UNIVERSITÄTSKLINIKUM HAMBURG-EPPENDORF

Klinik und Poliklinik für Hals-, Nasen- und Ohrenheilkunde
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Indication for vocal fold medialization in patients with unilateral vocal fold paralysis (thyroplasty versus fat injection)

Dissertation

zur Erlangung des Grades eines Doktors der Medizin
der Medizinischen Fakultät der Universität Hamburg.

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Hamburg 2010

Angenommen von der
Medizinischen Fakultät der Universität Hamburg am: 10.12.2010

Veröffentlicht mit Genehmigung der
Medizinischen Fakultät der Universität Hamburg.

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INHALTSVERZEICHNIS

1. INTRODUCTION

1.1. Introduction

Unilateral recurrent nerve paralysis results in inappropriate vocal cord vibration. This is leading to dysphonia, which is usually the major symptom of the paralysis. Furthermore glottal insufficiency may disturb both respiratory function and airway protection due to swallowing disorders. Patients with unilateral vocal fold paralysis (UVFP) exhibit a wide variability in phonatory, swallowing and airway dysfunction. This diversity makes a clinical classification difficult resulting in varying interpretation and treatment, depending on training and tradition.

The initial treatment of dysphonia in UVFP usually includes speech therapy. The surgical treatment is the second step in the therapy. The precise timing of a surgery is not well defined. The aim is a functional treatment, in order to medialize the vocal folds. Two major treatments are commonly used to treat UVFP: injection and thyroplasty. The indications for each treatment are imprecise and rarely addressed in literature.

The aim of the study is to analyze the indication of medialization in UVFP. Results of fibroscopic examination and measurements of acoustic and aerodynamic parameters are analyzed. The study analyzes patients with UVFP who were treated with a single fat injection or a single medialization thyroplasty and patients who required several procedures to improve their deficit.

1.2. Anatomic and physiological considerations

In health, the larynx is controlled by a sophisticated neural innervation. Motor, sensory, proprioceptive and parasympathetic nerve axons achieve its complex function. The vocals folds perform a high degree of versatility; they are capable of adjustment in length, tension and shape.

The immobility of vocal folds can be caused by impaired innervation or by a mechanic default (e.g. a tumor or immobility of the arytenoid).

1.2.1. Anatomy

The larynx is a tube shaped structure involving a complex system of muscle, cartilage, and connective tissue.

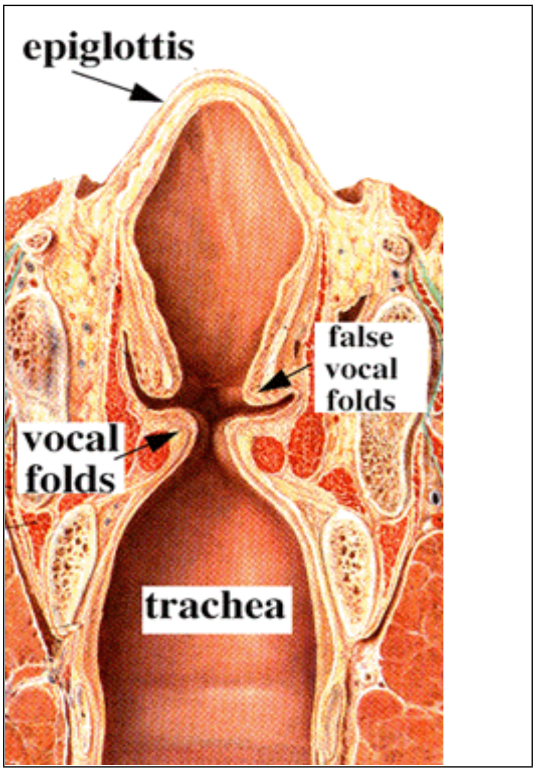


Fig 1. A human larynx (http://www.voice-center.com/voice_mecha.html)

Innervation of the larynx

During phonation and inspiration, neural impulses are transmitted from the nucleus ambiguous via the vagus nerve (Xth) to the intrinsic muscles of the larynx. Two branches of the vagus nerve are innervating the laryngeal muscles: the recurrent laryngeal nerve (RLN) and the superior laryngeal nerve (SLN). Both branches communicate via Galen's anastomosis (53); these branches are generally held to be sensory (47, 63). Mu et al (52) findings suggest motor components of the communicating nerves. Usually unineuronal innervation is present in adults; but also unineuronal multinnervation may be observed (58).

The SLN leaves the vagus at the base of the skull, descends behind the internal carotid artery, and divides into an external and an internal branch. The external branch descents on the larynx to innervate the cricothyroid muscle (CT). The internal branch, which is sensory to the supraglottic larynx, descends to the hyothyroid membrane and enters the laryngopharynx, where it spreads out (56). The SLN lies deep in the neck. Its anatomic position protects it from iatrogenic injury.

The RLN leaves the vagus in the chest and loops around the subclavian artery on the right and, deep in the thorax, around the aortic arch on the left side. Then, the RLN descends between trachea and esophagus, passes under the constrictor pharyngis inferior, and enters the larynx behind the cricothyroid articulation (67, 84). The posterior division of the RLN gives the sensory supply to the trachea, esophagus and pyriform sinus, before entering the larynx. The right and left RLN provides motor innervation for four intrinsic laryngeal muscles (posterior cricoarytenoid (PCA), thyroarytenoid (TA), lateral cricoarytenoid (LCA) and interarytenoid muscles (IA)) and sensory innervation of the upper trachea and subglottic. The RLN's redundant route exposes it at far more risk for traumatic and iatrogenic injury.

Laryngeal muscles

A complex structure of extrinsic and intrinsic laryngeal muscles are associated with the larynx: The extrinsic muscles raise the larynx via the suprahyoid group and lower it via the infrahyoid group. Five intrinsic muscles abduct and adduct the vocal folds. They include the PCA, TA, LCA, IA and CT muscles.

The paired PCA muscles are situated on the posterior larynx. The PCA is known as *the* abductor of the vocal folds. When the PCA contracts, it swings the muscular process of the arytenoid. This results in a sliding movement of the vocal folds along the mediolateral axis. Its important function is the vocal fold abduction during inspiration; it acts also as an antagonist to the adductors and as a balancer of the arytenoid during high-pitch phonation (44, 59, 64).

Three muscles interact to close the glottic gap during phonation and to protect the airway:

The TA muscle (also known as *vocalis muscle*) provides the main mass of the vocal fold. Tuning, tensing and thinning the vocal fold during normal phonation are its major function (11). The muscle appears to be divided into superior and inferior subcompartments, which have the ability to contract independently (17, 65). Denervation of the TA produces a decrease in tension and mass of the vocal folds. Those modifications produce changes in pitch and affect glottic closure by rounding the glottic edge (80).

The LCA muscle is the most important adductor muscle for the vocal folds. Phonation as well as coughing and the Valsalva's maneuver require a functional LCA that evokes a strong and permanent glottic closure (74). Once the LCA is denervated, it shows a loss of adduction, with a following inability to glottic closure. In some cases this dysfunction cannot be compensated by the contralateral larynx. This may result in aspiration (12).

The IA's primary function appears to control the size of the posterior glottic closure. Furthermore it assists the LCA in the vocal fold adduction and the PCA in some abductive and adductive maneuvers. Aibara (76) demonstrated that the IA is bilateral innervated by branches of the RLN. This results in less severe but more complicated affection after unilateral RLN paralysis (12).

The CT muscle, innervated by the SLN, does not insert directly on the arytenoid. It affects the vocal fold motion indirectly: By pitching the thyroid cartilage toward the cricoid ring ventrally with the result that the vocal folds are getting stretched. The muscle is innervated during adduction as well as in abduction.

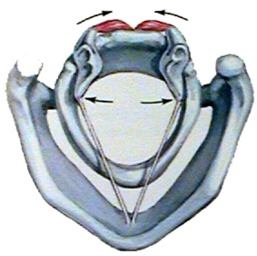
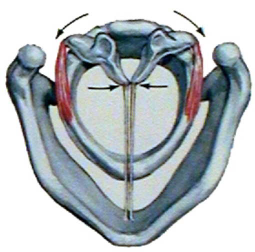
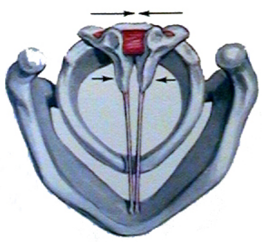
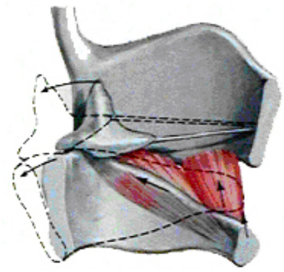
Muscles: 1. Posterior cricoarytenoid (PCA) 2. Ipsilateral thyroarytenoid (TA) 3. Lateral cricoarytenoid (LCA) 4. Interarytenoid muscle (IA) *5.* Cricothyroid (CT)	 Action of PCA Abduction of vocal folds	 Action of TA and vocalis muscle Shortening of vocal folds
 Action of LCA Adduction of vocal folds	 Action of IA Adduction of vocal folds	 Action of CT Tension of vocal folds

Fig 2. Anatomy and action of the muscles associated with the larynx (Atlas of Human Anatomy, Frank H. Netter, Saunders; 3rd edition)

1.2.2. Physiology

The upper aerodigestive tract serves the diverse purposes of airway protection, deglutition, respiration, and phonation. These activities require some orthogonal functions. To perform this role in humans, the larynx must be open during breathing and tightly closed during swallowing. The pharyngeal patency must be maintained during respiration, while the pharynx has to be forcibly constricted during swallowing. In addition, the anatomic structure of the upper aerodigestive tract is precarious, with ingested food and inspired air traversing the same space. Only the controlled interaction of innervation and muscle work and an appropriate response to sensory feedback can ensure their efficiency (35).

Phonation

Speech is audible communication that results from phonation, resonance, and articulation. For normal phonation, adequate respiratory support, appropriate glottal closure, a *regular* vocal fold cover, and instantaneous control of vocal fold length and tension are required. The phonation is based on instantaneous changes in mass, length and tension of the vocal folds. During phonation, the vocal folds act as an energy transducer that converts aerodynamic power generated by the chest, diaphragm, and abdominal musculature into acoustic power that is heard as our voice (1). This energy transformation takes place in the space between the vocal folds; and is also highly influenced by subglottic and supraglottic parameters.

The myoelastic-aerodynamic theory

At the beginning of the phonatory cycle, the air is moved out of the lungs. When the vocal folds come together, the flow is blocked and the air pressure from the lungs forces the adducted vocal fold to open momentarily. The abrupt high velocity of the air creates a lower pressure by the *Bernoulli Effect.* This brings first the bottom of the vocal cords back together, then followed by the top. The closure of the glottis cuts off the air column and decreases the air pressure toward the vocal cords and they can reopen. Repeated vibratory cycles produces “voiced sound”, which is than modified by resonance and articulation (56).

1.2.3. Pathophysiology

Neurological disorders may (but must not) impair upper aerodigestive tract function by diverse mechanisms, including motor weakness, atrophy, incoordination, and impairment of sensation.

The three-dimensional shape of the vocal fold is important to provide aerodynamic features to the glottis. Atrophy of the vocal fold causes concavity in the axial and coronal planes. This results in incomplete glottal closure, even during tight approximation of the vocal processes.

For a normal phonation, vocal folds should be appropriately approximated. If they are closed too tightly, excessive expiratory force is required. This results in a strained, harsh voice, or complete aphonia. If the vocal folds are too far apart, increased expiratory airflow volume is required. The voice becomes weaker, or even fades to a whisper.

The main symptoms of UVFP are dysphonia as well as swallowing and breathing disorders. The specific nature of dysphonia varies: vocal fatigue, insufficient loudness, non-specific ‘‘hoarseness“, effortful voicing, impaired singing quality, as well as sensation of breathlessness on exertion or speaking, and intermittent laryngospasm (4).

Beside total transaction of the RLN or/and SLN, a partial denervated nerve is a common clinical picture, evoked by partial cutting, electrocautery or crushing traumata. Once the Xth cranial nerve (X) is injured, a normal laryngeal neuromuscular function is rarely seen. As a nerve, containing motor, sensory and proprioceptive fibers, it is assumed that a regeneration chaos follows nerve injury. Even though Shindo et al (69) describe that the canine larynx becomes reinnervated via RLN regeneration after 3 month, despite removing a 2.5-cm segment. Crumley (11) declares that aberrant functioning reinnervation, rather than complete denervation, is the most common laryngeal problem in patients following RLN injury.

Beside these clinical pictures, a UVFP can be sometime asymptomatic. These patients probably never consult an otolaryngologist or speech pathologist concerning their paralysis and are not present in any statistic. This diversity of the clinical presentation of UVFP makes a classification difficult.

1.3. Management of UVFP

1.3.1. Diagnostic and assessment

The patient's history of the UVFP is important since it may influence the treatment. The assessment of the UVFP is based on a physical examination, which must include assessment of both voice and larynx. The differentiation of the impaired vocal fold movements' origin is a fundamental goal of the assessment: It can be either a paralysis or a mechanic problem, caused by a default of the cricoarytenoid articulation or a parietal lesion.

Key features of the history

Of particular importance in the origin of the UVFP is the knowledge about temporally related surgery in the neck and chest region and intubation, other neurological symptoms (weakness or numbness), history of neurological disease (e.g. multiple sclerosis or Guillain-Barré syndrome), and voice, swallowing, and breathing disorders. Information about onset, whether gradual or sudden, and classification of dysphagia symptoms can help to explain the history and the localization of the lesion.

Examination of the larynx and the vocal cords

Diagnostic and therapeutic decision-making in cases of UVFP is based on a visual and neurophysiological examination of the larynx. Indirect laryngoscopy, videostroboscopy and EMG are frequently used to assess the larynx.

