Remacle M, Hess M, Eckel HE, Young VN, Hantzakos A, Yung KC, Dikkers FG. Nomenclature proposal to describe vocal fold motion impairment. Eur Arch Otorhinolaryngol. 2015 Jun 3. [Epub ahead of print]

9. Benninger MS, Ahuja AS, Gardner G, Grywalski C. Assessing outcomes for dysphonic patients. J Voice. 1998 Dec;12(4):540-50.

10. Verdonck-de Leeuw IM, Kuik DJ, De Bodt M, Guimaraes I, Holmberg EB, Nawka T, Rosen CA, Schindler A, Whurr R, Woisard V. Validation of the voice handicap index by assessing equivalence of European translations. Folia Phoniatr Logop. 2008;60(4):173-8.

11. Dejonckere PH, Bradley P, Clemente P, Cornut G, Crevier-Buchman L, Friedrich G, Van De Heyning P, Remacle M, Woisard V; Committee on Phoniatrics of the European Laryngological Society (ELS). A basic protocol for functional assessment of voice pathology, especially for investigating the efficacy of (phonosurgical) treatments and evaluating new assessment techniques. Guideline elaborated by the Committee on Phoniatrics of the European Laryngological Society (ELS). Eur ArchOtorhinolaryngol. 2001 Feb;258(2):77-82.

12. Siu J, Tam S, Fung K. A comparison of outcomes in interventions for unilateral vocal fold paralysis: A systematic review. Laryngoscope. 2015 Oct 20. doi:10.1002/lary.25739. [Epub ahead of print] Review.

13. Lundy DS, Casiano RR, Xue JW. Can maximum phonation time predict voice outcome after thyroplasty type I? Laryngoscope. 2004 Aug;114(8):1447-54.

14. Jacobsen, Johnson, Grywalsky et al Am J Speech and Lang Pathol 1997 ; Criteria for determining disability in speech and langage disorders. Agency for healthcare research and Quality. Evidence report/technology assessment . January 2002, Number 52

15. Maertens K, de Jong FI. The voice handicap index as a tool for assessment of the biopsychosocial impact of voice problems. B-ENT. 2007;3(2):61-6. Erratum in: B-ENT. 2007;3(3):7 p preceding 113.

16. van Ardenne N, Vanderwegen J, Van Nuffelen G, De Bodt M, Van de Heyning P. Medialization thyroplasty: vocal outcome of silicone and titanium implant. Eur Arch Otorhinolaryngol. 2011 Jan;268(1):101-7.

17. Uloza V, Pribuisiene R, Saferis V. Multidimensional assessment of functional outcomes of medialization thyroplasty. Eur Arch Otorhinolaryngol. 2005 Aug;262(8):616-21.

18. Benninger MS, Crumley RL, Ford CN, Gould WJ, Hanson DG, Ossoff RH, Sataloff RT. Evaluation and treatment of the unilateral paralyzed vocal fold. Otolaryngol Head Neck Surg. 1994 Oct;111(4):497-508.

19 Sardesai MG, Merati AL, Hu A, Birkent H. Impact of patient-related factors on the outcomes of office-based injection laryngoplasty. Laryngoscope. 2015 Nov 24. doi: 10.1002/lary.25764. [Epub ahead of print] PubMed PMID: 26597519.

20. Laccourreye O, El Sharkawy L, Holsinger FC, Hans S, Ménard M, Brasnu D. Thyroplasty type I with Montgomery implant among native French language speakers with unilateral laryngeal nerve paralysis. Laryngoscope. 2005 Aug;115(8):1411-7.

21. Hsiung MW, Pai L, Wang HW. Correlation between voice handicap index and voice laboratory measurements in dysphonic patients. Eur Arch Otorhinolaryngol. 2002Feb;259(2):97-9.

22. Woisard V, Bodin S, Yardeni E, Puech M. The voice handicap index: correlation between subjective patient response and quantitative assessment of voice. J Voice. 2007 Sep;21(5):623-31.

23.Gillespie AI, Gooding W, Rosen C, Gartner-Schmidt J. Correlation of VHI-10 to voice laboratory measurements across five common voice disorders. J Voice. 2014 Jul;28(4):440-8.

24. Simpson C. B, Sulica L. Principles of medicalization thyroplasty in Sulica L, Blitzer A, Vocal Fold Paralysis, Springer Berlin Heidelberg New York 2006 , Chap 9 pg139

25. Aronson A.E., Bless D. M. Normal voice development in Clinical voice disorders4th Edition Thieme New York Stuttgart Chap. 2 pg 15

CHAPTER 7:

Accuracy of thyroid cartilage fenestration during Montgomery medialization thyroplasty

ABSTRACT

Introduction

Accuracy of thyroid cartilage fenestration during Montgomery Thyroplasty (MTIS) is considered a key success factor.

The primary aim of the study was to retrospectively evaluate the accuracy of fenestration.

Furthermore, recent publications indicate a possible discrepancy in MTIS voice outcomes related to gender.

The secondary aim of the study was to investigate whether the fenestration accuracy could explain this discrepancy.

Material and Method

Study was performed by virtually drawing the fenestration on a 3D CT-scan as proposed by the MTIS's instructions for use (the "expected window" (EW)), and comparing it to the actually realized fenestration (the "realized window "(RW)). Four position variables, (a) surface overlap (%), (b) the distances between RW and EW centers (mm), (c) the angle between RW and EW and (d) the orientation of RW's center, were studied and compared to MPT (Sec) and VHI-30 scores outcomes.

A descriptive statistical analysis and comparison between males and females were performed using a Mann-Whitney U test. Linear regression and multivariate analysis were also performed.

Results

The median overlapping surface was 58.8 % [34.6; 75.4]. The median Radius was 3.2 mm [1.7; 4.1]. The median angle was 16° [6.8; 21.2].

Results show no significant differences of overlapping surface percentage, distance or angle by gender. Data show no correlation between voice outcome and percentage overlap, distance or angle. However, data show better outcomes when fenestration was located in the infero-anterior orientation. All patients of this orientation were males.

Conclusions

Data provided by this study advocate a maximal infero-anterior positioning of the window during MTIS. This position is more difficult to obtain in female patients.

INTRODUCTION

Unilateral vocal fold paralysis (UVFP) can lead to breathy voice, voice fatigue, dysphagia and phonatory dyspnea [1-3]. Medialization Thyroplasty represents a well-established treatment option for UVFP in cases for which a permanent treatment solution is sought. It consists of restoring a glottic closure by pushing the immobile vocal fold medially by means of a material introduced into the para-glottic muscular space through a thyroid cartilage fenestration.

The Montgomery Implant System Thyroplasty (MTIS) represents a type of medialization thyroplasty that consists of a step-by-step operative procedure using a pre-molded hard silicone implant, which is per-operatively selected from a selection of 6 sizes of implants per gender [4-8].

Essentially the cartilage window, which has a fixed size for males and for females, is placed at a fixed distance from the lower border of the thyroid cartilage and a fixed distance from the anterior midline

The MTIS is reputed to have short learning curve and long-lasting benefits in terms of Voice Handicap Index (VHI-30) [9, 10]. However, some concerns regarding the results of female implants in terms of Maximum Phonation Time (MPT) were recently brought up [11]. Factors that could be of influence in this discrepancy in results are (a) the shape of the thyroid cartilage, (b) the shape and dimensions of the implant itself (c) the site at which the implant is placed, that is, the location of the cartilage fenestration. This study will investigate the last.

The primary aim of the study was to retrospectively evaluate the accuracy of fenestration taking as standard-reference the positioning proposed by MTIS instructions for use.

The secondary aim of study was to investigate whether the factor of fenestration accuracy could explain discrepancy in results by gender.

MATERIAL AND METHOD

This study was approved by the Institution Review Board (IRB) under the reference 2017/12M/266.

Studied variables were twofold: a) position variables, and (b) outcomes variables.

The position variables were: (a) the percentage of overlapping surfaces (PO in %) between EW and RW; (b) the distance between the center of EW and RW or Radius (R) (in mm), (c) the angle between EW and RW (Angle), and (d) the position of RW center respective to the EW center (Quadrants (Q)) called supero-anterior Q, supero-posterior Q, infero-anterior Q and infero-posterior Q).

The outcome variables were: (a) absolute (in sec.) and relative (in %) pre-post-op differences in MPT and (b) absolute (n/120) and relative pre-post op differences (in %) in VHI-30. The post-operative MPT and VHI-30 assessments took place one-month post-op as a standard procedure.

Measurement of accuracy of fenestration

The post-operative CT scans of 28 patients (16 males and 12 females) of MTIS as sole treatment for UVFP, as defined by the European Laryngological Society guidelines, were collected [13].

A post-operative 3D CT model of the thyroid cartilage with the realized fenestration, also called the realized window (RW), was segmented and reconstructed using ITK-Snap; an interactive open-source software that allows 3D medical image navigation and delineation of anatomical structures [12]. RW was defined by manually identifying the four corners in the post-operative 3D CT model (Fig. 1A). In practice, RW of each patient was recorded by storing the coordinates of the four corners of the realized fenestration stated in the reference frame of the CT images (Fig. 1A). For planning purposes, in order to define the expected window (EW), a pre-operative 3D model of the intact thyroid cartilage (before MTIS) was simulated by virtually filling the cartilage defect (caused by the fenestration) in the post-operative 3D CT model (Fig 1B). EW was then defined according to the instruction for use provided in the MTIS commercial documentation [14]. The input of the step-by-step MTIS procedure consisted of three anatomical landmarks to be identified manually in the pre-operative 3D model of the thyroid cartilage (Fig. 1B). Then the step-by-step MTIS procedure was implemented using numerical computation software (MatLab®, The MathWorks, Natick, MA) to compute automatically the output of the planning process as the EW (Fig. 1C). In practice, EW of each patient was recorded by storing the coordinates of the four corners of the expected fenestration stated in the same reference frame than that of RW. As a result, both RW and EW of each patient can be compared quantitatively in terms of relative positioning and orientation for accuracy measurement purposes (Fig. 1D).