Indirect laryngoscopy

Two methods of indirect laryngoscopy are used to examine the voice box and its surrounding larynx: mirror laryngoscopy and flexible laryngoscopy.

Using the traditional mirror laryngoscopy, the examiners can perform laryngeal examination on dysphonic patients. A strong gagging reflex can disturb the examination and a good visualization of the larynx. The mirror laryngoscopy is therefore only practicable for the first approach on voice disorders; further examinations should be done using an indirect videofibroscopy or videostroboscopy.

With the videofibroscopy, the entire larynx and pharynx can be observed. The flexible videofibroscopy allows a close exploration of the larynx and the recording of videos and images. The patient’s larynx can be observed during normal conversation, singing and swallowing. The fibroscopic exploration includes laryngeal structure, arytenoid and vocal-fold motion, color and quantity of mucous, vascularization, changes in laryngeal height or position during phonation, supraglottic activity or compression, and deformation of vocal-fold edges. The visualization of a videofibroscopy can be limited by patients who developed supraglottal hyper-function, compensating incomplete glottal closure. This compensation degrades the view of the “true” vocal folds and thereby makes clear visualization and evaluation of the larynx during phonation difficult.

Videostroboscopy

Videostroboscopy is another method of illuminating the vocal folds. The image is quasi-synchronized with the vocal fold vibration to provide what appears to be a slow-motion view of vocal fold movement and vibration (33). This is particularly helpful in assessment of completeness of laryngeal closure and the sharpness and shape of the vocal folds' edges. The most important limitation of the examination is its reliance on periodic vibration. Good imaging of mucosal wave dynamics requires synchronization of the strobe light with vocal fold vibration. This is especially in irregularly vibrating cords difficult to obtain.

Electromyography (EMG)

EMG has also been used to evaluate UVFP and is considered essential to the workup by some physicians. It is the only instrument for evaluating the integrity of the laryngeal motor unit. Laryngeal EMG is useful in separating mechanical from nerval causes of vocal fold immobility and for determining reinnervation potentials (38, 50). To examine the specific muscle activity the patient contracts the muscle in which the electrode rests (66, 72). This permits a distinction of the paralysis location, whether a RLN or a Xth cranial nerve paralysis.

Examination of voice

Degree of voice impairment can be determined by objective acoustic and aerodynamic parameters, as well as subjective clinical assessment based on the patient's symptoms such as breathiness and aspiration. Four parameters are essential to measure vocal function: acoustic and aerodynamic vocal-function, clinical assessment of vocal quality, and patient self-assessment.

The common acoustic and aerodynamic assessment includes phonatory function tasks such as maximum phonation time (MPT), acoustic parameters (e.g. spectrographic analysis, measurement of fundamental frequency, perturbation of frequency and amplitude, signal/noise ratio), and the measurement of airflow during phonation.

Clinical assessment of voice quality remains a fundamental component of the clinical examination despite problems like subjective measures, ear training, and low interrater reliability. The GRBAS score is the most frequently used vocal quality assessment (26, 79). ‘‘G’’, ‘‘R“, ‘‘B’’, ‘‘A’’, and “S” stand for *grade*, *roughness*, *breathiness*, *asthenia*, and *strain*. Kent (34), Kreiman et al (39, 40), and others have discussed the limitations of auditory perceptual measures in detail.

Patient‘s self-assessment provide outcome data from the patient’s subjective perspective. This is particularly important, because individuals have a broad variety of their perception of their voice. This is not always in a direct relation to their “objectively” evaluated voice quality. Rosen at al notice for example that patients with untreated UVFP tend to perceive greater vocal dysfunction than patients with other types of dysphonia (61).

The most frequently used dysphonia-specific self-assessment questionnaires are the Voice Handicap Index (VHI) (5, 29), Voice-Related Quality of Life (V-RQOL) (24), and Voice Outcome Survey (VOS) (21).

1.3.2. Treatment

Speech therapy

The initial treatment of UVFP is usually the speech therapy. There are only few studies regarding the efficacy of voice therapy for UVFP (68); nevertheless, this is a well established instrument to evaluate, observe and improve the patient’s voice. Therefore most otolaryngologists refer patients with UVFP to a speech pathologists who begins a trial therapy after a voice evaluation (10, 23). Different techniques are commonly used: pushing, hard glottal attack, half swallow boom, abdominal breathing, head and neck relaxation, lip and tongue trills, resonant voice, and the accent method are among the most widely used voice therapies (71).

Surgery

There are different techniques available to manage UVFP. The major medialization procedures are vocal fold injections, laryngeal framework surgery (thyroplasty, arytenoid adduction, adduction arytenoidopexy) (85), and reinnervation procedures. There are no precise guidelines for each specific surgical treatment. Selecting the appropriate procedure depends on tradition of the institution and the physician's training. Many variables, including duration of symptoms, degree of impairment, presence of anatomic or surgical defect, and potential for recovery have to be considered before starting a procedure.

Several surgical techniques are commonly described for improving glottic insufficiency due to UVFP:

1. Vocal fold surgery (injection of various substances into the paralyzed vocal fold)
2. Laryngeal framework surgery (medialization thyroplasty and arytenoid adduction)

(The classification used in this work is bases on a classification system proposed by the European Laryngological Society in 2007 (20).)

Augmentation of the vocal folds by injection

In 1911 Brünings (9) first introduced a vocal fold augmentation by endolaryngeal paraffin injection for the purpose of correcting glottic insufficiency due to UVFP. Although he achieved voice improvement, complications like inflammation, extrusion and migration came along with. This practice of injection laryngoplasty was abandoned shortly after its introduction.

In 1952 Meurman (48) performed a series of external medialization procedure, using autologous cartilage grafts placed between the thyroid ala and the inner perichondrium. Also this procedure had a high complication rate, probably due to mucosal and perichondrial perforations. In the 1960s Arnold (2, 3) reintroduced vocal fold injection using the alloplastic material Teflon. His goal was to inject a foreign substance laterally into the thyroarytenoid muscle to ‘‘reposition the edge of the cord from the intermediate or paramedian position medially to decrease or eliminate the gap during phonation’’ (15).

Teflon particles, mixed with glycerine into a paste, became popular as an injectable material. It became the *gold standard* between the late 1960s and early 1990s treating dysphonia due to UVFP. Stable vocal improvements were reported by several surgeons (31, 36, 45, 46, 60).

Over the years, the injection of Teflon demonstrated different problems: overinjection (25, 32, 51, 62), inaccurate placement (13, 51, 62) and granuloma formation (16, 30, 57), combined with the difficulty of revising patients with poor outcome (54, 55). This combination led to Teflon falling in the surgeon’s disgrace. In 1991 Mikaelian et al (49) first described the injection of autologous fat. Since then, fat has become a widely used substance for vocal fold injection (7, 8, 83). In spite of very encouraging long-term results of autologous fat injection, fat has been shown to be unpredictable with a success rate of 62% at 12 months (42).

Laryngeal framework surgery

In 1974 Isshiki conceptualized and introduced the laryngeal framework surgery as performed today (27). His "medialization thyroplasty type I" implicated the removal of the upper border of the thyroid ala to make a simple implant, which was inserted through the ''medialization thyroplasty window'' in the thyroid cartilage. Later on, using a silastic implant, he was the first introducing an alloplastic material for medialization. Koufman (37) modified the initial Isshiki medialization thyroplasty procedure by using a hand-carved silastic implant placed between the thyroid cartilage and the inner perichondrium for vocal fold medialization. Today, medialization laryngoplasty surgery has become the gold standard for the management of glottal incompetence. Type I medialization procedures result in improvement of glottal efficiency and sound production. Nevertheless a group of patients continue to have difficulties during phonation as a result of unequal levels of their vocal folds or large glottal gap.

To address this problem specifically, Isshiki et al also published in addition to the medialization thyroplasty the first article, describing a series of five patients who underwent an arytenoid adduction operation (28). In this procedure a suture is placed around the muscular process of the paralyzed arytenoid. It produces a traction on the lateral cricoarytenoid and thyroarytenoid muscles. This results in medial rotation of the arytenoid and descent of the vocal process, hence closing the posterior glottal chink and replacing the vocal folds at equal levels (18).

Both medialization thyroplasty and arytenoid adduction are usually performed under local anesthesia. This permits the surgeon to check up the patient's voice status during the operation.

1.4. Questions

About 100 years ago, Brünings (9) firstly described successful surgery for the functional treatment of UVFP by vocal fold augmentation. Since then, the surgical techniques, instruments and methods for treatment of UVFP have constantly been improved.

Arnold (2, 3) reintroduced in 1962 vocal fold injection using Teflon. It remained the gold standard for UVFP for over 30 years (41). Many other materials have been introduced; all of them have advantages and risks. After the initial surgical trials, the second major breakthrough was accomplished by Isshiki in 1974 with the introduction of the laryngeal framework surgery, a medialization thyroplasty. This technique is today the gold standard (27). In addition, diverse other treatments of UVFP such as arytenoid adduction (introduced by Isshiki) (28) and reinnervation were initiated.

Thus at present, the major controversial focuses are as follows:

1. Which treatment/surgery is the best method for UVFP? This is a current focus of controversy, since medialization thyroplasty became tremendously popular and many situations can be treated successfully with both methods.
2. How to achieve the best functional results?
3. Which clinical factors influence surgical results?

In order to precise indications of medialization and to figure out factors, that may influence surgical results different groups of patients with UVFP are analyzed in this study: Patients who did improve their voice qualities after having received either a single autologous fat injection or a single thyroplasty, and patients who did not show satisfactory results and required a second or third surgery. They are studied pre- and postoperatively to look for prognostic factors which may influence functional results. Twenty four patients are studied for this purpose.

The major points of this study are the following:

1. Which factors influence the postoperative functional results?
2. What are the reasons for unsuccessful treatment of UVFP?
3. Can a more precise indication for fat injection or medialization thyroplasty achieve better functional results for patients with UVFP?
4. Is a revision of a fat injection justified?

2. PATIENTS AND METHODS

2.1. Study Design

This investigation is a retrospective study.

2.2. Study Population

This study reviews a series of 24 patients who underwent medialization of unilateral vocal fold paralysis (UVFP) by medialization thyroplasty or autologous fat injection (36 procedures). Patients exhibiting mechanic default (e.g. cricoarytenoid ankylosis) are excluded from the study. The series is selected out of 127 medializations performed on 108 patients between May 1996 and January 2008 at the department of Otolaryngology Head and Neck surgery of Tenon's Hospital (Paris, France). The selection of patients is made after the following criteria: For each patient who needed a revision of its treatment a correspondent patient (sex and age) who was treated with a single fat injection and thyroplasty is selected.

This series is divided into three groups according to the treatment performed:

Group A: Single fat injection (n= 8)

Group B: Single thyroplasty (n=8)

Group C: Fat injection + revision (fat re-injection or thyroplasty) (n=8)

The patients of the groups A and B are treated with a single surgery. Group C includes patients who needed a revision following an initial fat injection since functional results were not sufficient. For all patients, complete pre- and postoperative data are required:

- Indirect laryngoscopy with videofibroscopy record
- Acoustic and aerodynamic analysis

2.3. Surgery

All medialization procedures are performed by one surgeon.

2.3.1. Fat Injection

All fat injections are performed under general anesthesia using a small endotracheal tube. The abdomen, as the selected donor place, is prepared and drapes in the usual sterile manner. Microlipoextraction (5-10cc) is performed in the right or left fossa iliac. The content of the syringe is places on a sterile piece of fine-mesh gauze, covering a small metal container. The fat globules remain on the surface of the tissue, after the fluid has drained through the gauze. The fat is then removed from the gauze with a little spatula and placed into the barrel of a Brunings vocal cord injector to which an 18-gauge needle on a straight shaft has been attached. A microlaryngoscopy is performed to expose the larynx. The injection needle is places into the superior surface of the vocal fold and then directed into the thyroarytenoid muscle. The fat is injected in at least two sites of the paralyzed vocal cord (in general at the midthird of the vocal cord and at the lateral aspect of the vocal process). The injection is performed slowly, progressively, avoiding dilatation of the injection point and a minimal loss of infected fat. The injected fat is observed to readily diffuse into the thyroarytenoid muscle, resulting in a medialization of the cord. Injection is continued until an overcorrection with a convex bowing of the involved vocal cord becomes visible.

2.3.2. Thyroplasty

All thyroplasties are performed with loco regional anesthesia (except for one patient who wished an operation under general anesthesia), supplemented by intravenous sedation. The larynx is exposed through a small skin incision, located at the inferior third on the midline of the thyroid cartilage. The sternocleidohyoid muscles are displaced aside. The sternothyroid and thyrohyoid muscles are getting dissected and the thyroid cartilage is getting liberated. A rectangle window of the thyroid cartilage is performed, located 7 mm (female: 5mm) from the median line, on a length of 11mm (female: 9mm) and height of 7mm (female: 5mm). The external perichondrium is elevated from the delineated window. In patients with no calcification of the cartilage, a sharp elevator is used to remove the cartilage. When calcified, the cartilage is removed from the outlined window using a Lindeman fraise. All cartilage from the window is getting removed. The internal perichondrium is getting detached.

A pre-carved silastic implant (fashioned by the surgeon from a silastic block) is then placed: After the posterior side of the implant is placed into the window, the implant is rotated into position. The implant can be removed and adjusted appropriately depending of the vocal results and the breath tolerance obtained. The hyoid muscles are getting replaced and may be sutured on the midline before the skin is closed without aspiration drainage.

2.4. Pre- and postoperative assessment

Fibroscopy examination and clinical measurements of acoustic and aerodynamic parameters were recorded within 2 weeks before vocal fold medialization.