The sensitivity of the step-by-step MTIS planning procedure was analyzed by applying random noise to the input of the automatic algorithm. In practice, each of the three anatomical landmarks identified manually in the pre-operative 3D model of the thyroid cartilage was numerically perturbed by a random noise of maximum 2 millimeters. We arbitrarily chose the 2mm measure as error postulate. This measure corresponded to a surface covering approximately half of the length of the cartilage lower border between the inferior tuberculum and the respective extremities of the Thyroid ala. The impact of these random errors on the definition of the expected fenestration was small. Variations in the dimensions of the computed EW were estimated to be within a 15% interval centered on the nominal geometry of EW.

Statistical analysis:

A descriptive statistical analysis and comparison between males and females were performed using a Mann-Whitney U test for each studied variable except for the Quadrants variable.

Linear regression models were performed to assess the relationship between several variables on the outcome variables, i.e. the absolute increase of MPT and the relative decrease in VHI-30 before and after the surgery. All variables associated with a p-value <0.20 in univariate model were candidate for the multivariable model. The final multivariable model was chosen through stepwise selection using the Akaike's Information Criteria. In addition, multicolinearity was checked through variance inflation factor.

Line graphs were made comparing pre-op and post-op VHI-30 according to their position in terms of quadrants. Likewise, line graphs were made comparing pre-op and post-op MPT according to their position in terms of quadrants.

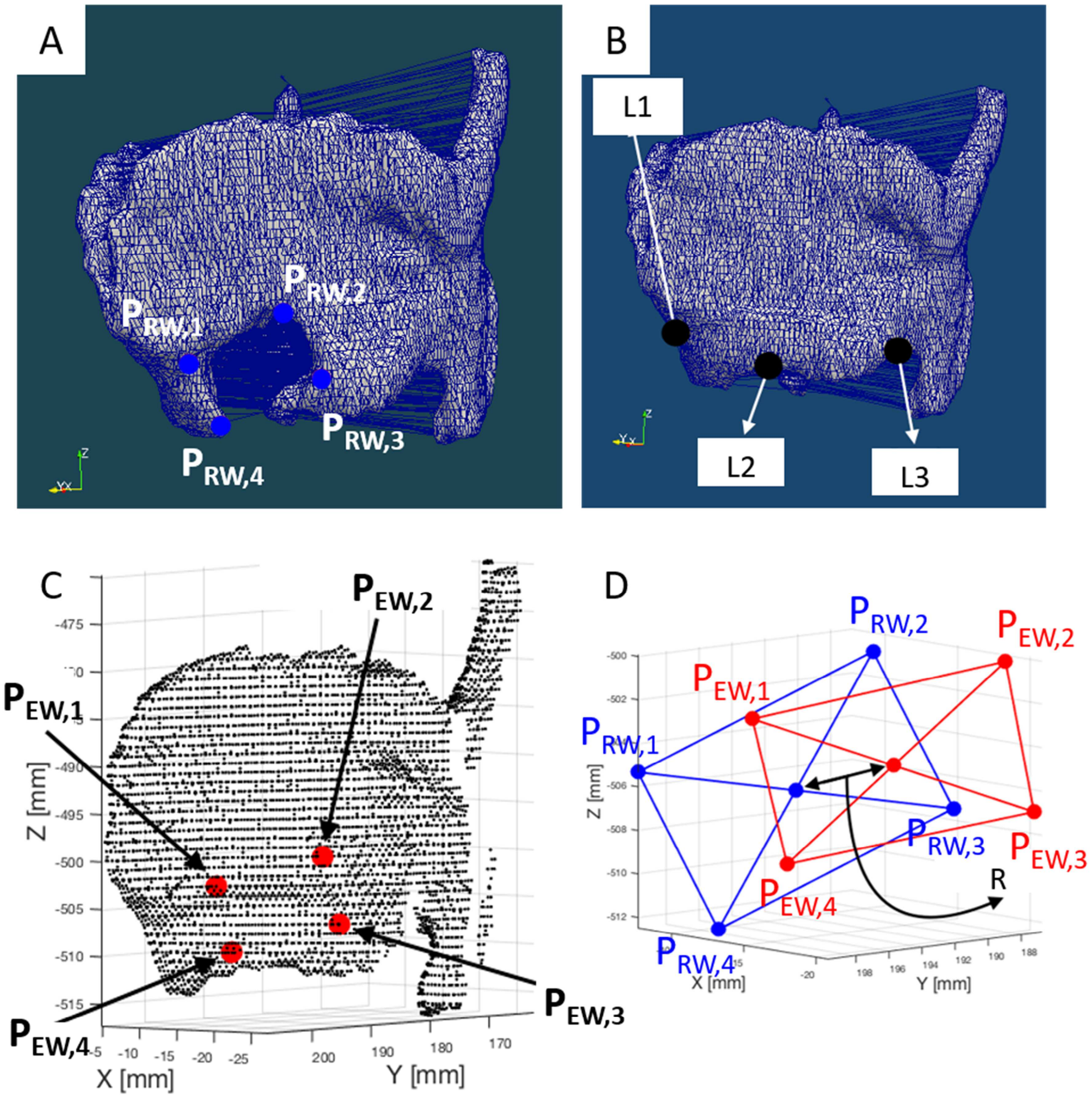


Figure 1: Illustrations showing (A) the thyroid cartilage with the realized fenestration - blue points ($P_{RW,1}$, $P_{RW,2}$, $P_{RW,3}$, $P_{RW,4}$) are the four corners of RW -, (B) the simulated intact thyroid cartilage and the three anatomical landmarks (L1, L2, L3) identified manually, (C) the simulated intact thyroid cartilage and the computed expected fenestration - red points ($P_{EW,1}$, $P_{EW,2}$, $P_{EW,3}$, $P_{EW,4}$) are the four corners of EW -, and (D) example of comparison between EW in red and RW in blue – R is the distance between EW and RW centers.

RESULTS

The increase of MPT and the decrease in VHI-30 were respectively of 6.6 sec (164% increase) and 45 points (77% decrease). There was a difference of results unfavorable to female for both outcome measures although only significant in terms of VHI-30 decrease.

Table 1 summarizes these descriptive statistics and comparison between males and females.

	Total (n=28) Median [P25 ; P75]	Males (n=16) Median [P25 ; P75]	Females (n=12) Median [P25 ; P75]	p-value
Overlapping surface (%)	58.8 [34.6 ; 75.4]	60.0 [54.8 ; 81.3]	56.2 [32.2 ; 67.7]	0.246
Radius (mm)	3.2 [1.8 ; 4.9]	3.0 [1.7 ; 4.1]	3.7 [2.0 ; 5.3]	0.330
Angle (°)	14.0 [6.8 ; 21.2]	16.0 [9.5 ; 21.2]	7.5 [4.0 ; 18.7]	0.099
VHI, absolute decrease (Pts)	45.0 [24.3 ; 66.8]	63.0 [33.3 ; 70.8]	35.0 [20.8 ; 44.0]	**0.027**
VHI, relative decrease (%)	77.0 [49.8 ; 88.8]	85.8 [72.0 ; 91.4]	56.8 [48.7 ; 75.8]	**0.029**
MPT, absolute increase (Sec)	6.6 [0.2 ; 12.4]	8.0 [0.8 ; 17.1]	3.1 [-0.3 ; 8.3]	0.255
MPT, relative increase (%)	164.2 [5.0 ; 344.6]	235.0 [39.2 ; 368.8]	80.0 [-1.6 ; 218.8]	0.378

Table 1: Table displays the descriptive statistics and the comparison between males and females, topographical and outcome variables.

Results showed a median PO of 59 % that is 60% for male and 56% for female, showing no significant difference of window overlapping surface between genders.

The Radius, standing for the distance between the EW center and the RW center, showed a median of 3.2mm, 3.0 mm for males and 3.7 mm for females showing no significant difference between genders.

The angle between EW and RW, showed a median of 14°, 16° for males and 7.5° for females, showing a clear difference between genders, however not significant.

As displayed in figure 2, there is no correlation between outcome (MPT and VHI-30) and three position variables: PO, Radius and Angle.