Group C was reexamined in the period 02/2008 - 04/2008. In addition to the standard physical examination including a videofibroscopy examination, an acoustic and aerodynamic analysis before and after each medialization and a patient's self-assessment (VHI) were performed after the last surgery.

2.4.1. Fibroscopy

The UVFP was studied by general ENT and videofibroscopic examinations. All patients underwent a pretreatment and posttreatment videofibroscopy, using a flexible laryngoscope (Olympus, ENF type PIII or Machida, ENT-30 type PIII). This videofibroscopy also included a functional assessment of the larynx during swallowing of thick cream and methylene blue water.

Videofibroscopy examination realized before May 2003 had been archived on videotapes. Videofibroscopy examination realized from May 2003 on had been digitally archived for documentation purpose (.mpeg).

2.4.2. Acoustic and aerodynamic parameters

Aerodynamic and acoustic parameters were registered by a speech-language pathologist, using S.Q. Lab workstation and an EVA analyzer (French acronym for Assisted Voice Evaluation). All of the subjects were recorded in a sound-treated room.

For acoustical analysis, a mouth-to-microphone distance of 30 cm was maintained during production of the vowel /a/ voiced at a comfortable pitch and loudness level. Acoustical parameters included measurements of jitter, shimmer, number of harmonics, and the aperiodic component of voice expressed by the "1-ratio signal". The number of harmonics and the “1-ratio signal” were calculated from spectrum analysis. For aerodynamic parameters, both oral and nasal airflows were assessed by separate airflow transducers.

All results of the aerodynamic and acoustic examination are digitally archived for documentation purpose.

2.5. Data collection

In the following, all preoperative data are called T0. The first surgery is called T1, as well as the first postoperative assessment. Concerning the revision group, the second surgery and the following postoperative assessment are called T2, the third intervention and the following postoperative assessments are called T3.

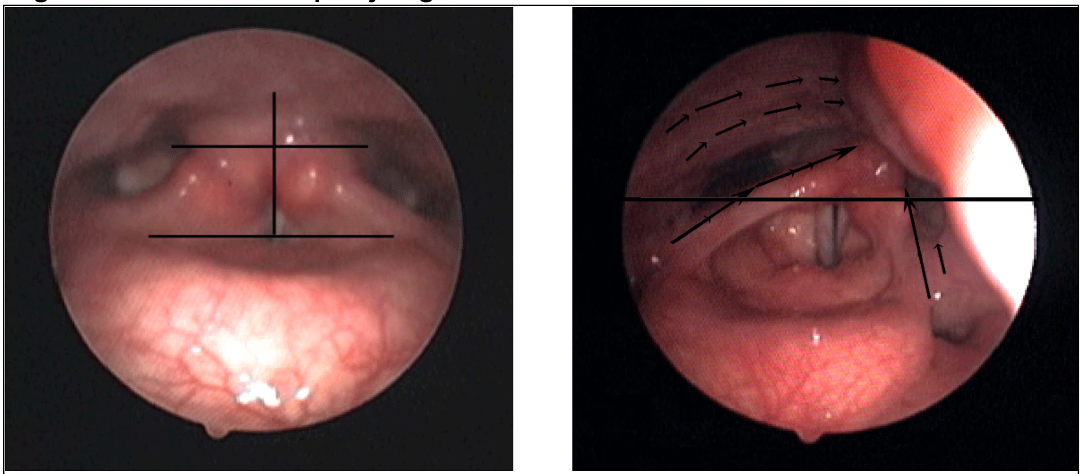
2.5.1. Fibroscopic assessment

Perceptual judgments of the larynx are made independently by two raters (one otolaryngologist with more than 10 years professional experience and me, medical student), using a nominal scale designed to rate severity of larynx abnormally, applied on fibroscopic recordings. The jury judged “larynx rotation”, “false vocal fold” and “glottic closure“, on a scale 0 to 3. The scale 0 represents a “normal” larynx, the rating 1 to 3 represents “mild”, “moderate” and “severe” visual disturbance. Examples for grade 0 and 3 are given in the figures 3 to 5 (Fig 3.-5.).

The video samples were presented on a computer in random order and through loudspeakers at a comfortable loudness level. All testing were carried out in a quiet room. Great care was taken to evaluate each examination in a blinded fashion. All videos were seen three times. At the first sequence all videos were judged about their *larynx rotation*, in the second about their *false vocal folds* and in the third about their *glottic closure*. The two judges were asked to mark their answers on a score sheet that was provided for them. To make the decision on the score, the recordings were replayed as many times as necessary for the judges. At the end of the session, the recordings were review. The scores were discussed in the event of different judgements, to achieving a final score to avoid inter-individual variability. This consensus was achieved in all cases.

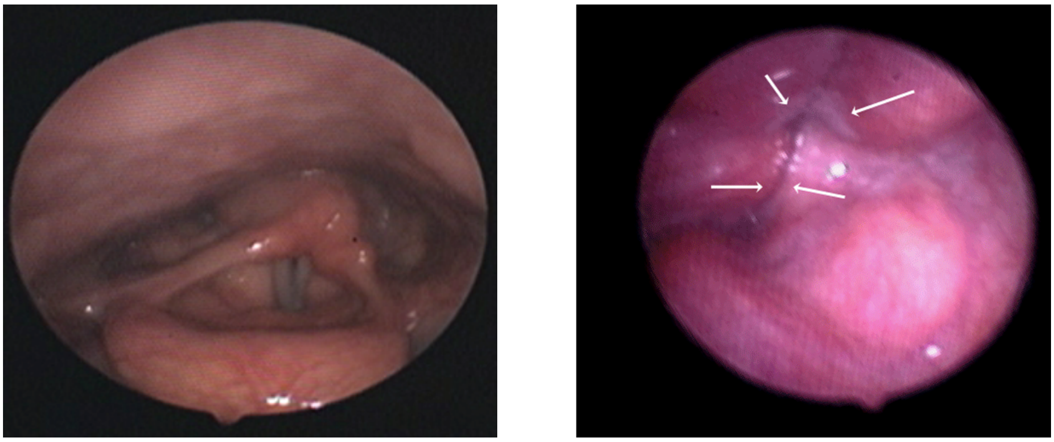
The judgements were performed in two sessions, two weeks apart.

Figure 3-5: Fibroscopic judgement criteria for UVFP



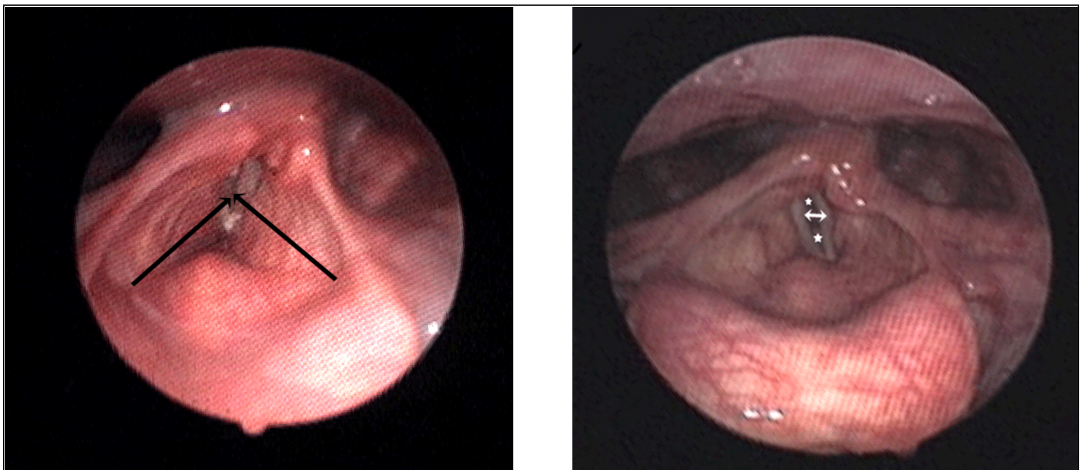
No larynx rotation- Grade 0 | Important larynx rotation- Grade 3

Fig 3. Fibroscopy, judgement of the grade of **larynx rotation** in two examples of left UVFP



Normal false vocal folds Grade 0 | False vocal folds cover completely the vocal cords - Grade 3

Fig 4. Fibroscopy, judgement of the grade of false **vocal folds** in two examples of left UVFP



Normal glottic closure- Grade 0 | Severely limited glottic closure- Grade 3

Fig 5. Fibroscopy, judgement of the grade of **glottic closure** in two examples of left UVFP

TABLE 1. Interpretation criteria of fibroscopic assessment

Grade		Interpretation criteria of the glottic gap size
0	Normal	No appreciable gap
1	Mild	Small gap extending up to 1/3 of the posterior membranous vocal folds
2	Moderate	Moderate gap extending up to 2/3 of the posterior membranous vocal folds
3	Severe	Severe gap without observable contact between the vocal fold
Grade		**Interpretation criteria of larynx rotation**
0	Normal	No appreciable larynx rotation
1	Mild	Mild larynx rotation extending up to <5% of the midline of the vocal folds
2	Moderate	Moderate gap extending 5-20% of the midline of the vocal folds
3	Severe	Severe gap extending >20% of the midline of the vocal folds
Grade		**Interpretation criteria of false vocal folds**
0	Normal	No appreciable false vocal folds
1	Mild	Small false vocal folds extending up to 1/3 of the vocal folds
2	Moderate	Moderate false vocal folds extending up to 2/3 of the vocal folds
3	Severe	Severe false vocal folds where no observable vocal fold during phonation

2.5.2. Acoustic and aerodynamic parameters

The figure 6 (Fig 6) shows the instruments, used to record and evaluate the following parameters:

- glottic gap: airflow measured during production of a sustained /a/ (cm3/dB(sec)),
- maximum phonation time during production of a sustained /a/ (sec)
- expiratory volume during the sentence, "c'est une affaire intéressante, qu'en pensez-vous ?" (L) (the French translation of “this is a very interesting subject, what do you think about?”)

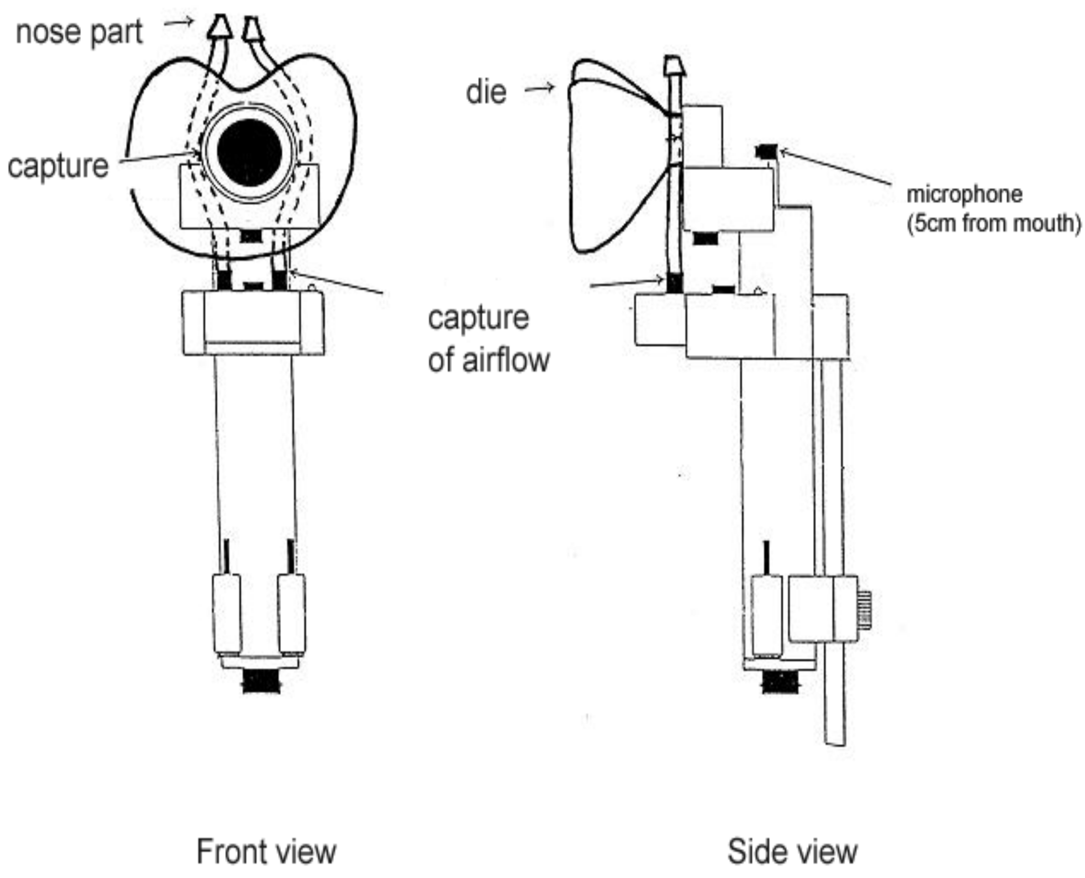


Fig 6. Aerodynamic capture

2.5.3. Perceptual analysis- GRBAS score

Three judges made independently a perceptual judgment of the patients‘ voice using the familiar nominal GRBAS scale designed to rate severity of voice abnormally. The judges were two speech-language pathologists with more than 10 years professional experience and me, medical student. The scale was applied on the recorded sentence “C’est une affaire intéressante, qu’en pensez-vous?”. The “GRBAS” represents the *G*rade, *R*oughness, *B*reathiness, *A*sthenia, and *S*train of the patient’s voice. It is rated on a scale 0 to 3, 0 represents a “normal” voice, the rating 1 to 3 represents “mild”, “moderate” and “severe” voice disturbance.

All testing were carried out in a quiet room. The voice samples were presented through loudspeakers at a comfortable loudness level. Each examination was evaluated independently and in a blinded fashion.