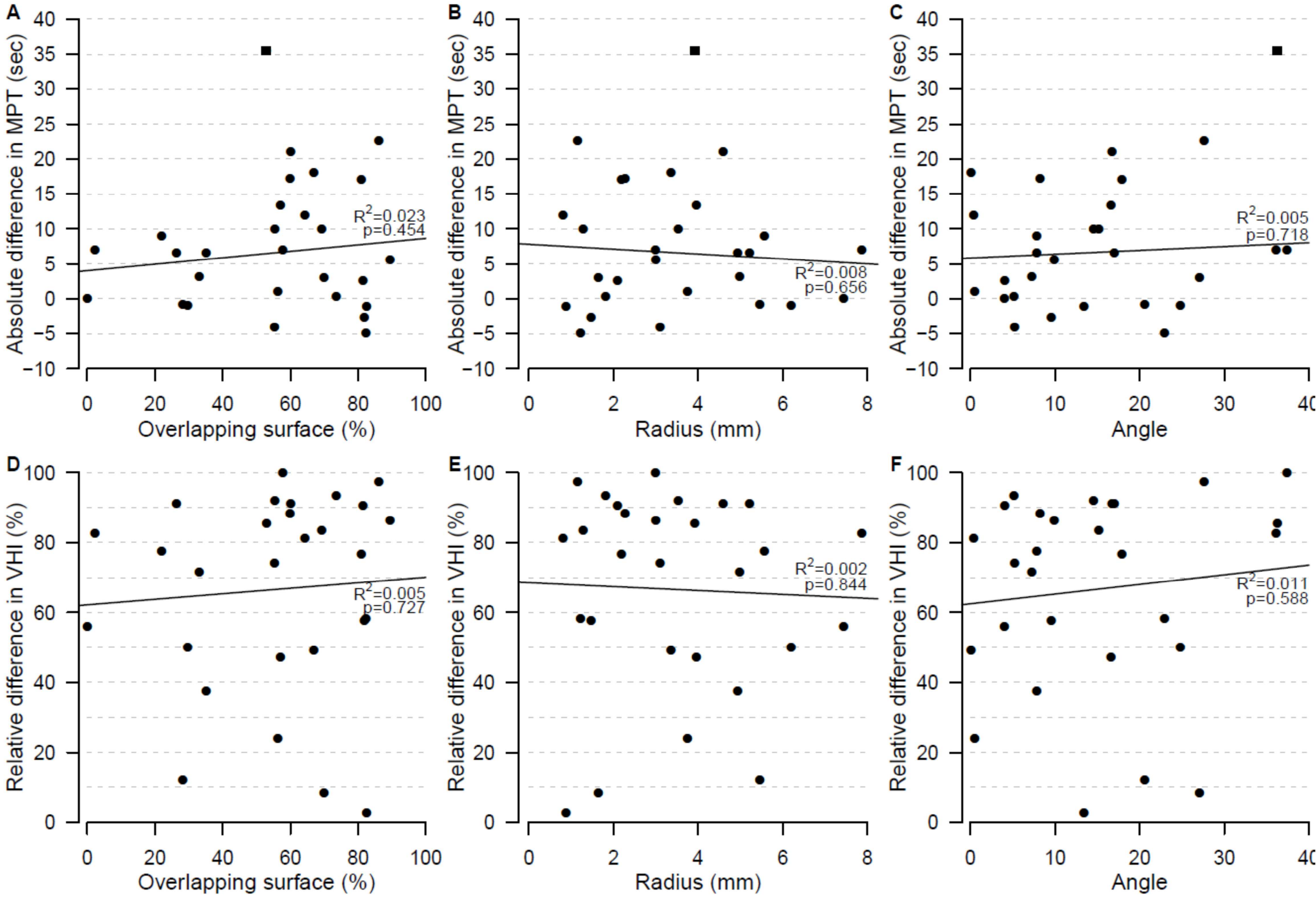


Figure 2: Scatter plots graphs showing (A) the association between MPT and PO, (B) the association between MPT and R, (C) the association between MPT and Angle, (D) the association between VHI-30 and PO, (E) the association between VHI-30 and R, (F) the association between VHI-30 and Angle.

Figure 3 displays a three-dimensional representation of RW centers with respect to their EW centers, showing X coordinates and Y coordinates along with the voice outcome groups they belong to. A color was attributed to their respective post-operative voice outcomes groups in terms of relative decrease of VHI-30 and absolute increase of MPT. For this specific figure, the choice for a relative change in VHI-30 rather than an absolute one, was made to minimize subjective self-perception differences that exists between individuals.

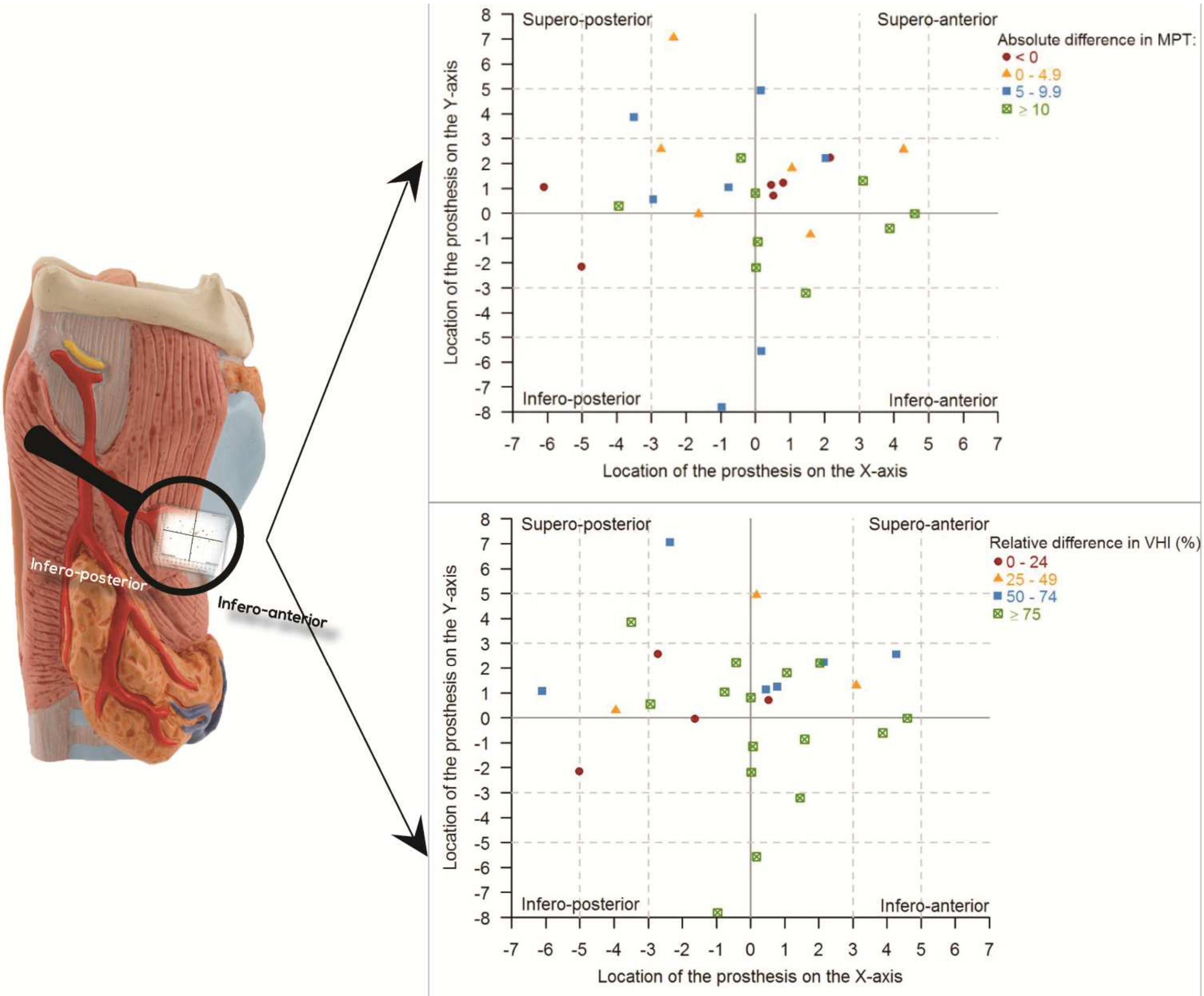


Figure 3: topographical plotting of RW centers with respect to their EW centers. A color was attributed to their respective post-operative outcomes in terms of absolute increase of MPT (above) and in terms of relative decrease of VHI-30 (below).

Figure 4 displays linear graphs showing pre and post-op results in terms of (A) absolute increase of MPT and (B) absolute decrease of VHI-30 by Quadrants. For this specific graphic representation of results the use of relative changes of VHI-30 was impossible. Results of Figure 4 are aligned with results of Figure 3.

Indeed, according to both Figure 3 and 4 the infero-anterior Q location of implants centers shows better voice outcomes. Accordingly, infero-anterior Q will, by postulate, be considered as the reference Q within the consecutive multi-variate analysis.

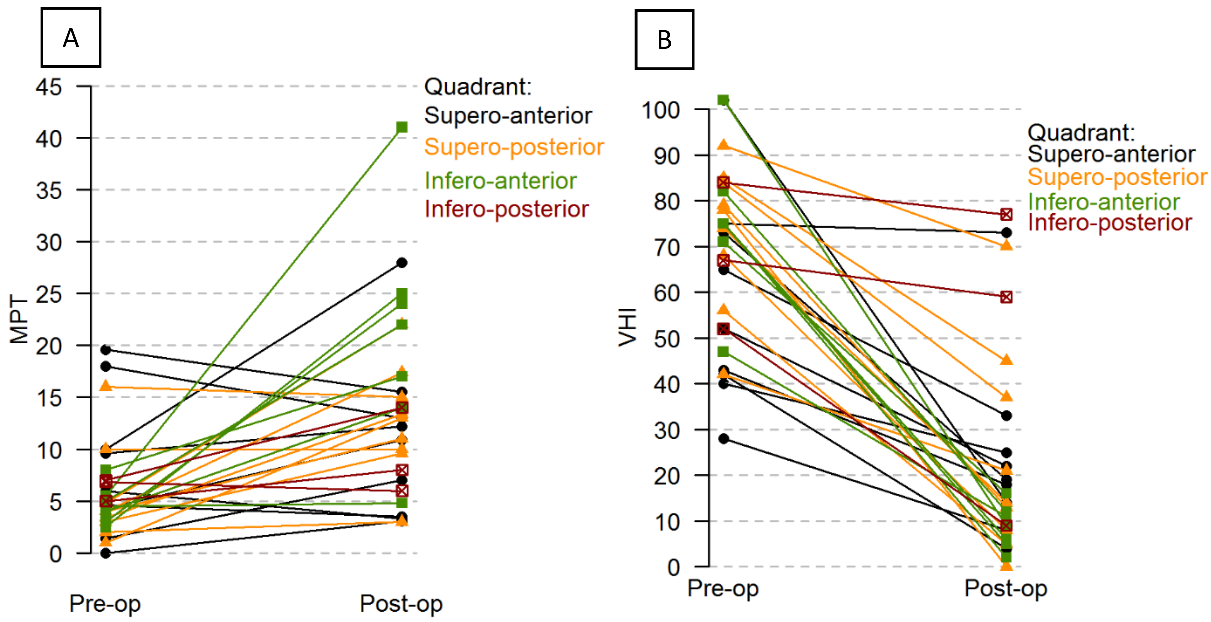


Figure 4: Linear graphs showing pre and post-op differences by Quadrant (Q), in terms of (A) absolute increase of MPT and (B) in terms of absolute decrease of VHI-30.

Table 2 displays the results of the univariate and multivariable regression analysis of variables associated with the absolute increase of MPT and with the relative decrease in VHI-30.

The multivariate analysis confirms a significant correlation between a positioning of the fenestration within the infero-anterior Q and voice results in terms of absolute increase of MPT and relative decrease of VHI-30.

A Variables associated with the absolute increase of MPT (Sec.)

	Univariate model		Multivariable model	
Variable	Regression coefficient (95%CI)	p-value	Regression coefficient (95%CI)	p-value
Male vs female	4.91 (-2.34 ; 12.16)	0.176		
Implant size	1.58 (-0.69 ; 3.84)	0.165		
Side of surgery: right vs left	0.53 (-7.52 ; 8.58)	0.893		

Overlapping surface (%)	0.04 (-0.11 ; 0.19)	0.578		
Radius (mm)	-0.22 (-2.14 ; 1.70)	0.816		
Angle (°)	0.24 (-0.09 ; 0.57)	0.153		
Quadrant				
Infero-anterior	1.00 (ref)		1.00 (ref)	
Infero-posterior	-13.42 (-24.84 ; -2.00)	0.023	-15.47 (-28.85 ; -2.10)	**0.025**
Supero-anterior	-13.92 (-22.26 ; -5.58)	0.002	-14.86 (-25.14 ; -4.58)	**0.007**
Supero-posterior	-9.12 (-17.46 ; -0.78)	0.033	-10.01 (-19.89 ; -0.12)	**0.047**

B Variables associated with the relative decrease of VHI-30 (%)

	Univariate model		Multivariable model	
Variable	Regression coefficient (95%CI)	p-value	Regression coefficient (95%CI)	p-value
Male vs female	13.66 (-8.40 ; 36.72)	0.214		
Implant size	5.78 (-0.84 ; 12.40)	0.084	4.25 (-2.15 ; 10.64)	0.182
Side of surgery: right vs left	3.35 (-20.71 ; 27.42)	0.776		
Overlapping surface (%)	0.08 (-0.38 ; 0.54)	0.727		
Radius (mm)	-0.56 (-6.37 ; 5.25)	0.844		
Angle (°)	0.28 (-0.76 ; 1.31)	0.588		
Quadrant				
Infero-anterior	0.00 (ref)		0.00 (ref)	
Infero-posterior	-53.29 (-88.86 ; -17.72)	0.005	-50.66 (-86.04 ; -15.28)	**0.007**
Supero-anterior	-29.01 (-54.99 ; -3.03)	0.030	-22.61 (-50.03 ; 4.82)	0.101
Supero-posterior	-18.63 (-44.60 ; 7.35)	0.152	-17.52 (-44.52 ; 9.48)	0.192

Table 2: Univariate and multivariate regression analysis of variables associated with (A) the absolute increase of MPT and (B) the relative decrease of VHI-30. All variables associated with a p-value of <0.2 in univariate model were candidate for the multivariable model.

DISCUSSION

Fenestration accuracy

The 2 mm EW determination error postulate corresponds to the measured lowest R variability of the surgeon (1.8 mm). This validates, post-hoc, the chosen error postulate.

The overall percentage of surface overlap between RW and EW is rather low (59%). Likewise, the median distance separating RW centers with EW centers is rather high (3.2 mm). Finally, the median Angle between EW and RW is also rather large (14°). These data demonstrate the presence of variability in terms of fenestration location when compared with the MTIS instructions for use provided by Bess Inc.

Nonetheless, no correlation was found between these two position variables and voice outcome variables.

Three hypotheses could explain this variability that does not affect outcome: (a) the MTIS procedure, as described by Bess Inc., does not represent a "one-fits-all" procedure but rather a guideline procedure that needs to be interpreted by surgeons, (b) the MTIS procedure does represent indeed a "must-follow" procedure that allows some variability before affecting outcome and finally, (c) surfaces of overlap, radius and angle does not represent pertinent position variables.

The results obtained by the last position variable, the Quadrant, give some credit to this very last hypothesis. Indeed, data show evidence that patients that benefited from a more anterior and inferior fenestration positioning have better voice outcomes.

These data may confirm an MTIS surgeon's intuition that is that a most infero-anterior fenestration will avoid any protrusion of the implant within the Morgani's ventricle as well any exaggerated interaction with the arytenoid cartilage posteriorly.

These study findings are aligned with a very recent study published by C. Storck et al. that focused on the impact of the MTIS implant on the arytenoid cartilage [15]. Authors demonstrated that the MTIS implant causes a gentle superior and posterior push on the cricoidal facet of the arytenoid cartilage causing a medialization and a rising of the paralyzed vocal fold. Achieving this arytenoid move will require an implant positioning that is low and anterior.

Finally, while RW are homogeneously distributed between three of the quadrants, one can observe that almost none of the RW –independent of patient gender- where located into the infero-posterior quadrant. Authors believe that is due to the presence of the thyro-hyoid muscle that surgeons tend to approach very conservatively. No other operative pattern that the surgeon would have developed with the time could be identified.

Outcome discrepancy between genders

There is a notable, although not significant, difference of Angle between EW and RW related to gender. Authors think this might be related to the respective usable area for implantation; this is the area beneath a horizontal line through the midpoint, and the anterior border of the thyro-hoid muscle. This area is smaller in females than in males, allowing less angle variability.

Furthermore, this study shows that none of cohort's patients that had their RW centers in the infero-anterior quadrant were female.

This could represent a factor affecting MTIS outcome in female individuals.

Two hypotheses can be formulated to explain this gender discrepancy: (a) the MTIS instruction for use are simply wrong for female individuals or (b) size and/or shape of the stabilizing mid-plate of the MTIS implant does not allow a maximal infero-anterior positioning of the fenestration.

Finally, some limitations of the study have to be underscored.

Window location does certainly not represent the sole factor influencing voice outcome. Factors such as volume of the inner part of the prosthesis, induced tissue compression [16] and eventually shape of the implant that possibly influences [17-19] the arytenoid cartilage position, represent others outcomes factors to consider.

The population of the study is rather limited and CT images were collected retrospectively with some variability in image acquisition parameters. Furthermore, EW location was defined by one sole engineer, potentially inducing a single-evaluator bias. Nonetheless, the sensitivity analysis performed by applying the 2mm random noise on the input of the numerical MTIS planning process has shown a small impact on the definition of the expected fenestration.

CONCLUSION

Despite good overall outcome results, window positioning accuracy of MTIS fenestration is rather low for both genders. Therefore, the MTIS, landmarks, provided by Bess Inc. step-by-step procedure should, to a certain extent, not be considered as too rigid.

Data provided by this study advocate a maximal infero-anterior positioning of the window during MTIS. This maximal infero-anterior positioning is more difficult to obtain for female patients. Authors hypothesize that an improper design of female rectangle base and/or an improper female step-by-step surgical procedure impedes upon maximal infero-anterior location of the female prosthesis.

Further prospective studies should investigate the rectangle base, as well as the intra-laryngeal portion of the MTIS prosthesis as a possible determinant of voice outcome by gender, with a maximal infero-anterior fenestration position as standard.

REFERENCES

1.Mattei A, Desuter G, Roux M, Lee BJ, Louges MA, Osipenko E, Sadoughi B,Schneider-Stickler B, Fanous A, Giovanni A. International consensus (ICON) on basic voice assessment for unilateral vocal fold paralysis. Eur Ann Otorhinolaryngol Head Neck Dis. 2018 Feb; 135(1S):S11-S15.

2. Bonilla-Velez J, Small M, Bonilla-Escobar FJ, Sharum M, Tulunay-Ugur OE. Voice and Swallowing Outcomes of Unilateral Vocal Fold Paralysis: Comparing Younger Adult and Geriatric Patients. Otolaryngol Head Neck Surg. 2018May;158(5):904-911.

3. Rosen CA, Mau T, Remacle M, Hess M, Eckel HE, Young VN, Hantzakos A, Yung KC, Dikkers FG. Nomenclature proposal to describe vocal fold motion impairment. Eur Arch Otorhinolaryngol. 2016 Aug;273(8):1995-9.

4. McLean-Muse A, Montgomery WW, Hillman RE, Varvares M, Bunting G, Doyle P, Eng J. Montgomery Thyroplasty Implant for vocal fold immobility: phonatory outcomes. Ann Otol Rhinol Laryngol. 2000 Apr;109(4):393-400.

5. Montgomery WW, Blaugrund SM, Varvares MA. Thyroplasty: a new approach. Ann Otol Rhinol Laryngol. 1993 Aug;102(8 Pt 1):571-9.

6. Laccourreye O, Benkhatar H, Ménard M. Lack of adverse events aftermedialization laryngoplasty With the montgomery thyroplasty implant in patientswith unilateral laryngeal nerve paralysis. Ann Otol Rhinol Laryngol. 2012Nov;121(11):701-7.

7. Laccourreye O, El Sharkawy L, Holsinger FC, Hans S, Ménard M, Brasnu D.Thyroplasty type I with Montgomery implant among native French language speakers with unilateral laryngeal nerve paralysis. Laryngoscope. 2005 Aug;115(8):1411-7.

8. Nouwen J, Hans S, De Mones E, Brasnu D, Crevier-Buchman L, Laccourreye O.Thyroplasty type I without arytenoid adduction in patients with unilaterallaryngeal nerve paralysis: the montgomery implant versus the Gore-Tex implant.Acta Otolaryngol. 2004 Aug;124(6):732-8. .

9. Desuter G, Henrard S, Boucquey D, Van Boven M, Gardiner Q, Remacle M. Learning curve of medialization thyroplasty using a Montgomery™ implant. Eur ArchOtorhinolaryngol.2015 Feb;272(2):385-90.

10. Desuter G, Zapater E, Van der Vorst S, Henrard S, van Lith-Bijl JT, van Benthem PP, Sjögren EV. Very long-term Voice Handicap Index Voice Outcomes after Montgomery Thyroplasty: A cross-sectional study. Clin Otolaryngol. 2018 Apr 6.doi: 10.1111/coa.13113. [Epub ahead of print]

11. Desuter G, Henrard S, Van Lith-Bijl JT, Amory A, Duprez T, van Benthem PP, Sjögren E. Shape of Thyroid Cartilage Influences Outcome of Montgomery Medialization Thyroplasty: A Gender Issue. J Voice. 2017 Mar;31(2):245.e3-245.e8.

12. Yushkevich PA, Piven J, Hazlett HC, Smith RG, Ho S, Gee JC, Gerig G. User-guided 3D active contour segmentation of anatomical structures: significantly improved efficiency and reliability. Neuroimage. 2006 Jul 1;31(3):1116-28.