The three judges were asked to mark their answers on a score sheet that was provided for them.

To come to a final decision on the score, the audio recordings were replayed as many times as wished.

Final scores were assigned by consensus of two or more jury members to avoid inter-individual variability. This consensus was achieved in all cases.

The judgements were performed in two sessions, two weeks apart.

2.6. Statistical analysis

The results were calculated using SPSS® statistical software (version 14.0 for windows, SPSS Inc., Chicago, Illinois, USA).

Descriptive statistics including the mean, standard deviation and ranges for each group were computed.

The differences in fibroscopic and acoustic judgements and acoustic and aerodynamic measurements were compared to determine whether significant differences existed between the groups. A Mann-Whitney *U*-test with a significance level of $p < 0.05$ was performed to evaluate the significance.

The statistical analysis were performed to analyze and compare both changes in the fibroscopic and acoustic judgements and acoustic and aerodynamic measurements before and after treatment with medialization using Wilcox Signed Ranks tests, with a significance level of $p < 0.05$.

3. RESULTS

3.1. Population

The population includes 24 patients, 9 males and 15 females, ranging in age from 21 to 82 years with a mean of 55 years. The mean age of the male and female patients is similar (mean 54,8 and 55,1 years). The age pattern of male population is evenly spread from 21 to 82 years. 12 of 15 female patients are between 42 and 67 years old.

TABLE 2. Population

	Age at T1		**Sex**		**Type of paralysis**			**Operated Side**	
Study group	Mean	Median	M	F	RLN	X	X+	R	L
Group A	57	55,5	1	7	8	0	0	3	5
Group B	62	69	5	3	7	0	1	3	5
Group C	46	49	3	5	6	1	1	4	4
all patients	55	55	9	15	21	2	1	10	14

M: male; F: female; RLN: recurrent laryngeal nerve; X: Xth cranial nerve; X+: Xth cranial nerve and other associated cranial nerve paralysis; R: right; L: left

Group A

Group A (*Fat Injection*) includes 8 patients, 1 male and 7 females. The age ranges from 48 to 73 years (median 56 years) at time of the fat injection (T1).

Group B

Group B (*Medialization thyroplasty*) includes 8 patients, 5 males and 3 females. The age ranges from 21 years to 82 years (median 69 years) at time of the medialization thyroplasty (T1).

Group C

Group C (*Revision*) includes 8 patients who received at least two treatments for their vocal folds paralysis. The group includes 3 males and 5 females. Age ranges from 22 years to 60 years (median 49 years) at time of the first intervention (T1). The first treatment is in all cases a fat injection.

3.2. Preoperative characteristics

3.2.1. Patient data

Table 3 shows preoperative data of the 24 patients. It contains both information about type, side and etiology of paralysis and the duration of paralysis before medialization.

TABLE 3. Patient preoperative data

Group	Case no.	Sex	Age T1 (years)	Paralysis	Side	Etiology	Etiology (Cf. Table 4)	Paralysis onset to T1 (months)
GROUP A	1	F	58	RLN	L	Loboisthmectomy *	2,1	94
	2	F	73	RLN	L	Thyroidectomy *	2,1	21
	3	F	48	RLN	R	Thyroidectomy *	2,1	17
	4	F	66	RLN	L	Unknown	3	26
	5	F	50	RLN	L	Thyroid	2,1	24
	6	F	53	RLN	R	Cervicotomy *	2,4	12
	7	F	60	RLN	R	Unknown	3	5
	8	M	48	RLN	L	Pneumonectomy *	2,2	68
GROUP B	9	M	82	RLN	L	Thoracic aortic aneurysm	2,3	9
	10	M	21	RLN	L	Pneumonectomy *	2,2	137
	11	F	67	RLN	R	Parathyroidectomy *	2,1	10
	12	M	71	RLN	L	Thoracic aortic aneurysm	2,3	9
	13	F	54	RLN	L	Pneumonectomy *	2,2	7
	14	F	78	RLN	L	Thoracic aortic aneurysm	2,3	7
	15	M	77	RLN	R	Loboisthmectomy *	2,1	8
	16	M	42	X+	R	Cervical neck dissection *	2,4	29
GROUP C	17	F	60	RLN	R	Thyroidectomy *	2,1	16
	18	F	22	X	R	Glomic tumor *	1	30
	19	M	52	RLN	L	Pneumonectomy *	2,2	10
	20	F	42	RLN	L	Thyroidectomy *	2,1	24
	21	F	59	RLN	L	Thyroidectomy *	2,1	20
	22	F	36	RLN	R	Thyroidectomy *	2,1	9
	23	M	55	RLN	L	Lung cancer	2,2	20
	24	M	45	X+	R	Schwannoma *	1	41
	MEAN		55					27

*surgical cause

M: male; F: female; RLN: recurrent laryngeal nerve; X: Xth cranial nerve; X+: Xth cranial nerve and other associated cranial nerve paralysis; R: right; L: left; Etiology (Cf. Table 4)

Paralysis and side of UVFP

Out of the 24 patients with UVFP, 14 have paralysis on the left and 10 on the right side: The incidence of RLN paralysis on the left side is 58%, that on the right side 42% of the population.

Group A

The paralysis of the vocal cord is in 8 out of 8 cases due to a paralysis of the RLN, 5 patients present a paralysis on the left, 3 on the right side.

Group B

There are 7 recurrent laryngeal paralyses and one Xth nerve paralysis associated with a paralysis of the XIth cranial nerve. Like Group A, 5 patients have paralysis on the left, 3 on the right side.

Group C

There are 6 recurrent laryngeal nerve paralyses, one Xth nerve paralysis and one Xth nerve paralysis associated with an associated paralysis of the VIII, IX, XI and XIIth cranial nerves. 4 patients present left, 4 patients right UVFP.

Etiology of UVFP

The causes of vocal fold paralysis are shown in table 3. A classification concerning the major etiologies of UVFP is recorded in table 4.

Thyroid and parathyroid etiologies are the most important causes of UVFP with a rate of 42% (10/24). The other major cause is related to lung cancers (21%, 5/24) and aortic aneurysm (13%, 4/24).

71% of the paralyses are the consequence of surgery (17/24).

TABLE 4. Classification of etiology of UVFP

1. Nuclear or troncular etiologies	n=2
2. Distal etiologies:	n=20
2.1. Neck: thyroid or parathyroid	n=10
2.2. Thorax: lung cancer	n=5
2.3. Thorax: aortic aneurysm	n=3
2.4. Neck: esophagus, cervical neck dissection	n=2
3. Unknown	n=2

Group A

In this group 4 UVFP (50%) are due to thyroid or parathyroid cause.

Group B

There are 3 out of 8 cases due to thoracic aortic aneurysm, 2 out of 8 cases due to lung cancer, 2 out of 8 cases to thyroid etiologies.

Group C

Like in the group A, 50% (n=4) of UVFP are related to thyroid or parathyroid surgery.

Paralysis onset to T1 (time interval)

Group A

The duration of paralysis before medialization ranges from 6 to 94 months (median 23 months).

Group B

The duration of paralysis before medialization ranges from 7 to 137 months (median 9 months).

Group C

The paralysis' duration before T1 ranges from 9 to 41 months (median 20 months).

3.2.2. Fibroscopic assessment

Figure 7 (Fig 7.) shows the results of the fibroscopic assessment.

The assessment of *larynx rotation* and ventricular fold closure shows statistically significant differences between the groups:

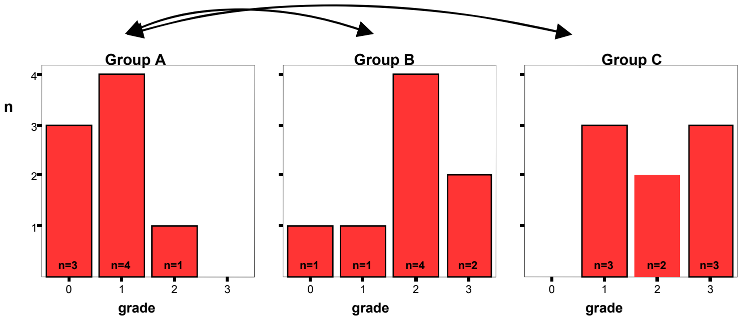
In group A, no patient shows a severe *larynx rotation*, and only one patient is judged to have a “moderate“ *larynx rotation*; 7 patients (88%) are judged as normally or only mildly disturbed. In group B, 6 patients (75%) are judged as moderately or severely disturbed. In group C *larynx rotation* is observed in all patients (100%). The judgement of *larynx rotation* shows statistically significant differences between the groups A and B (p=0.025) and the groups A and C (0.015).

False vocal folds are found in all subjects of group A and in 7 cases of group B. In group C only two patients present mild or moderate *false vocal folds*, the others 6 patients are judged as normal (75%).

The judgement of *false vocal folds* of group C is significantly different to group A (p=0.006) and B (p=0.014).

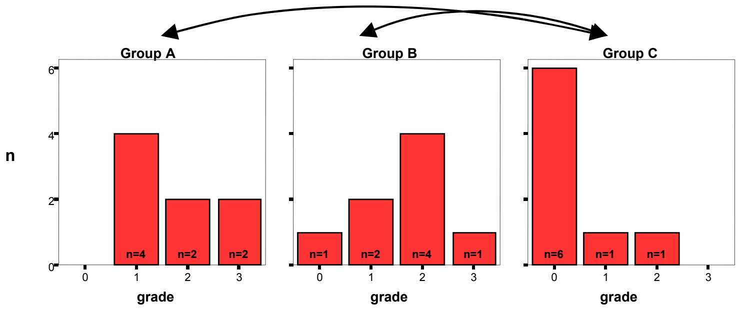
The assessment of the *glottic closure* shows no significantly different results between the three groups. Group A shows in all cases a mild or moderate disturbance in the *glottic closure*. In group B 2 patients are judged as normal, 3 as moderately and 3 as severely disturbed. In group C, there is no patient exhibiting a normal *glottic closure*; 6 patients are judged as normally or mildly disturbed, and two patients as severely disturbed.

Fibroscopic assessment, PRETREATMENT
Group A (Fat Injection), Group B (Medialization thyroplasty), Group C (Revision)



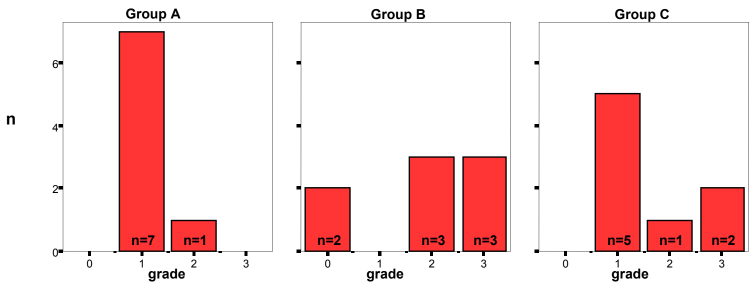
LARYNX ROTATION T0

Mann-Whitney U	Group A *v* B	Group A *v* C	Group B *v* C
Significance	0,025	0,015	NS



FALSE VOCAL FOLDS T0

Mann-Whitney U	Group A *v* B	Group A *v* C	Group B *v* C
Significance	NS (0,911)	0,006	0,014



GLOTTIC CLOSURE T0

Mann-Whitney U	Group A *v* B	Group A *v* C	Group B *v* C
Significance	NS	NS	NS

Significance is marked by ($p<0.05$)

Fig 7. Preoperative fibroscopic assessment, Group A, B and C: larynx rotation, false vocal folds and glottic closure assessed on a scale 0 to 3. (n= 8 subjects/group)

3.2.3. Acoustic and aerodynamic parameters

Preoperative acoustic and aerodynamic parameters are presented in table 5, summarized in table 6 and visualized in figure 8 (Fig 8.):

The population mean of glottic gap is 6.7 cc/dB/sec. The results of group A (mean=3.01 cc/dB/sec) are better than the population mean, those of group B are worse (mean=7.61 cc/dB/sec). In group C, the result of the glottic gap is falsified by two measurements (patient 18, 20.43 cc/dB/sec, and patient 24, 26.42 cc/dB/sec), which are impractically high for this parameter. Without those outliners, the mean glottic gap is 4.83 cc/dB/sec (with outliers 9.48 cc/dB/sec).

The results of group A in Maximum Phonation Time (MPT) are 10.3 sec (mean), that means higher than the average (population mean=7.67 sec). The results of group B (mean=4.48 sec) are inferior, and the results of group C (mean=8.19 sec) lie in between the results of group A and B.

The measurement of expiratory volume in group A (mean=0.56 L) is smaller than the population mean (0.855 L). Group B presents more disturbed results (mean=1.2 L), and group C's results (0.81 L) lie in between the groups A and B.

The comparison of group A and B shows significantly different results in glottic gap, MPT and expiratory volume (cf. Fig 8.). Comparing the acoustic and aerodynamic parameters, group C cannot be statistically significant distinguished from group A or group B.