13. Rosen CA, Mau T, Remacle M, Hess M, Eckel HE, Young VN, Hantzakos A, Yung KC, Dikkers FG. Nomenclature proposal to describe vocal fold motion impairment. Eur Arch Otorhinolaryngol. 2016 Aug;273(8):1995-9.

14. Montgomery® Thyroplasty Implant System: Instructions for Use. Boston Medical Products, Shrewbury,MA,USA; MK-THYCAT-C; 05-2016

15. Storck C, Lüthi M, Honegger F, Unteregger F. Surgical Impact of the Montgomery Implant System on Arytenoid Cartilage and the Paralyzed Vocal Fold. J Voice. 2018Aug 29. pii: S0892-1997(18)30232-7. doi: 10.1016/j.jvoice.2018.07.019. [Epub ahead of print] PubMed PMID: 30172670.

16. Benninger MS, Chota RL, Bryson PC, Drake RL. Custom implants for medicalization laryngoplasty: a model that considers tissue compression. J Voice. 2015, May;29(3):363-9.

17. Chester MW, Stewart MG. Arytenoid adduction combined with medicalization thyroplasty: an evidence-based review. Otolaryngol Head Neck Surg. 2003, Oct;129(4):305-10.

18. Li AJ, Johns MM, Jackson-Menaldi C, Dailey S, Heman-Ackah Y, Merati A, Rubin AD. Glottic closure patterns: type I thyroplasty versus type I thyroplasty with arytenoid adduction. J Voice. 2011 May;25(3):259-64.

19. Chang J, Schneider SL, Curtis J, Langenstein J, Courey MS, Yung KC. Outcomes of medialization laryngoplasty with and without arytenoid adduction. Laryngoscope. 2017 Nov;127(11):2591-2595.

CHAPTER 8:

General discussion, summary and future perspectives

General discussion:

The ultimate goal of this work is to contribute to the improvement of the voice, and consequently the quality of life, of the patient suffering from dysphonia due to paralysis of a vocal cord.

Basically, there are three kinds of surgical treatments for UVFP considered effective in the literature. Regardless of their duration of effectiveness, these are: injection laryngoplasty, non-selective reinnervation and laryngeal framework surgery including arytenoid modifications.

Temporary injection laryngoplasty appears to be highly effective in an early phase, all be it temporary. Some authors even attribute to it, an effectivity beyond the time of substance resorption. This hypothesis that injection augmentation thyroplasty perhaps stimulates reinnervation, induces adaptation of the central nervous system and/or gives rise to long-term beneficial laryngeal adaptations remains disputed and is the subject of studies in progress.

Improvement of voice results with a non-selective nerve transfer using the ansa cervicalis is based on reinitialization of reinnervation and recovery of tonus. Reports show more favorable results than those obtained during the initial spontaneous reinnervation, but results also appear somewhat unpredictable. Such reinnervation procedures are regularly combined with temporary injection augmentation, using various injectable materials. It then becomes less clear to what intervention the final effect can be attributed: injection, reinnervation or the combination of both?

Laryngeal framework surgery is generally considered as the "gold standard" for the treatment of UVFP, the technique is effective an relatively simple. Such a surgical procedure, as medialization thyroplasty, practiced since the first intervention by *Payr* in 1915, whatever its exact technique or the implant used, does not have to prove its effectiveness, the number of the studies underlining its good results are numerous.

So, *ite missa est*? Has everything been said? Are we satisfied on the pretext that some postoperative voice quality indicators have only a 5% chance of being identical to their preoperative value ($p < 0.05$)?

Regarding laryngeal medialization framework surgery, this thesis puts this complacency back into question. A specific type of thyroplasty -the MTIS- was chosen for two reasons; firstly, because the author had good experience with the technique, secondly the MTIS not only represents a type of implant but also a codified surgical technique, supposed to reduce the variability related to the surgeon.

The author of this thesis has also made an effort to use alternative and innovative research techniques in order to *critically consider the nature of the knowledge claims of their discipline (sic)*[1]. The originality lies in the choice of the Pareto technique as literature review, in the technique of the e-mail survey as to the use of voice indicators by practitioner, in a proof-of-concept study of an innovative (perhaps even disruptive) endoscopic measuring technique, and finally in the development of a new concept, the α -ratio with the use of virtual CT scan reconstruction to study the interactions between thyroid cartilage morphology and post-operative voice results.

Only one non-innovative research technique –a classical multi-centric cross-sectional study- was used, applied in the case of the long-term results. In the latter case, is it then a coincidence that its conclusions are as expected and gender differences did not become apparent?

Such innovative approaches, called for by the scientific community [2], offer alternative perspectives of the same reality. They allowed, as ambitioned, to further improve what is perceived as already satisfactory.

Here within lies the basis of our research.

Regarding the Voice Outcome Indicators

The literature review and the survey of surgeons (Studies 1 and 2, Chapter 2 & 3) indicate that two VOIs are widely used: the MPT and the VHI-30. These are both VOIs that are easily accessible. Nevertheless, the methodology to collect MPT should be further standardized. VOI acoustic measurements such as Jitter and Shimmer, although widely cited in literature and acclaimed important by speech-language pathologists, appear less relevant to surgeons. The survey among surgeons shows an interest in aerodynamic measurements - MeAF in particular - for UVFP assessment. This is in line with the work of Dastolfo et al. who consider the average airflow in the all-voiced sentence as a disease-specific VOI for UVFP [3].

Finally, two frequently used VOIs, should not be part of a minimum UVFP set of outcome indicators. These are the fundamental frequency (F0) and the estimated subglottic pressure (ESGP). Although frequently reported, F0 and ESGP do not change as a function of UVFP treatment (Study1). The same seems to be true of the Peak Direct Subglottic Pressure (PDSGP) that shows a poor agreement rate between PDSGP and Choice of Implant Size (62.5%) [4].

One of the possible reasons why F0 and ESGP are not relevant is that it does not only reflect the severity of the UVFP but rather a combination of the severity and the way the patient tries to overcome the limitation.

TAKE HOME MESSAGE 1:

Most commonly used VOIs to determine the effectiveness of surgical UVFP treatment are: MPT and VHI. MeAF is a VOI deserving further investigations.

Regarding the Advantages of the MTIS

Question 1: Is the MTIS a simple technique? What is its "learning-curve"?

An article, published in 2015, by G. Desuter et al. showed the easiness of the technique. The post-operative voice outcomes are good from the first patient on and remain at the same level [5]. Only the operating time improves with increasing experience of the surgeon. In conclusion; yes, the MTIS is a simple operating procedure.

Question 2: Does the MTIS offer permanent results?

Although MT is considered a definitive treatment of UVFP by the majority of authors [6], some have expressed doubts about the permanence of its benefits in the very long term [7]. According to these authors, glottic atrophy would cause a reappearance of symptoms. Our multi-centric cross-sectional study demonstrates the opposite (Chapter 4). It shows particularly stable results over the years. These results are independent of the patient's gender, his age at the time of the procedure and the size of the implant. The work of Ryu et al. had already reached the same conclusions regarding the medialization thyroplasties realized with self-carved silastic implants [8]. Our work shows that the same is true for MTIS. To conclude, the MTIS must be considered as offering a permanent result and can be presented as such during the pre-operative discussion with the patient.

Question 3: Does the MTIS make additional arytenoid cartilage surgery unnecessary? In other words, does the MTIS also achieve posterior glottis closure?

The authors expected to see this issue addressed by other teams during the course of this thesis. Indeed, Storck et al. answered this question by superimposing pre and post-operative 3D images with an imagery software (MIMICS) [9]. They concluded that MTIS can, in the case of a paralyzed vocal fold, adequately close the posterior glottis by imposing a postero-superior gliding movement of the arytenoid on the shoulder of the crico-arytenoid joint.

The authors, together with engineers, have chosen a non-irradiating and cheaper approach. An on-board laser measuring system on a flexible video-endoscope was developed and tested. In conducting a "proof of concept" study on human post mortem larynx, the question was whether this type of instrument would be clinically applicable and whether it had sufficient resolution to determine difference in height and position between vocal folds. The answer is affirmative and the Larynx Ruler is expected to be tested in clinical practice in the coming years.

TAKE HOME MESSAGE 2:

MTIS is a simple technique, offering permanent results with the possibility of treating posterior glottal gaps in most UVFP configurations.

Regarding the limitations of the MTIS

<u>Question 4: Considering the large variation in laryngeal anatomy, do 6 sizes of implants per gender allow to satisfactory treatment of all the UVFP patients?</u>
Study 5 (Chapter 6) shows poorer MPT results in female patients. Localization of the cartilage fenestration, the angle between the implant free edge and the middle plate, and the implant length are possible factors influencing results in females. Design of study 5 supports the implication of prosthesis angulation.

This discrepancy of outcome in disfavor of females exists since the initial article written on MTIS by W. Montgomery. Their argument for this finding is that normal MTP values are lower in women.

Unfortunately, very few studies comparing pre- and post-operative results after MT by another technique or implant stratify their results by gender. A comparison with other MT techniques is therefore impossible.

<u>Question 5: What is the accuracy of cartilage fenestration by following the "instruction for use" provided by the MTIS?</u>

Study 6 demonstrates a difference in the results for female patients as well. In this case, the VHI-30 difference was significantly poorer.

Study 6 shows variability in the realization of cartilage fenestration during MTIS. This variability had very limited effect on results of the whole cohort. A careful examination of these, however, asserts that the best vocal results are obtained when the implant is placed the most anterior and inferior on the thyroid ala. Again, there is a gender difference in results. None of the patients implanted antero-inferiorly were female.

As a matter of fact, length of the prosthesis and cartilage fenestration location, represent collinear factors as they both may influence the implant versus arytenoid interaction.

It is important to note that these results relate to separate cohorts of a limited number of patients (n = 20 for study 5 and n = 28 for study 6). Multi-centric studies will need to verify these findings.

TAKEHOME MESSAGE 3:

MTIS provides excellent results for male individuals. Female patients have a lower benefit after MTIS. The depth of the implant, as well as cartilage fenestration location, are factors influencing this gender discrepancy.

General conclusions of the thesis.

From studies 2 and 3, it can be deduced that the outcome indicators used in studies 4 to 7 are adequate. Moreover, a specific indicator, the mean airflow, seems of particular interest and at present is underused.

The MTIS was confirmed to be highly effective in the very long term and its high performance can even be considered to be permanent.

Besides for MTIS, no other preliminary studies on thyroplasty have shown slightly poorer vocal results in female patients compared to those found in male patients. Although in the majority of laryngology studies, the question of statistical power remains, these findings are nonetheless challenging and deserve further research.

In view of the results of studies 6 and 7, this difference in results could possibly be reduced by modifying both the shape of the endo-laryngeal portion of the implant (allowing a better α-ratio) and the size of its anchoring base (allowing maximum anterolateral cartilage fenestration for anchoring).

In any case, the MTIS is a valid technique that should benefit from these research data to improve its qualification of vocal results from good to excellent for both genders.

Perspectives

One of my mentors, Professor Yves Guerrier, from the University of Montpellier in France, once said to me that good research led to more questions than answers.
This is certainly the case at the end of this thesis.

Regarding the VOIs

The conclusions of this work (Chapter 2 & 3) served as a basis for the discussion of the establishment of an International Consensus on Basic Voice Assessment for UVFP [10].
New studies will focus on the creation and validation of a French and Dutch version of MeAF in the all-voiced sentence.
A correlation study of MeAF and Phonatory Quotient before and after MTIS is also planned.

Regarding the Larynx Ruler

A team of engineers from the Université Libre de Bruxelles (ULB) led by Mr B. Mertens is working on the production of LR fiberscopes and their EU certification. Once this is obtained, a clinical study comparing the results provided by the LR with the results obtained by MIMICS processed CT imagery will be launched. This will make it possible to carry out other prospective studies concerning the treatment of posterior glottic leaks.

Concerning the improvement of MTIS results in women

A preliminary study of 3D printed template for cartilage fenestration localization is ongoing.

Fully customized 3D printed implants study based on pre-operative planning imagery will have to be done subsequently. Depending on the outcome of this study it will be necessary to decide on a switch to a custom-made 3D printing model or the development of different sizes of a new female prosthesis.

References

1. Bárdardóttir E. Time is on my side, yes it is. Scand J Prim Health Care. 2008;26(1):3-4.doi: 10.1080/02813430801905672.

2.Baerheim A. Limits of medical research - some considerations. Scand J Prim Health Care. 2010 Dec;28(4):197-8. doi: 10.3109/02813432.2010.530739.

3.Dastolfo C, Gartner-Schmidt J, Yu L, Carnes O, Gillespie AI. Aerodynamic Outcomes of Four Common Voice Disorders: Moving Toward Disorder-Specific Assessment. J Voice. 2016 May;30(3):301-7. doi: 10.1016/j.jvoice.2015.03.017. Epub 2015 May 20.

4.Almohizea MI, Prasad VM, Fakhoury R, Bihin B, Remacle M. Using peak direct subglottic pressure level as an objective measure during medialization thyroplasty: a prospective study. Eur Arch Otorhinolaryngol. 2016 Sep;273(9):2607-11. doi: 10.1007/s00405-016-4059-5. Epub 2016 Apr 30.

5.Desuter G, Henrard S, Boucquey D, Van Boven M, Gardiner Q, Remacle M. Learning curve of medialization thyroplasty using a Montgomery™ implant. Eur Arch Otorhinolaryngol. 2015 Feb;272(2):385-90. doi: 10.1007/s00405-014-3292-z. Epub 2014 Sep 24.

6.Vinson KN, Zraick RI, Ragland FJ. Injection versus medialization laryngoplasty for the treatment of unilateral vocal fold paralysis: follow-up at six months. Laryngoscope. 2010 Sep;120(9):1802-7. doi: 10.1002/lary.20982.

7.Siu J, Tam S, Fung K. A comparison of outcomes in interventions for unilateral vocal fold paralysis: A systematic review. Laryngoscope. 2016 Jul;126(7):1616-24. doi: 10.1002/lary.25739. Epub 2015 Oct 20. Review.

8.Ryu IS, Nam SY, Han MW, Choi SH, Kim SY, Roh JL. Long-term voice outcomes after thyroplasty for unilateral vocal fold paralysis. Arch Otolaryngol Head Neck Surg. 2012 Apr;138(4):347-51.

9.Storck C, Lüthi M, Honegger F, Unteregger F. Surgical Impact of the Montgomery Implant System on Arytenoid Cartilage and the Paralyzed Vocal Fold. J Voice. 2018 Aug 29. pii: S0892-1997(18)30232-7. doi: 10.1016/j.jvoice.2018.07.019. [Epub ahead of print).

10.Mattei A, Desuter G, Roux M, Lee BJ, Louges MA, Osipenko E, Sadoughi B, Schneider-Stickler B, Fanous A, Giovanni A. International consensus (ICON) on basic voice assessment for unilateral vocal fold paralysis. Eur Ann Otorhinolaryngol Head Neck Dis. 2018 Feb;135(1S): S11-S15. doi: 10.1016/j.anorl.2017.12.007. Epub 2018 Feb 3. Review.

Chapter 9

Samenvatting

In dit proefschrift wordt een behandelingstechniek voor eenzijdige stembandverlamming (UVFP) geëvalueerd, het gaat om de stem verbeterende Montgomery thyroplastiek. Na een stembandverlamming blijft de aangedane stemband stilstaan, waardoor het vaak onvoldoende lukt om de stembanden bij de stemgeving te sluiten, met heesheid als gevolg. Met behulp van een implantaat kan de aangedane stemband naar mediaal worden verplaatst en in deze positie worden gefixeerd. Hierdoor kunnen de stembanden beter sluiten en verbeterd van de stemkwaliteit. Het betreft hier een siliconenimplantaat dat wordt verankerd op het schildkraakbeen. Zowel het implantaat als de implantatietechniek, is vernoemd naar zijn ontwerper: Montgomery, of beter gezegd het "Montgomery Implant Thyroplasty System" (MTIS™). Dit proefschrift geeft een 360 ° evaluatie van de resultaten met deze techniek.
Hiertoe werden verschillende onderzoeksvragen gesteld:
Biedt MTIS een permanente of een op zijn minst lange termijnoplossing voor UVFP-patiënten? Biedt MTIS voldoende medialisatie en sluiting van de stembanden bij alle patiënten en is er ook voldoende sluiting in de posterieure glottis (achterste deel van de stembanden)? Bieden de zes door MTIS voorgestelde implantaatgroottes afdoende oplossing ongeacht het geslacht en de grote verscheidenheid aan de larynxanatomie? Ten slotte, heeft de exacte locatie van de implantaatverankering in het schildkraakbeen, zoals beschreven in de MTIS-techniek, invloed op het stemresultaat?
Allereerst de vraag: wat zijn de relevante uitkomstindicatoren met betrekking tot MTIS. Verschillende auteurs hebben reeds het multidimensionale karakter van stemevaluatie benadrukt. De richtlijnen van de ELS stellen een hetero-perceptieve, auto-perceptuele, akoestische, aerodynamische en strobo-endoscopische evaluatie voor. Yung et al. deden twee tegengestelde constateringen, namelijk dat de meeste chirurgen helemaal geen stemevaluaties uitvoerden, vóór chirurgische correctie van de UVFP, terwijl anderen vijf dimensionele evaluaties hanteerden. Het nadeel van multidimensionale benadering ligt in het feit dat ze dubbelzinnig kunnen zijn, waarbij elk type indicator op zichzelf staat en vaak in uiteenlopende richtingen evolueren. Hoe moeten we onder deze omstandigheden onze MTIS evalueren? Multidimensionale evaluatie wordt al snel een potpourri waarin iedereen ziet wat ze willen zien. De auteur heeft getracht om chirurgen aan te moedigen hun resultaten te meten, door op rationele wijze de indicatoren te kiezen en om vervolgens vergelijking tussen verschillende behandelingen van de UVFP mogelijk te maken.

Hoofdstuk 2 keek naar het type uitkomst indicatoren die worden gebruikt in de literatuur voor pre- en postoperatieve evaluatie van chirurgische UVFP-behandeling. Het totale aantal werd gekwantificeerd en gerangschikt op 'populariteit' met behulp van een Pareto-techniek. Elf indicatoren vertegenwoordigden, door hun cumulatieve gebruik, tachtig procent van het totale aantal gerapporteerde indicatoren. Van deze elf indicatoren waren er 5 niet gestandaardiseerd of niet vergelijkbaar tussen verschillende onderzoeken. Er bleven slechts 6 indicatoren over die werden voorgelegd aan de mening van chirurgen die de UVFP behandelden (hoofdstuk 3).

In hoofdstuk 3 bleek er onder de chirurgen, een voorkeur voor drie indicatoren (VHI30, MPT en GRABAS) en daarbij speciale aandacht voor de MeAF. De indicatoren Jitter en Shimmer, hoewel gevalideerd door de literatuur, genoten slechts een beperkte voorkeur onder de chirurgen die hebben deelgenomen aan het onderzoek.
In hoofdstuk 4 heeft de auteur de duurzaamheid van de stemresultaten onderzocht en of de duurzaamheid aan de MTIS kan worden toegeschreven. In een multi-center studie waar drie Europese teams aan mee werkten, werden subjectieve zelfevaluaties verzameld van de stem van patiënten die 2 jaar of langer geleden een MTIS hadden ondergaan. De resultaten laten een opmerkelijke stabiliteit zien van de stemverbetering door de jaren heen, ongeacht hun leeftijd, geslacht of prothesegrootte. Daarbij zijn de verkregen resultaten vergelijkbaar, ongeacht het centrum waar de operatie werd uitgevoerd.