TABLE 5. Objective voice measurements before intervention for vocal folds paralysis (n=24)

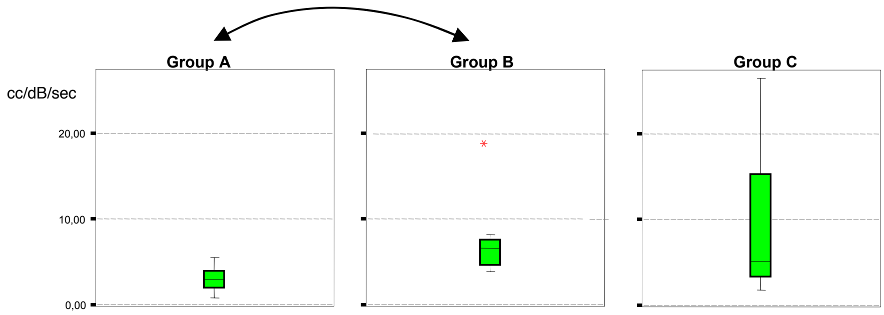
Group	Case no.	**Glottic Gap** (cc/dB/sec)	**MPT** (sec)	**Expiratory Volume** (L)
GROUP A	1	1,54	15	0,44
	2	3,74	7,2	0,5
	3	2,9	9,5	0,7
	4	2,93	15	0,58
	5	4,23	5	0,76
	6	2,48	15	0,44
	7	0,83	10,5	0,4
	8	5,4	5,2	0,63
GROUP B	9	7	3	1,2
	10	5	8,6	0,65
	11	4,5	2	1,8
	12	6,7	4,7	1,5
	13	6,7	1,4	1
	14	8,3	3	0,9
	15	18,8	1,8	1,98
	16	3,9	11,3	0,6
GROUP C	17	1,75	14,0	0,5
	18	*20,43*	3,7	1,3
	19	6,52	4,3	1,2
	20	3,1	18	0,38
	21	3,6	6	0,85
	22	3,64	15	0,47
	23	10,34	2,6	0,96
	24	*26,42*	1,9	0,78
	MEAN (SD)	**6.7 (±6.4)**	**7.67 (±5.3)**	**0.855 (±0.44)**
	Median	**4,37**	**5,6**	**0,73**

TABLE 6. Objective voice measurements (mean and median value) before intervention for vocal folds paralysis (n= 24)

	GROUP A		**GROUP B**		**GROUP C**	
	Mean (SD)	Median	Mean (SD)	Median	Mean (SD)	Median
Glottic Gap (cc/dB/sec)	3.01 ± 1.5	2,92	7.61 ±4.8	6,7	9.48 ±9.15	5,08
MPT (sec)	10.3 ±4.32	10	4.48 ±3.6	3	8.19 ±6.41	5,15
Expiratory Volume (L)	0.56 ± 0.13	0,54	1.2 ±0.51	1,1	0.81 ±0.34	0,82

Acoustic and Aerodynamic Parameters, PRETREATMENT;

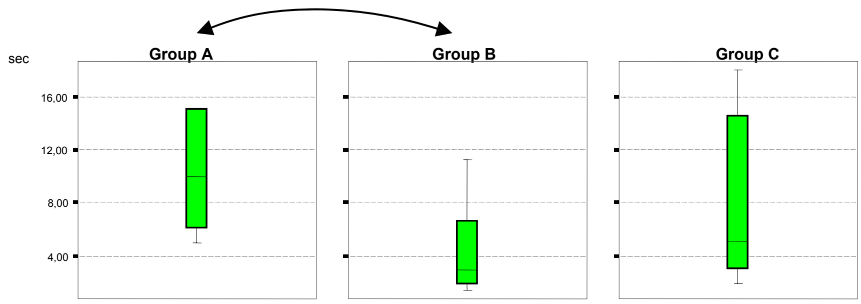
Group A (Fat Injection), Group B (Medialization thyroplasty), Group C (Revision)



GLOTTIC GAP (cc/dB/sec) T0

Flow rate measured during production of a sustained /a/ (cc/dB/sec)

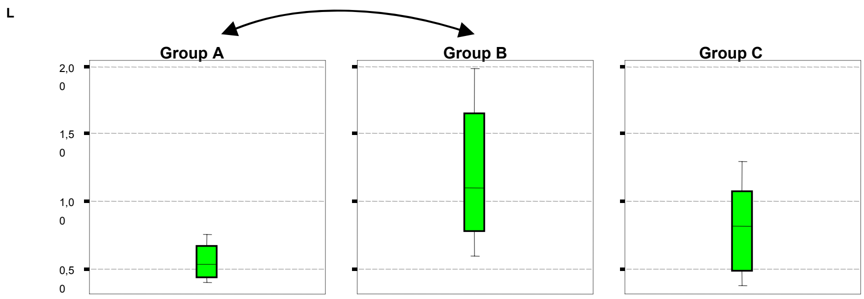
Mann-Whitney U	Group A *v* B	Group A *v* C	Group B *v* C
Significance	**0,003**	NS (0,074)	NS



MPT (sec) T0

Maximum phonation time during production of a sustained /a/ (sec)

Mann-Whitney U	Group A *v* B	Group A *v* C	Group B *v* C
Significance	**0,011**	NS	NS



EXPIRATORY VOLUME (L) T0

Expiratory volume during a sentence ("c'est une affaire interessante, qu'en pensez-vous?") (L)

Mann-Whitney U	Group A *v* B	Group A *v* C	Group B *v* C
Significance	**0,005**	NS	NS

Significance is marked by a (p<0.05)

Fig 8. Preoperative Acoustic and Aerodynamic Parameters, Group A, B and C; Glottic Gap (cc/dB/sec), Maximum Phonation Time (MPT, sec) and Expiratory Volume (L); (n= 8 subjects/group)

3.2.4. Perceptual Analysis (GRBAS score)

No statistically significant differences are found between the three groups among any of the judged voice qualities (p>0.05 in all cases). Nevertheless, the groups show different tendencies: While group A shows better and group B worse results in *grade*, *roughness*, *breathiness* and *asthenia* than the population mean, group C cannot be classified. The judgements of group C are evenly spread over the grades 0 to 3.

The *strain* (GRBAS) of the patients' voice was evaluated but not used for the following analysis: Only 1 patient's voice-strain is judged as mildly disturbed.

Annex 1 shows the results of the perceptual judgment of voice recordings.

3.3. Postoperative characteristics

3.3.1. Patient data

Table 7 shows postoperative (T1) data of the 24 patients. It contains the time interval between T1 and the postoperative assessment (in the following called "postoperative evolution"). Furthermore, the table shows the time interval between the last surgery (T1, T2 or T3) and the last follow up in the ENT department of Tenon's Hospital - in the following called "follow-up period".

Supplement data of group C (T2 compared to T3) are displayed in table 8: The T2-postoperative evolution, the T1 - T2-time interval (equal T2 - T3 for two patients), and the patient‘s age at T2 and T3.

TABLE 7. Patient postoperative data

Group	Case no.	T1-postoperative evolution (month)	last surgery-last follow up (months)
Group A	1	4	17
	2	3	10
	3	21	18
	4	4	4
	5	5	71
	6	64	64
	7	1	12
	8	6	13
Group B	9	3	3
	10	6	35
	11	3	3
	12	4	13
	13	18	18
	14	9	13
	15	3	11
	16	16	32
Group C	17	14	6
	18	19	12
	19	4	70
	20	3	9
	21	2	40
	22	1	34
	23	+	12
	24	20	79
MEAN		**10,1**	**25**
MEDIAN		**4**	**13**

+ no assessment available

TABLE 8. Group C, supplement postoperative data (T2/T3)

Group	Case no.	T1	T2	T3	T2-postoperative evolution (month)	T1-T2-time interval (month)	T2-T3-time interval (month)	Age T2 (years)	Age T3 (years)
Group C	17	Fat	Fat	TP	37	39	33	63	66
	18	Fat	TP	-	12	117	-	32	
	19	Fat	TP	Fat	+	12	22	52	55
	20	Fat	TP	-	9	29	-	45	
	21	Fat	TP	-	40	13	-	60	
	22	Fat	TP	-	34	3	-	36	
	23	Fat	TP	-	12	1	-	55	
	24	Fat	Fat	-	79	41	-	48	
MEAN					*32*	*32*		*49*	
MEDIAN					*34*	*21*		*50*	

Fat: fat injection; TP: thyroplasty

+ no assessment available

Group A

The timing of the postoperative evaluation ranges from 1 to 64 month, with a median of 4.5 month. The follow-up period of group A ranges from 3 to 64 month (median 16 months).

Group B

The timing of the postoperative evaluation ranges from 3 to 18 month, with a median of 5 month. The follow-up ranges from 3 to 35 months (median 13 months).

Group C

The timing of the postoperative evaluation of T1 ranges from 1 to 20 month, with a median of 4 month. The timing of the postoperative evaluation of T2 ranges from 9 to 79 month (median 34 month). The follow-up period ranges from 6 to 79 months (median 23 months).

The T1-T2 time interval is 21 month on average (median), it ranges from 1 to 117 month. The two patients with a T3 have a T2-T3 interval of 33 month (patient 17) and 22 month (patient 22).

The patient‘s age at T2 ranges from 32 to 63 years (median 50 years). The second treatment is in 2 cases a fat re-injection, and in 6 cases a medialization thyroplasty. Two patients receive a third treatment (T3), patient 17 a medialization thyroplasty (after fat injections in T1 and fat injections in T2, 66 years old at T3), and patient 19 a fat injection (after fat injection in T1 and medialization thyroplasty in T2, 55 years old at T3).

3.3.2. Fibroscopic assessment

The figure 9 (Fig 9.) shows the result of the postoperative fibroscopy.

In the postoperative assessment neither *larynx rotation*, nor *false vocal folds* and *glottic closure* are judged in any group as severely disturbed.

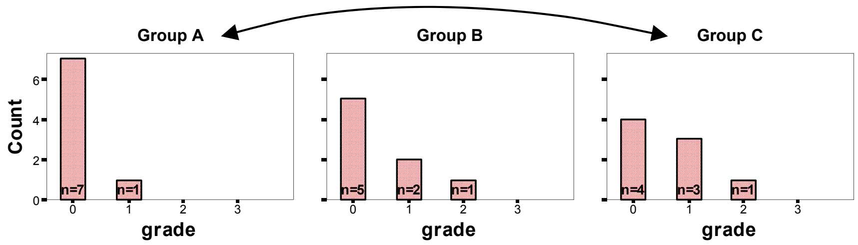
Seven patients (88%) of group A show a normal *larynx rotation* and only one patient presents a mild disturbance. In group B, 5 patients are judged as normal; 3 patients show a mild (n=2) or moderate rotation (n=1). The *larynx rotation* in group C is judged 4 times as normal, 3 times as mild and one time as moderate. The judgement of *larynx rotation* shows statistically significant differences between group A and C (p=0.027).

In group A, 3 patients do not present any *false vocal folds* (grade 0), while 3 patients show mild and two moderate *false vocal folds*. Group B presents 5 patients without, 2 patients with mild and one patient with moderate *false vocal folds*. Group C exhibited no moderate or severe ventricular folds closure; all 8 patients demonstrate normal (n=6) or mild (n=2) *false vocal folds*. The comparison of the results of *false vocal folds* shows no significantly different results between the three groups.

The *glottic closure* of group A and B shows in all cases a normal (n=5/n=6) or mild disturbance (n=3/n=2). In group C 4 patients are judged as normal, 2 as mildly and 2 as moderately disturbed. The assessment of the *glottic closure* shows no significantly different results between the three groups.

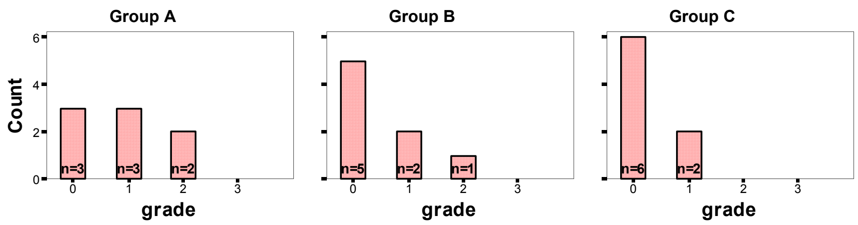
Fibroscopic assessment, POSTTREATMENT;

Group A (Fat Injection), Group B (Medialization thyroplasty), Group C (Revision)



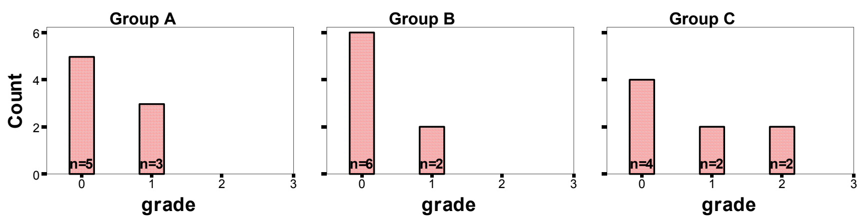
LARYNX ROTATION T1

Mann-Whitney U	Group A *v* B	Group A *v* C	Group B *v* C
Significance	NS	,027	NS



FALSE VOCAL FOLDS T1

Mann-Whitney U	Group A *v* B	Group A *v* C	Group B *v* C
Significance	NS	NS	NS



GLOTTIC CLOSURE T1

Mann-Whitney U	Group A *v* B	Group A *v* C	Group B *v* C
Significance	NS	NS	NS

Significance is marked by a ↶↷ ($p<0.05$)

Fig 9. Postoperative fibroscopic assessment, Group A, B and C: larynx rotation, false vocal folds and glottic closure assessed on a scale 0-3. (n= 8 subjects/group)

3.3.3. Acoustic and aerodynamic parameters

Postoperative acoustic and aerodynamic parameters are presented in table 9, summarized in table 10 and visualized in figure 10 (Fig 10.):

TABLE 9. Objective voice measurement after intervention for vocal folds paralysis (n = 24)

Case	**Group**	**Glottic Gap** (cc/dB/sec)	**MPT** (sec)	**Expiratory Volume** (L)
1	GROUP A	2,56	15	0,38
2		1,76	11,7	0,35
3		5,2	7,2	0,4
4		1,8	18	0,5
5		0,35	11,4	0,47
6		2,5	13	0,46
7		1,36	10,5	0,29
8		2,8	8,8	0,44
9	GROUP B	2	11,7	0,8
10		4	10,6	0,66
11		4,43	3,8	1,82
12		3,63	11,5	1,2
13		1,33	4,9	0,49
14		1,49	6,3	0,4
15		2,7	11	0,9
16		3,4	18,7	0,72
17	GROUP C	1,5	19	0,42
18		3,31	12	0,35
19		10,5	1,43	1,17
20		2,3	27	0,35
21		2,8	9,5	0,56
22		*	*	*
23		15,18	15	0,26
24		2,37	15	0,53
MEAN (SD)		**3.45 (±3.24)**	**11.87 (±5.6)**	**0.605 (±0.37)**
Median		**2,56**	**11,5**	**0,47**

**no available data*

The results of glottic gap in group A (mean=2.29 cc/dB/sec) and group B (mean=2.87 cc/dB/sec) are inferior to those of the population mean (mean=3.45 cc/dB/sec). Group C has more elevated results (mean=5.42 cc/dB/sec) than group A and B.