Een hoogteverschil tussen de gezonde en aangedane stemband kan leiden tot verticale lekkage tussen de stembanden aan het achterste deel van de glottis. Evaluatie van door de MTIS bewerkstelligde hoogte herstel werpt de vraag op hoe dit hoogteverschil te meten. Radiologische technieken bestaan, waarvan de nauwkeurigheid, toegankelijkheid van de techniek, morbiditeit en kosten, vragen oproepen. In hoofdstuk 5 werkt de auteur samen met een ingenieursteam van de *Université Libre de Bruxelles* (ULB) om een lasermeter in te bouwen in een flexibele fiberscope. Het uiteindelijke doel is om een tool te ontwikkelen die toegankelijk, makkelijk toepasbare is, en betaalbaar, zonder stralingsbelasting. Hiermee zouden prospectieve studies kunnen worden uitgevoerd naar de effectiviteit van de behandeling, vermindering of liefst oplossen van glottislekkage en uiteindelijk het gebruik van deze tool in de huidige praktijk. In een haalbaarheidsonderzoek met behulp van een in vitro larynx preparaat wordt de validiteit van de techniek voldoende bevestigd om de gestelde onderzoeksvraag te beantwoorden.
In hoofdstukken 6 en 7 van dit proefschrift werd getracht de vraag te beantwoorden of zes implantaatgroottes voldoende zijn om patiënten van beide geslachten en alle verscheidenheid aan larynxanatomie te behandelen.
In Hoofdstuk 6 worden de stemresultaten bekeken in relatie tot de axiale anatomie van het schildkraakbeen en de grootte van het geplaatste MTIS- implantaat. De anatomie van het schildkraakbeen wordt gekenmerkt door de zogenaamde alfa-hoek, de hoek tussen twee rechte lijnen, die ieder door de voorste commissuur en een van de achterste randen van het schildkraakbeen worden getrokken. De verhouding -alfa-hoek: grootte van de geplaatste prothese- wordt de -alfa-ratio- genoemd en deze wordt vergeleken met de stem resultaten. De resultaten van deze studie laten een verschil zien in stemresultaten in termen van MPT in het nadeel van vrouwelijke patiënten. De omgekeerde correlatie tussen de alfa-ratio en de achtergebleven verbetering van MPT bij vrouwen, suggereert dat de vorm van de vrouwelijke implantaat voor verbetering vatbaar is.

Tot slot, Hoofdstuk 7 richt zich op de exacte locatie van het kraakbeenluikje (fenestratie) waarin het implantaat is geplaatst en de hoek met het sagittale vlak. Bij 28 patiënten werd de postoperatieve CT-scan van het strottenhoofd bekeken en daarna virtueel gereconstrueerd door de fenestratie op te vullen. Een ingenieur realiseerde virtueel een nieuwe fenestratie, de lokalisatie hiervan werd bepaald door nauwgezet de door de MTIS beschreven werkwijze te volgen. De gerealiseerde en geïdealiseerde fenestraties werden over elkaar gelegd. De verschillende uitkomstvariabelen werden bestudeerd met betrekking tot stemresultaten. Deze variabelen zijn: de afstand tussen het centrum van elk gerealiseerd venster en het ideale venster, de hoek tussen deze twee fenestraties, het percentage overlap tussen de twee vlakken en ten slotte de richting van de verplaatsing van het midden van het luikje ten opzichte van het geïdealiseerde centrum. Slechts één variabele bleek geassocieerd met een beter postoperatief stemresultaat. Deze was aanzienlijk beter wanneer de fenestratie werd uitgevoerd in relatief anterieure en inferieure positie. Geen enkele vrouwelijke patiënt had de fenestratie in dit kwadrant.

Chapter 10:

Thesis at a glance

Objective	Methods	Conclusions	Reference
STUDY 1: Voice Outcome Indicators for Unilateral Vocal Fold Paralysis Surgery: A Review of the Literature		**STUDY 1: Voice Outcome Indicators for Unilateral Vocal Fold Paralysis Surgery: A Review of the Literature**	
Literature review to identify which VOIs are most frequently used and most relevant, in terms of significant change in pre- and post-operative measurements, in order to assess UVFP surgical treatments.	A Medline/Pubmed literature review was performed and the most frequently used VOIs were identified using a Pareto diagram. For these most frequently used VOI's the number of studies that showed a statistically significant change in pre and post-operative results were compared to the total number of studies found, this portion was expressed in percent. This percentage was defined as the "percentage of significance" and used to assess changes of each VOI.	The results indicate that MPT, MeAF and GRBAS-I, represent the top-three most frequently used and the most relevant VOIs in terms of "percentage of significance". VHI showed a relatively low rate of use and low "percentage of significance". The role of Jitter and Shimmer remains unclear. Finally, MSGP and the F0 appear to be less relevant VOIs for the evaluation of UFVP surgical treatments in terms of significant change in pre- and post-operative measurements.	Desuter G, Dedry M, Schaar B, van Lith-Bijl J, van Benthem PP, Sjögren EV. Voice outcome indicators for unilateral vocal fold paralysis surgery: a review of the literature. Eur Arch Otorhinolaryngol. 2018 Feb;275(2):459-468.
STUDY 2: Voice Outcome Indicators for Unilateral Vocal Fold Paralysis Surgery: A Survey Among Surgeons		**STUDY 2: Voice Outcome Indicators for Unilateral Vocal Fold Paralysis Surgery: A Survey Among Surgeons**	
A survey was launched among the European laryngologists to acquire surgeons' opinions on the above mentioned preselected VOIs.	Three general questions were asked about surgeon's practice setting(s) and experience. The eleven next questions concerned (a) surgeon's VOIs preference and (b) their estimates of post-operative target values, they would consider being satisfactory.	Three VOIs are favored by surgeons: VHI-30, MPT and GRBAS-I. Jitter and Shimmer, although very frequently reported and statistically valid in the literature, come last concerning surgeon's choice as VOI for UVFP treatment assessment.	Desuter G, Dedry M, Schaar B, van Lith-Bijl J.T, van Benthem P. P, Sjögren E.V. Voice Outcome Indicators for Unilateral Vocal Fold paralysis Surgery: a survey among surgeons Eur Ann Otorhinolaryngol Head Neck Dis. 2018 (Accepted for publication)
STUDY 3: Very Long Term Voice Handicap Index Voice Outcomes after Montgomery Thyroplasty: a cross-sectional study.		**STUDY 3: Very Long Term Voice Handicap Index Voice Outcomes after Montgomery Thyroplasty: a cross-sectional study.**	
The aim of this multi-centric cross-sectional study was to examine the permanency of Montgomery Thyroplasty (MTIS) results from a patient's perspective.	The study consisted of collecting Voice Handicap Index (VHI-30) questionnaires from patients who had been previously been operated with MTIS between 2 and 12 years before. Very long term (>2 years) post-operative data were compared to the previously acquired pre-operative and early post-operative VHI results. Influence of factors such as age, gender, size/side of the prosthesis, and length follow-up were also analyzed.	Age differences, gender differences and size/side differences of the prosthesis, centres where surgery took place and length of the follow-up showed no significant influence. MT (medialization thyroplasty) overall and MTIS in particular, should be considered as a possible standard of care for UVFP when permanency of voice results is sought.	Desuter G, Zapater E, van der Vorst S, Henrard S, van Lith-Bijl JT, van Benthem PP, Sjögren EV. Very Long Term Voice Handicap Index Voice Outcomes after Montgomery Thyroplasty: a cross-sectional study. Clin Otolaryngol. 2018 Apr 6.doi: 10.1111/coa.13113. [Epub ahead of print] PubMed PMID: 29624876.

STUDY 4: The Larynx Ruler to measure height and profile of vocal folds: a proof of concept.		**STUDY 4: The Larynx Ruler to measure height and profile of vocal folds: a proof of concept.**	
The Larynx Ruler (LR) is a laser based, measuring device that could meet the previously stated need. This study represents a proof of concept regarding the use of LR in assessing vocal fold height and profile.	One fresh male human cadaver larynx was explored with the LR system through the operative channel of a gastroenterology video-endoscope. The tip of the video-endoscope was located in the laryngeal vestibule. Experimentally induced arytenoid motions were compared with measurements provided by the LR	The LR system represented a feasible technique to evaluate vocal fold's heights and bulk in humans. A few technical limitations were identified that will require improvements before experimental use on human.	Desuter G, Mertens B, Delchambre A, van Lith-Bijl J, van Benthem PP, Sjögren E. The larynx ruler to measure height and profile of vocal folds: a proof of concept. Med Devices (Auckl). 2017 Jul 5;10:149-155.
STUDY 5: Shape of Thyroid Cartilage Influences Outcome of Montgomery Medialization Thyroplasty. A Gender Issue.		**STUDY 5 : Shape of Thyroid Cartilage Influences Outcome of Montgomery Medialization Thyroplasty. A Gender Issue.**	
This study aimed to determine whether the shape of the thyroid cartilage and/or the gender influence voice outcomes after Montgomery thyroplasty (MTIS).	A retrospective cohort study was performed on 20 consecutive patients that underwent MTIS. Voice outcome variables were the relative decrease in VHI (%) and the absolute increase in MPT (sec.). Material variables were the angle between the thyroid cartilage lamiae (α-angle), the size of the prosthesis and a combination of both (the α-ratio). Continuous variables were analyzed using medians, and were compared between groups using the Mann-Whitney test. Factors associated with the outcome variables were assesses by multivariable linear regression. A Pearson coefficient was calculated between material variables.	The MTIS is a good thyroplasty modality for male patients but inadequate design of MTIS female implants leads to poor MPT outcomes. This represents a gender issue that needs to be further studied and eventually tackled.	Desuter G, Henrard S, Van Lith-Bijl JT, Amory A, Duprez T, van Benthem PP, Sjögren E. Shape of Thyroid Cartilage Influences Outcome of Montgomery Medialization Thyroplasty: A Gender Issue. J Voice. 2017 Mar;31(2):245.e3-245.e8
STUDY 6: Accuracy of Thyroid Cartilage Fenestration during Montgomery Medialization Thyroplasty		**STUDY 6: Accuracy of Thyroid Cartilage Fenestration during Montgomery Medialization Thyroplasty**	
The primary aim of the study was to retrospectively evaluate the accuracy of cartilage fenestration. Furthermore, recent publications indicate a possible discrepancy in MTIS voice outcomes related to gender. The secondary aim of the study was to investigate whether the fenestration accuracy could explain this discrepancy.	Study was performed by virtually drawing the fenestration on a 3D CT-scan as proposed by the MTIS's instructions for use (the "expected window" (EW)), and comparing it to the actually realized fenestration (the "realized window "(RW)). Four position variables, (a) surface overlap (%), (b) the distances between RW and EW centers (mm), (c) the angle between RW and EW and (d) the orientation of RW's center, were studied and compared to MPT (Sec) and VHI-30 scores outcomes.	Data provided by this study advocate a maximal infero-anterior positioning of the window during MTIS. This position is more difficult to obtain in female patients.	Desuter G, Cartiaux O, Pierard J, Henrard S, van Lith-Bijl J, van Benthem PP, Sjögren E. Accuracy of Thyroid Cartilage Fenestration During Montgomery Medialization Thyroplasty. J Voice. 2019 Jan 15. pii: S0892-1997(18)30499-5. doi: 10.1016/j.jvoice.2019.01.005. [Epub ahead of print]

Curriculum Vitae

Publications

Word of thanks

Gauthier René Raymond DESUTER was born in Berchem-Ste-Agathe, Brussels, Belgium on March 12th 1968. In 1986 he graduated of Latin-sciences studies from the Collège Saint-Michel in Etterbeek, Brussels, Belgium. He studied medicine at the Université catholique de Louvain (UCL) in Louvain-en-Woluwe, Brussels, Belgium. During his studies he launched, as founding-treasurer, the European Medical Students Association (EMSA). The constituent general assembly of EMSA took place in Brussels in 1991. EMSA represents nowadays the entire European medical student community towards the European institutions. During the final year of his medical studies, he spent one month in the department of Otolaryngology Head & Neck Surgery of the Clinica Universitaria de Navarra, Pamplona, Spain (Pr. R. Garcia-Tapia). He was graduated from the UCL medical school cum laude in 1994. The same year he has been ranked first of the Otolaryngology Head and Neck Surgery specialty selection process and started his residency in Otolaryngology Head & Neck Surgery at the Cliniques Universitaires Saint-Luc (CUSL) in Brussels (Pr. M. Gersdorff). In 1995 he performed a clinical observership of 2 months at the Sloan Kettering Cancer Center of New-York, NY, USA. In 1997-98 he spent a one-year residency in Head & Neck Surgery at the Centre Hospitalier Universitaire de Montpellier, France (Pr. B. Guerrier). In 1999, he finished his residency in Otolaryngology Head & Neck Surgery cum laude and started to work as a faculty member of the Otolaryngology Head & Neck Dpt. of the CUSL, affiliated to the UCL, in Brussels, Belgium. He benefited in 2003 of an Eisenhower Fellowship that allowed him to travel across the USA for three months investigating safety and quality policies among US hospitals. During his clinical career, he completed his expertise by pursuing an Executive MBA at the Solvay Business School of the Free University of Brussels in 2001 and a Master of Science in Health Care Management of Harvard School of Public Health, Cambridge, MA, USA in 2007. He was seven years elected by his peers as member of the Medical Council of the CUSL and acted from 2007 to 2010 as president of the Quality and Safety Council of the CUSL. In 2008, he was appointed "Chargé de Cours" at the Medical School, the School of Pharmacy and the Speech and Language Dpt. of the Psychology School of the UCL. In 2016, Doctor E.V. Sjögren and Professor P.P. van Benthem extended to him an offer of admission to the PhD program of the Leids Universitair Medisch Centrum (LUMC), Leiden, The Netherlands. He has published extensively and is member of numerous scientific societies, both within the field of Head & Neck Surgery, Laryngology and Phoniatry.

Gauthier Desuter is married to Angelica Chiarini since 2000. They have two sons, Maximilien and Léopold.

List of Publications

1: **Desuter G**, Henrard S, van Lith-Bijl JT, Amory A, Duprez T, van Benthem PP, Sjögren E. Shape of Thyroid Cartilage Influences Outcome of Montgomery Medialization Thyroplasty: A Gender Issue. J Voice. 2017 Mar;31(2):245.e3-245.e8. doi: 10.1016/j.jvoice.2016.08.010. Epub 2016 Oct 18. PubMed PMID: 27769698.

2: **Desuter G**, Mertens B, Delchambre A, van Lith-Bijl J, van Benthem PP, Sjögren E. The larynx ruler to measure height and profile of vocal folds: a proof of concept. Med Devices (Auckl). 2017 Jul 5;10:149-155. doi: 10.2147/MDER.S136561. eCollection 2017. PubMed PMID: 28740437; PubMed Central PMCID: PMC5505612.

3: **Desuter G**, Dedry M, Schaar B, van Lith-Bijl J, van Benthem PP, Sjögren EV. Voice outcome indicators for unilateral vocal fold paralysis surgery: a review of the literature. Eur Arch Otorhinolaryngol. 2018 Feb;275(2):459-468. doi:10.1007/s00405-017-4844-9. Epub 2017 Dec 20. PubMed PMID: 29264655.

4: **Desuter G**, Zapater E, van der Vorst S, Henrard S, van Lith-Bijl JT, van Benthem PP, Sjögren EV. Very Long Term Voice Handicap Index Voice Outcomes after Montgomery Thyroplasty: a cross-sectional study. Clin Otolaryngol. 2018 Apr 6.doi: 10.1111/coa.13113. [Epub ahead of print] PubMed PMID: 29624876.

5: **Desuter G**, Dedry M, Schaar B, van Lith-Bijl, van Benthem PP, Sjögren E. Voice outcome indicators for unilateral vocal fold paralysis: a survey among surgeons. Eur Ann Otorhinolaryngol Head Neck Dis. 2019 Oct;136(5):343-347. doi: 10.1016/j.anorl.2018.07.009. Epub 2019 Apr 19.

6: **Desuter G**, Cartiaux O, Pierard J, Henrard S, van Lith-Bijl J, van Benthem PP, Sjögren E. Accuracy of Thyroid Cartilage Fenestration during Montgomery Medialization Thyroplasty.JVoice.2019Jan5.pii:S08921997(18)304995.doi:10.1016/j.jvoice.2019.01.005. [Epub ahead of print] PMID:30658874

Thesis related articles

1: **Desuter G**, Henrard S, Boucquey D, Van Boven M, Gardiner Q, Remacle M. Learning curve of medialization thyroplasty using a Montgomery™ implant. Eur Arch Otorhinolaryngol. 2015 Feb;272(2):385-90. doi: 10.1007/s00405-014-3292-z. Epub 2014 Sep 24. PubMed PMID: 25248912.

2: Mattei A, **Desuter G**, Roux M, Lee BJ, Louges MA, Osipenko E, Sadoughi B, Schneider-Stickler B, Fanous A, Giovanni A.
International consensus (ICON) on basic voice assessment for unilateral vocal fold paralysis.
Eur Ann Otorhinolaryngol Head Neck Dis. 2018 Feb;135(1S):S11-S15. doi:10.1016/j.anorl.2017.12.007. Epub 2018 Feb 3. PubMed PMID: 29398504.

Word of thanks

Praesidium Libertatis, *bastion of freedom* ... the motto of the Universiteit Leiden ...
the words are right and true.

Like the reception given by the city to the Walloons persecuted at the end of the 16th Century, the University of Leiden welcomed me. It allowed me to express myself and develop my critical and scientific sense. I would like to thank the University, its spirit and excellence. In particular, I would like to thank Professor Peter Paul van Benthem, Head of the Department of Otolaryngology, who did me the honor of accepting my doctoral project. **Maxime Gratus Sum.**

Dr. Elisabeth Sjögren. There are decisive encounters in a man's life. The meeting with Elisabeth Sjögren was. She trusted me and left me a certain autonomy while improving my rigor and my structure of thought. You really gave me the taste of research. I benefited from your support and your listening despite your many professional and societal responsibilities. Elisabeth ... "you rock"!

Dr Antoon Langeveld. Dear Ton, thank you for your humor and lucidity. These qualities have sprinkled the time of the thesis of breathing moments.

Dr Julie van Lith-Bijl. Dear Julie, you have been my guide in the mysteries of Dutch society and Dutch academic culture. Thank you for your calm, patience and your endless encouragements. May our, truly European, professional collaboration lasts for many years to come.

Dearest Radboud van den Akker, you have agreed to be my paranimph as a token of friendship. Thank you. Your presence reassures.

Surgery is also a craftmanship made of fellow apprentices and mentors. I think it is important to thank some of my mentors when closing this doctoral thesis. Prof. R. Garcia-Tapia (†), Pamplona, Spain, let me operate for the first time. Prof. Y. Guerrier, Montpellier, France, taught me everything I know about head and neck surgery. Professor M. Remacle, Luxembourg, instilled in me his visionary spirit, Professor G. Lawson, Mont-Godinne, Belgium, taught me his soft-skills-based management style, finally, Prof. H. Mahieu, Amsterdam, the Netherlands, and N. Maragos, Rochester, MN, USA introduced me to this magnificent surgery that is Thyroplasty.

Thank you to the confreres, doctors, engineers and speech therapists who participated in this work. Thank you for your daily work: Enrique, Sebastien, Benjamin, Séverine, Jonathan, Olivier, Marie, Donatienne, Bérénice, Sylvie, Valentine, Catherine, Anna, Audrey, Thierry ... and many others. Thank you from the heart.

Thank you my friends, Gabriela, Xavier, Nicolas, Vinciane, Parla, Jean-Paul, Michel, Lionel, Heikki, Michal, Ramon, Matsu, Benny, Daniel, Albert and many more ... who understood my absences and who supported me during this bet a little crazy to cumulate full-time clinical activity and doctoral thesis.

I am thankful to my dear mother Yvette Antonia van den Bossche-Desuter. Mom, thank you for your love and your unwavering support. There are no words to express my gratitude. Long life to you!

Finally, these thanks are addressed to the dearest beings. This trio offers a base to my life.
Angelica; thank you for your patience, your enthusiasm and your love! Thank you for giving me two wonderful sons.
Maximilien and Leopold, lights of mom's and dad's lives; be good, be brave, do not be satisfied with little and cherish freedom in the service of others.