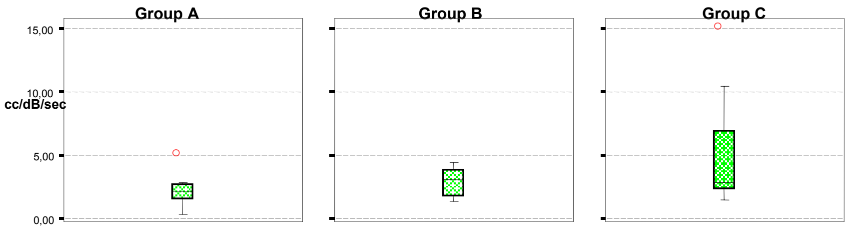
The population mean of the expiratory volume is 0.605 L. Group A's results (mean=0.411 L) are inferior, group B's results (mean=0.874 L) are superior (more disturbed) and the group's C results (mean=0.52 L) are statistically significant superior of group A and significantly inferior of group B. The comparison of the groups A and B shows only in the parameters of the expiratory volume significantly different results. (cf. Fig 10.).

The MPT of group A (11.95 sec) is similar to the population mean (11.87 sec). Group B presents with a MPT of 9.81 sec a less elevated result. The MPT of group C (14.13 sec) is longer than the mean and is the highest result of all groups.

TABLE 10. Objective voice measurements (mean and median value) after intervention for vocal folds paralysis (n = 23)

	GROUP A		**GROUP B**		**GROUP C**	
	Mean (SD)	Median	Mean (SD)	Median	Mean (SD)	Median
Glottic Gap (cc/dB/sec)	2.29 ±1.41	2,15	2.87 ±1.17	3,05	5,42 ±5.27	2,8
MPT (sec)	11.95 ±3.42	11,55	9.81 ±4.78	10,8	14.13 ±7.94	15
Expiratory Volume (L)	0.411 ±0.07	0,42	0.874 ±0.455	0,76	0.52 ±0.305	0,42

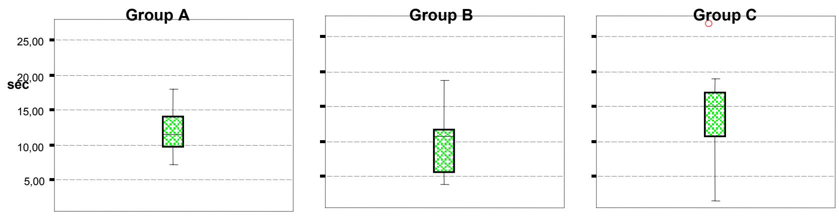
Acoustic and Aerodynamic Parameters, POSTTREATMENT;
Group A (Fat Injection), Group B (Medialization thyroplasty), Group C (Revision)



GLOTTIC GAP (cc/dB/sec) T1

Flow rate measured during production of a sustained /a/ (cc/dB/sec)

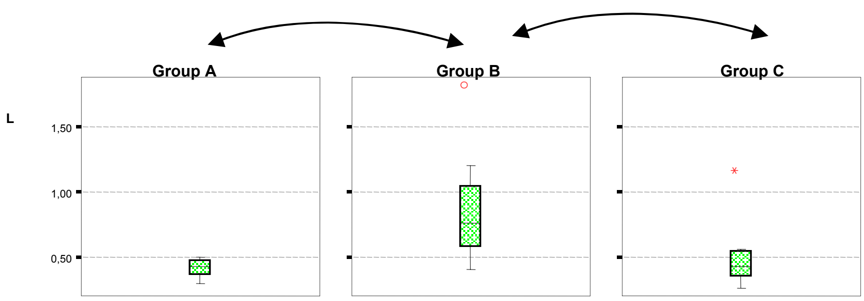
Mann-Whitney U	Group A *v* B	Group A *v* C	Group B *v* C
Significance	NS	NS	NS



MPT (sec) T1

Maximum phonation time during production of a sustained /a/ (sec)

Mann-Whitney U	Group A *v* B	Group A *v* C	Group B *v* C
Significance	NS	NS	NS



EXPIRATORY VOLUME (L) T1

Expiratory volume during a sentence ("c'est une affaire interessante, qu'en pensez-vous?")(L)

Mann-Whitney U	Group A *v* B	Group A *v* C	Group B *v* C
Significance	0,005	NS	0,049

Significance is marked by a ↶↷ (p<0.05)

Fig 10. Postoperative acoustic and aerodynamic parameters, Group A, B and C; glottic gap (cc/dB/sec), maximum phonation time (MPT, sec) and expiratory volume (L); (n= 8 subjects/Group)

3.3.4. Perceptual analysis (GRBAS score)

All patients of group A achieve at least a mildly disturbed (n=5) or normal (n=3) grade. The results of group B and C are evenly spread over the grades 0 to 3. The results of the judgment of *roughness*, *breathiness* and *asthenia* are correlating in the three groups. All patients of group A show a normal or mildly disturbed *roughness*, *breathiness* and *asthenia* of their voice. The judgments of *roughness*, *breathiness* and *asthenia* of group B and C are evenly spread over the grades 0 to 3.

No statistically significant differences are found between the three groups among any of the judged quality of voice (p>0.05 in all cases). The postoperative results of patients' *strain* is not analyzed: All patients' *strain* are judged as normal.

Annex 2 shows the results of the perceptual judgment GRBAS of postoperative voice recordings.

3.4. T0-T1 Comparison

3.4.1. Fibroscopic assessment

Group A

Postoperatively none of the patients present a *larynx rotation*; all 8 subjects achieve a normal result. Compared with the preoperative fibroscopy results, *larynx rotation* improved in 4 cases (50%) and remained unchanged in 4 patients (50%) (p=0.034). *False vocal folds* improved in 6 cases (75%) and remained unchanged or worsened in 2 cases (p=0.047), 5 patients achieved a normal result.

Postoperative *glottic closure* improved in 6 cases (75%) and remained unchanged in 2 cases, 6 subjects achieved a normal result (p=0.008).

All changes are statistically significant.

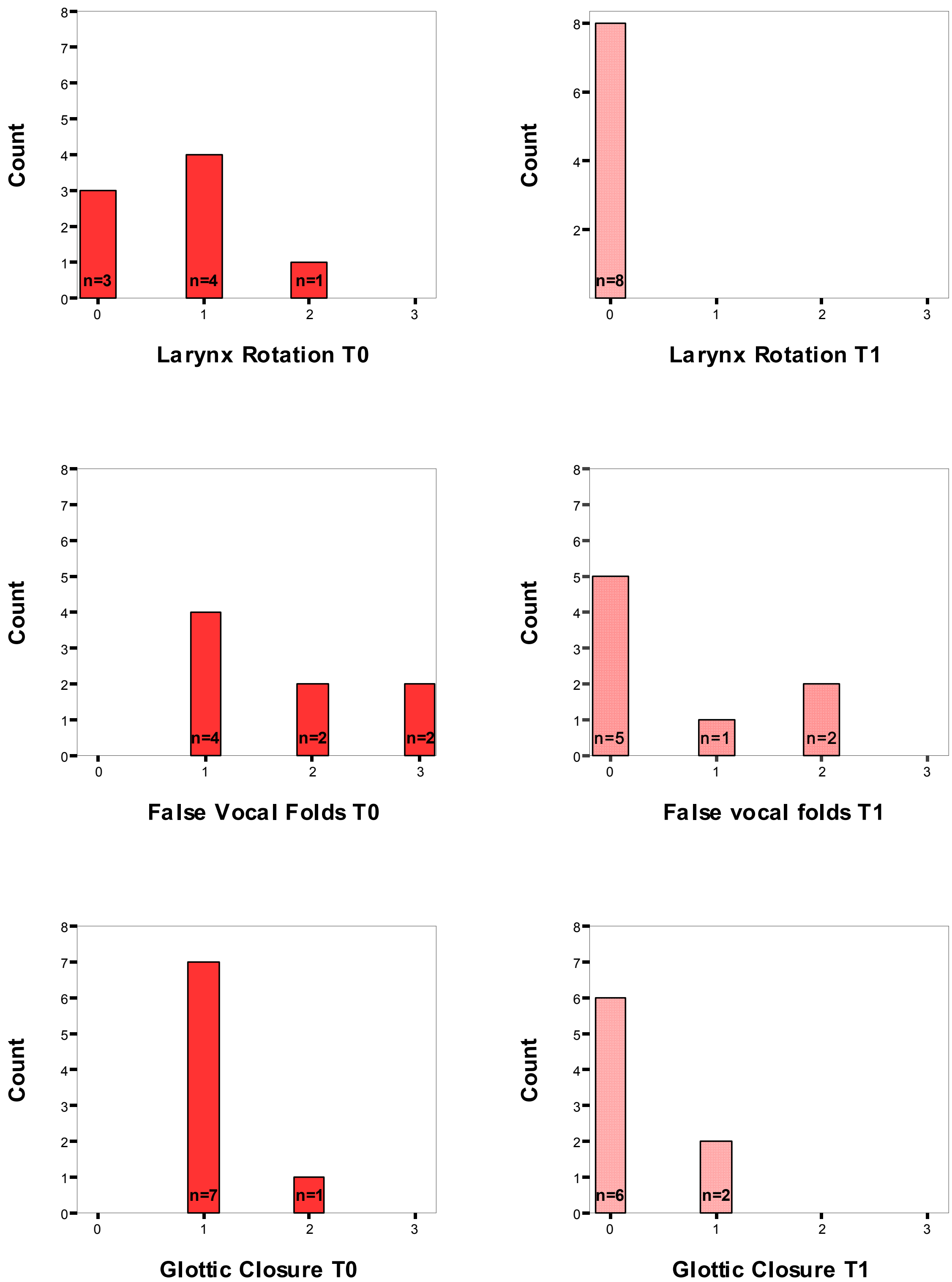


Fig 11. Group A, Fibroscopic assessment T0-T1: larynx rotation, false vocal folds, glottic closure assessed on a scale 0 to 3. (n= 8 subjects/group)

TABLE 11. Group A T0-T1

Wilcoxon Signed Ranks Test	Larynx rotation T0 - Larynx rotation T1	False vocal folds T0 - False vocal folds T1	Glottic closure T0 - Glottic closure T1
Z	-2,121(a)	-1,983(a)	-2,646(a)
Significance	0,034	0,047	0,008

Group B

Compared with the preoperative fibroscopy results, postoperative *larynx rotation* improved in 7 cases (88%) and remained unchanged in 1 patient. 5 patients achieved grade 0.

False vocal folds improved in 6 cases (75%) and remained unchanged in 2 cases, 5 patients presented a normal result.

Glottic closure improved in 6 cases (75%) and remained unchanged or worsened in 2 cases. A normal result was achieved in 6 patients.

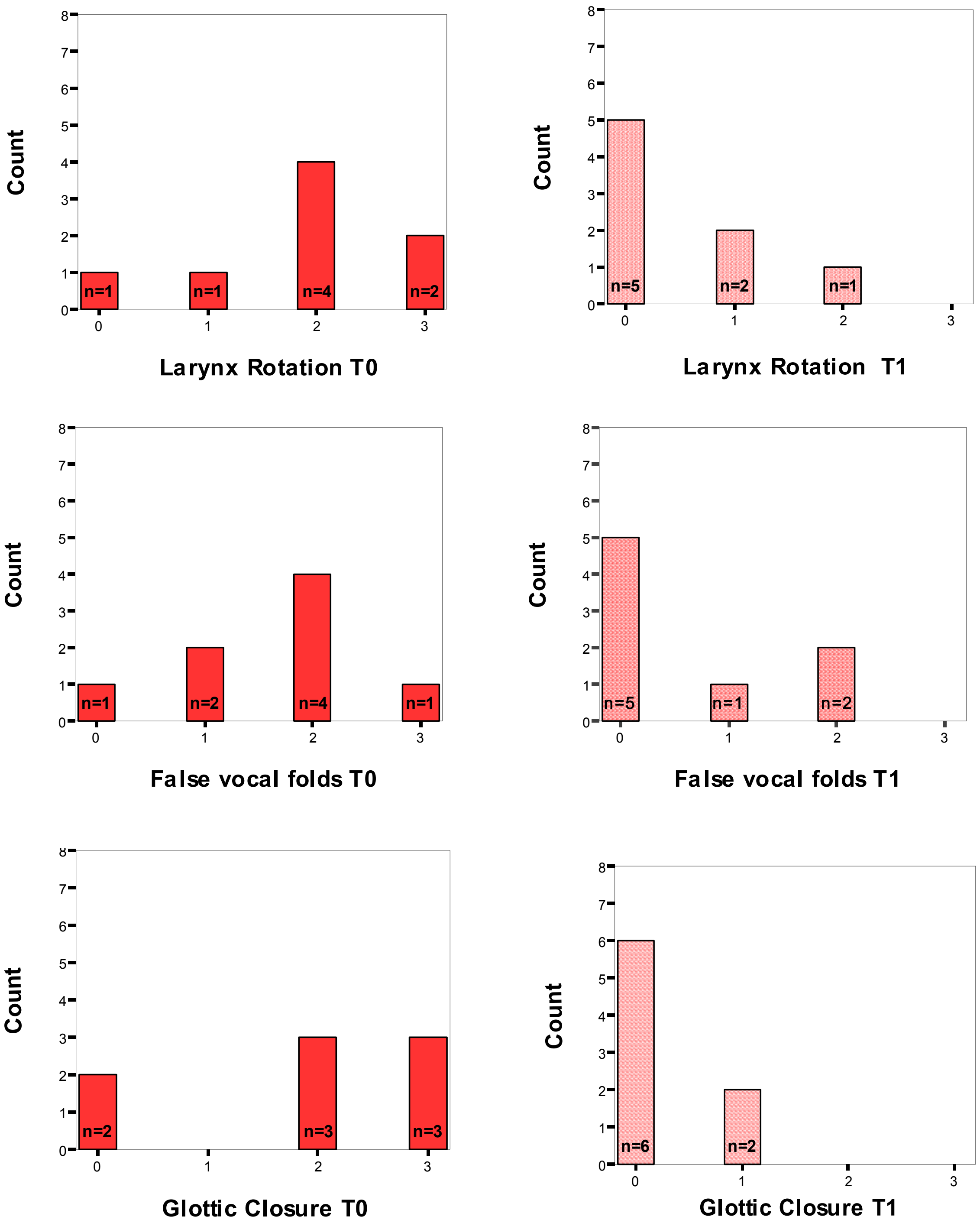


Fig 12. Group B, Fibroscopic assessment T0-T1: larynx rotation, false vocal folds, glottic closure assessed on a scale 0-3. (n= 8 subjects/group)

TABLE 12. Group B T0-T1

Wilcoxon Signed Ranks Test	Larynx rotation T0 - Larynx rotation T1	False vocal folds T0 - False vocal folds T1	Glottic closure T0 - Glottic closure T1
Z	-2,414(a)	-2,251(a)	-2,136(a)
Significance	0,016	0,024	0,033

Group C

T0-T1

Compared to the preoperative fibroscopy results, *larynx rotation* improved in all cases (100%). 4 patients achieved a normal result. This improvement shows statistically significance between T0-T1 (p=0.009).

False vocal folds improved in 2 cases, remained in 4 cases unchanged and became more important in 2 cases. Both in T0 and in T1 6 out of 8 patients did not present *false vocal folds*. *Glottic closure* improved in 6 cases (75%) and remained unchanged (n=1) or worsened (n=1) in 2 cases. A normal result was achieved by 4 patients.

The judgement of *false vocal folds* and *glottic closure* shows no statistically significant differences between T0 and T1.

T1-T2

Comparing the results of T1 and T2, *larynx rotation* improved in 7 patients and remained unchanged in 1 case.

2 patients present in T2 less *false vocal folds* than in T1, 5 show the identical result (4 of them grade 0) and 1 patient became more important *false vocal folds* in T2.

In T2 all 8 patients showed a better result in *glottic closure* than in T1. There is no statistically difference between T1 and T2.

T0-T2

Compared with the T0 fibroscopy results, the *larynx rotation* improved in T2 in 7 cases (88%), and worsened in 1 case (statistically significant difference (p=0.014)). 3 patients achieved grade 0.

False vocal folds improved in 1 case, remained unchanged in 5 cases and became more important in 2 cases (p=NS).

Postoperative *glottic closure* improved in all 8 cases (100%). 6 of them show a normal result. This improvement is statistically significant (p=0.009).

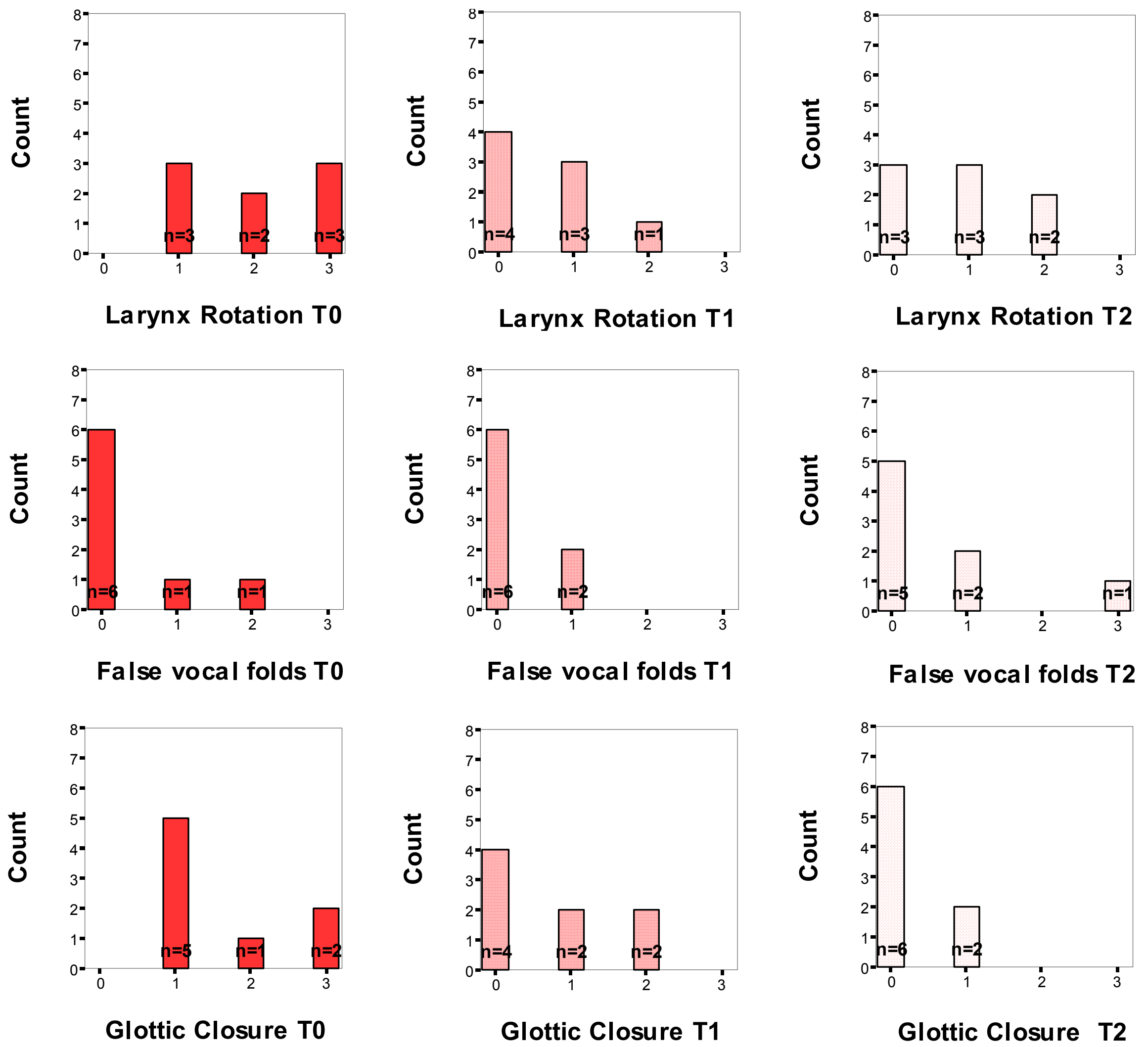


Fig 13. Group C, Fibroscopic assessment T0-T1-T2: larynx rotation, false vocal folds, glottic closure assessed on a scale 0-3. (n= 8 subjects/group)

TABLE 13. Group C T0-T1

Wilcoxon Signed Ranks Test	Larynx rotation T0 - Larynx rotation T1	False vocal folds T0 – False vocal folds T1	Glottic closure T0 – Glottic closure T1
Z	-2,598(a)	-0,378(a)	-1,933(a)
Significance	0,009	NS	NS (0,053)

TABLE 14. Group C T1-T2

	Larynx rotation T1- Larynx rotation T2	False vocal folds T1 – False vocal folds T2	Glottic closure T1 – Glottic closure T2
Z	-1,414	0,816	-1,633
Significance	NS (0,157)	NS (0,414)	NS (0,102)

TABLE 15. Group C T0-T2

	Larynx rotation T0- Larynx rotation T2	False vocal folds T0 – False vocal folds T2	Glottic closure T0 – Glottic closure T2
Z	-2,46 (a)	-0,535(b)	-2,598(a)
Significance	0,014	NS	0,009

3.4.2. Acoustic and aerodynamic parameters

Group A

T0-T1

Comparing the objective voice measurements of T0 and T1, all parameter improved: Glottic gap decreased from 3.01 cc/dB/sec to 2.29 cc/dB/sec (all means), MPT improved from 10.3 sec to 12 sec, and expiratory volume decreased from 0.56 L to 0.411 L. The expiratory volume is the only parameter that changed statistically significant (p=0.017).

TABLE 16. Group A - Objective voice measurements - T0, T1 (n=8)

Group	Case no.	**Glottic Gap** (cc/dB/sec)		**MPT** (sec)		**Expiratory Volume** (L)	
		T0	T1	T0	T1	T0	T1
GROUP A	1	1,54	2,56	15	15	44	0,38
	2	3,74	1,76	7,2	11,7	5	0,35
	3	2,90	5,2	9,5	7,2	7	0,4
	4	2,93	1,8	15	18	58	0,5
	5	4,23	0,35	5	11,4	76	0,47
	6	2,48	2,5	15	13	44	0,46
	7	0,83	1,36	10,5	10,5	4	0,29
	8	5,40	2,8	5,2	8,8	63	0,44

TABLE 17. Group A - Objective Voice Measurements (Mean and Median Values) T0-T1 (n=8)

GROUP A	**T0**		**T1**		**Comparison Wilcoxon signed rank test**
	Mean (SD)	Median	Mean (SD)	Median	
Glottic Gap (cc/dB/sec)	3.01 ± 1.5	2,92	2.29 ±1.41	2,15	NS
MPT (sec)	10.3 ±4.32	10	12 ±3.42	11,55	NS
Expiratory Volume (L)	**0.56 ± 0.13**	**0,54**	**0.411 ±0.07**	**0,42**	⬂ **p = 0.017**

Note: ⬂ = significant decrease; ⬀ = significant increase; NS: not significant; {⬀}:limit of significant increase

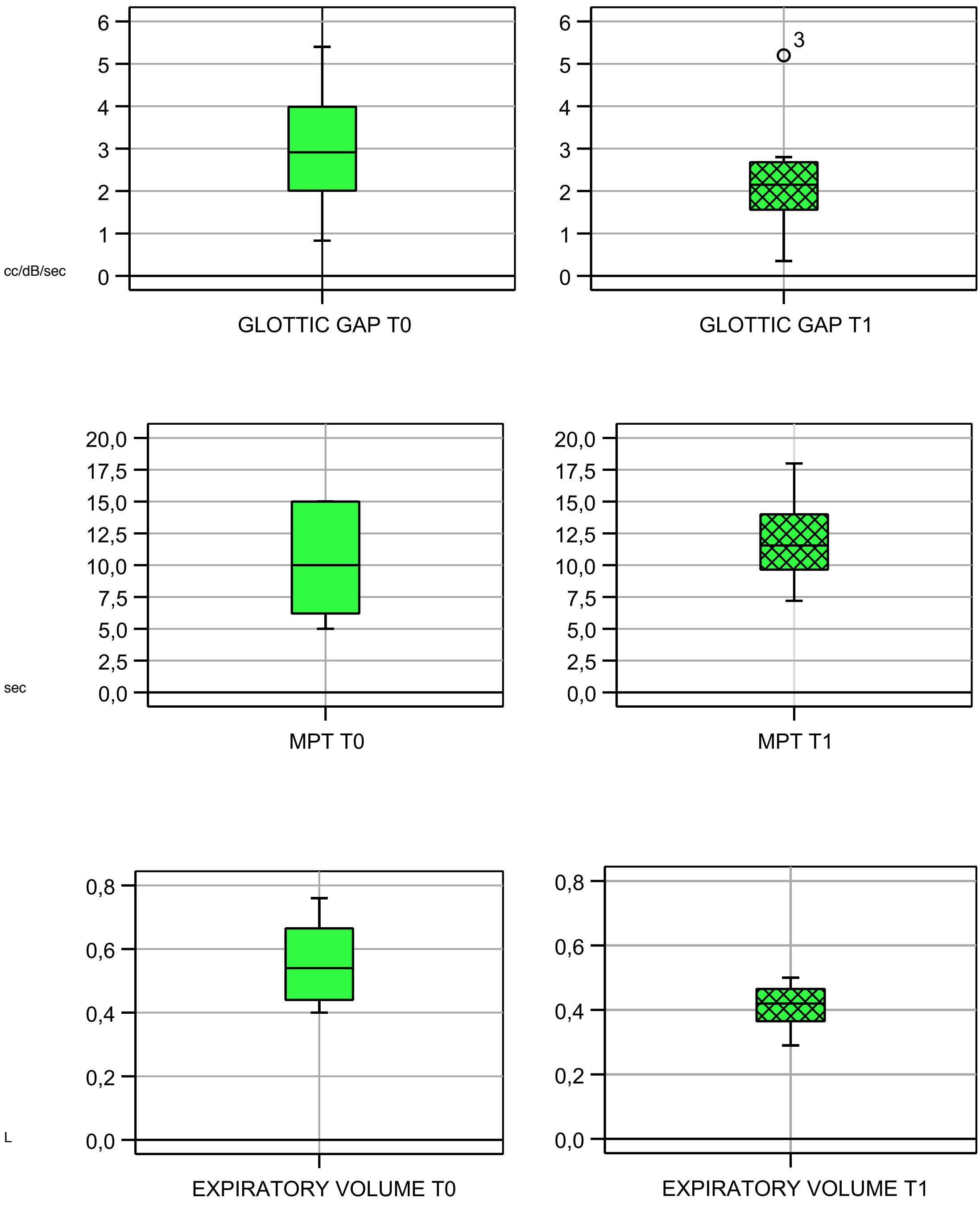


Fig 14. Group A, Acoustic and Aerodynamic Parameters T0-T1; Glottic Gap (cc/dB/sec), Maximum Phonation Time (MPT, sec) and Expiratory Volume (L); (n= 8 subjects/group)

Group B

T0-T1

Compared to the preoperative fibroscopy results all parameters improved in T1. The measurements of glottic gap decreased from 7.61 cc/dB/sec to 2.87 cc/dB/sec, MPT improved from 4.48 sec to 9.81 sec, and expiratory volume decreased from 1.2 L to 0.87 L (all means). The improvements of glottic gap (p=0.012) and MPT (0.012) are statistically significant.

TABLE 18. Group B- Objective voice measurements - T0, T1 (n=8)

Group	Case no.	**Glottic Gap** (cc/dB/sec)		**MPT** (sec)		**Expiratory Volume** (L)	
		T0	**T1**	**T0**	**T1**	**T0**	**T1**
	9	7,00	2	3	11,7	1,2	0,8
	10	5,00	4	8,6	10,6	0,65	0,66
	11	4,50	4,43	2	3,8	1,8	1,82
	12	6,70	3,63	4,7	11,5	1,5	1,2
GROUP B	13	6,70	1,33	1,4	4,9	1	0,49
	14	8,30	1,49	3	6,3	0,9	0,4
	15	18,80	2,7	1,8	11	1,98	0,9
	16	3,90	3,4	11,3	18,7	0,6	0,72

TABLE 19. Group B - Objective Voice Measurements (Mean and Median Values) T0-T1 (n=8)

GROUP B	**T0**		**T1**		**Comparison Wilcoxon signed rank test**
	Mean (SD)	Median	Mean (SD)	Median	
Glottic Gap (cc/dB/sec)	**7.61 ±4.8**	**6,7**	**2.87 ±1.17**	**3,05**	⇘ **p = 0.012**
MPT (sec)	**4.48 ±3.6**	**3**	**9.81 ±4.78**	**10,8**	⇗ **p = 0.012**
Expiratory Volume (L)	1.2 ±0.51	1,1	0.874 ±0.46	0,76	NS

Note: ⇘ = significant decrease; ⇗ = significant increase; NS: not significant; {⇗}:limit of significant increase

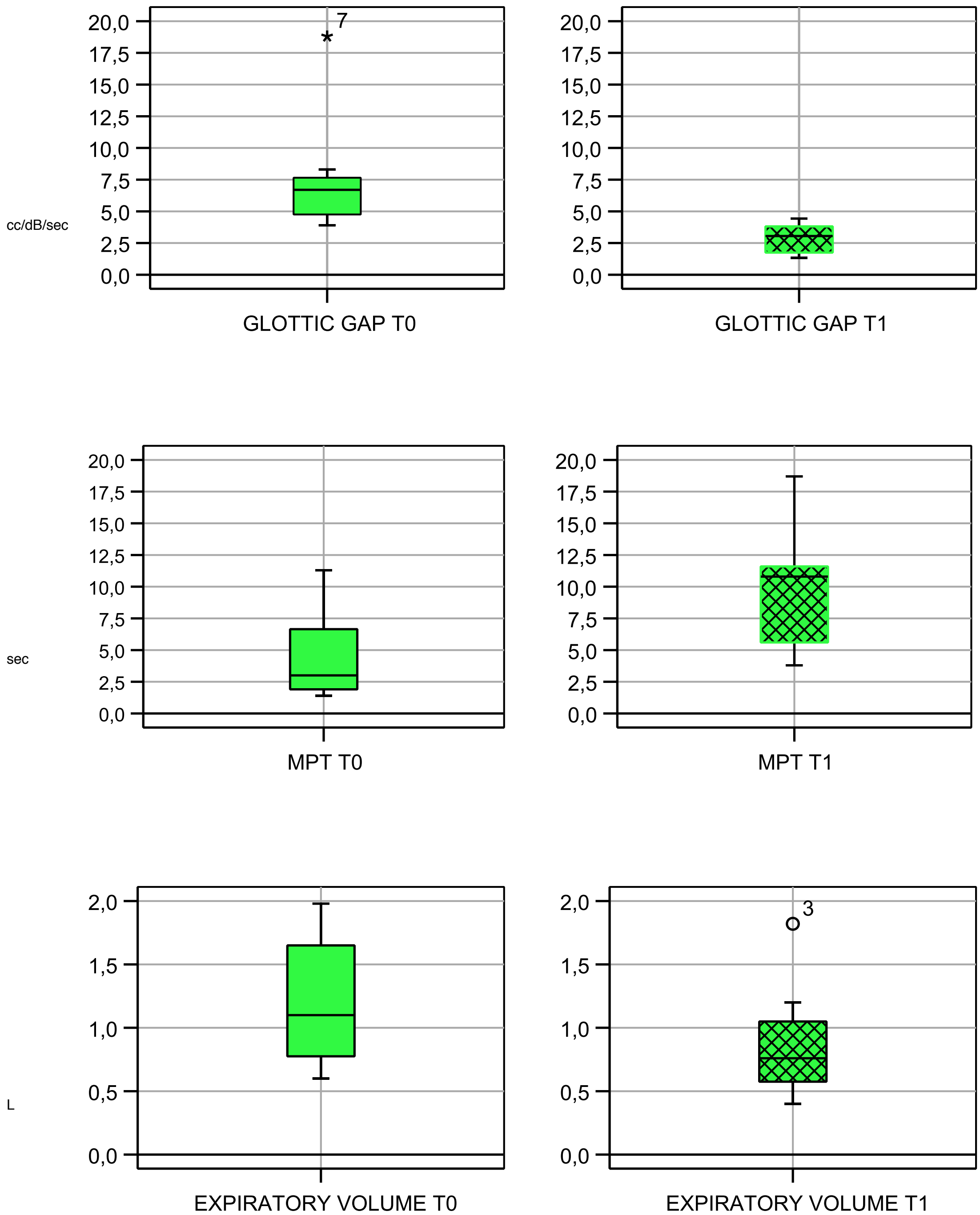


Fig 15. Group B, Acoustic and Aerodynamic Parameters T0-T1; Glottic Gap (cc/dB/sec), Maximum Phonation Time (MPT, sec) and Expiratory Volume (L); (n= 8 subjects/group)

Group C

T0-T1

Compared to the fibroscopy results of T0, all parameters improved in T1: Glottic gap decreased from 9.18 cc/dB/sec to 5.42 cc/dB/sec (all means), MPT improved from 8.19 sec to 14.13 sec, and expiratory volume decreased from 0.81 L to 0.52 L. The improvement of MPT is statistically significant, the significance of the decrease of expiratory volume is limited (p=0.063)

T1-T2

The improvements from T1-T2 are not statistically significant. Nevertheless, a decrease of glottic gap from 5.42 cc/dB/sec to 3.01 cc/dB/sec, a decrease of the MPT from 14.13 sec to 12.08 sec and an identical (0.5 L) expiratory volume are notable.

T0-T2

Comparing the results of T0 and T2, all parameters improved in T2.

Glottic gap decreased from 9.18 cc/dB/sec to 3.01 cc/dB/sec, MPT improved from 8.19 sec to 12.08 sec, and expiratory volume decreased from 0.81 L to 0.5 L (all means)

The decrease of glottic gap is statistically significant (p=0.018), the significance of the decrease of expiratory volume is limited (p=0.063)

TABLE 20. Group C Objective voice measurements - T0, T1, T2 (n=8)

Group	Case no.	**Glottic Gap** (cc/dB/sec)			**MPT** (sec)			**Expiratory Volume** (L)		
		T0	T1	T2	T0	T1	T2	T0	T1	T2
GROUP C	17	1,75	1,5		14,0	19		0,5	0,42	
	18	*20,43*	3,31		3,7	12		1,3	0,35	
	19	6,52	10,5		4,3	1,43		1,20	1,17	
	20	3,10	2,3		18,0	27		0,38	0,35	
	21	3,60	2,8		6,0	9,5		0,85	0,56	
	22	3,64	*		15,0	*		0,47	*	
	23	10,34	15,18		2,6	15		0,96	0,26	
	24	*26,42*	2,37		1,9	15		0,78	0,53	

* DATA LOST

TABLE 21. Group C Objective Voice Measurements (Mean and Median Values) T0-T1-T2 (n=8)

GROUP C	**TO**		**T1**		**T2**	
	Mean (SD)	Median	Mean (SD)	Median	Mean (SD)	Median
Glottic Gap (cc/dB/sec)	9.18 ±9.15	5,08	5.42 ±5.27	2,8	3.01 ± 1.26	2,62
MPT (sec)	**8.19 ±6.41**	**5,15**	14.13 ±7.94	15	12.08 ±4.32	10,3
Expiratory Volume (L)	**0.81 ±0.34**	**0,82**	0.52 ±0.305	0,42	0.5 ±0.27	0,4

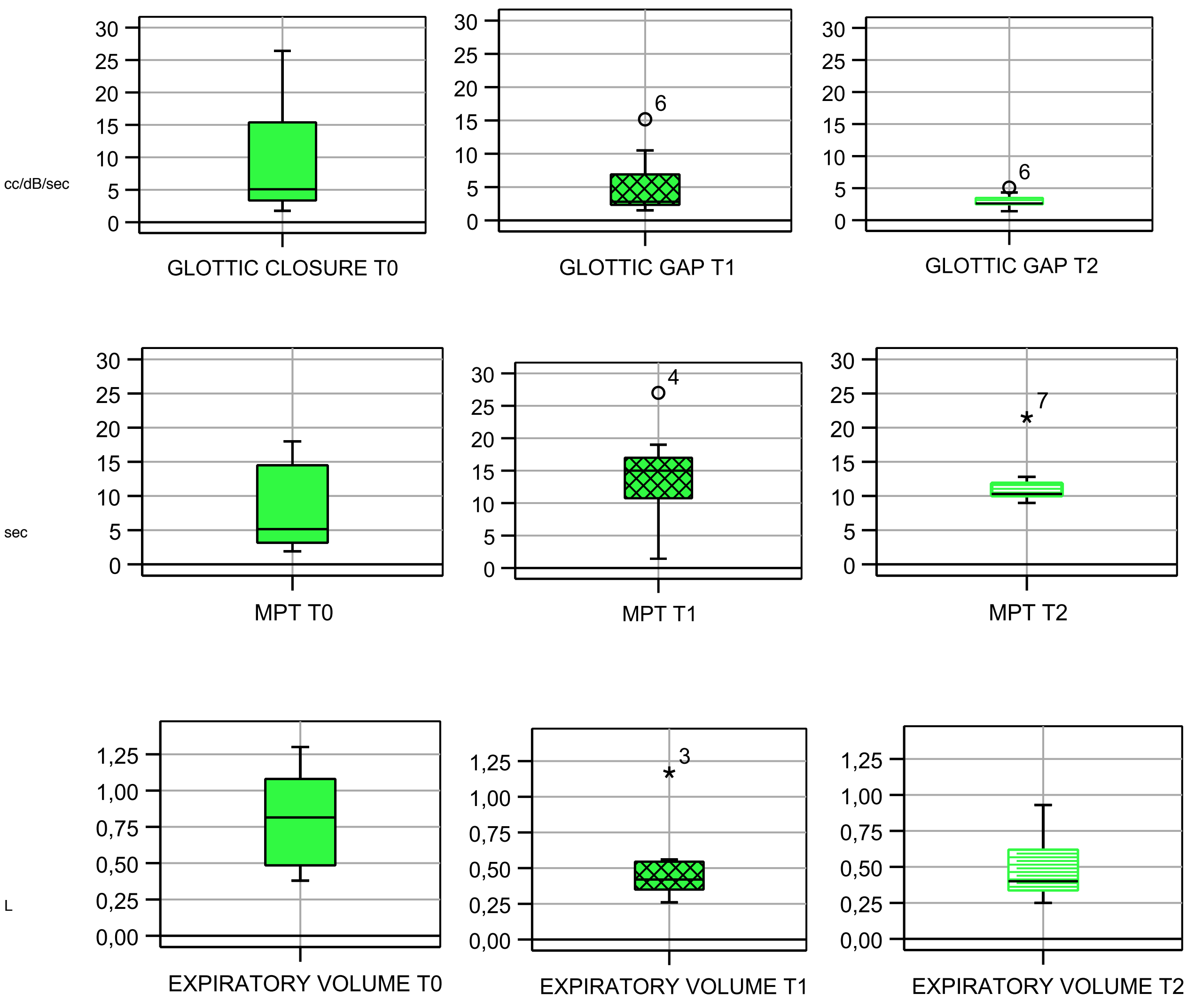


Fig 16. Group C, Acoustic and Aerodynamic Parameters T0-T1-T2; Glottic Gap (cc/dB/sec), Maximum Phonation Time (MPT, sec) and Expiratory Volume (L); (n= 8 subjects/group)

TABLE 22. Group C Wilcoxon signed rank test T0-T1, T1-T2, T0-T2

	Comparison Wilcoxon signed rank test		
	TO-T1	**T1-T2**	**T0-T2**
Glottic Gap (cc/dB/sec)	NS	NS	**⇘ p = 0.018**
MPT (sec)	**⇗ p = 0.012**	**{⇘} p = 0.08**	NS
Expiratory Volume (L)	**{⇘} p = 0.063**	NS	**{⇘} p = 0.063**

Note: ⇘ = significant decrease; ⇗ = significant increase; NS: not significant; {⇘}:limit of significant decrease

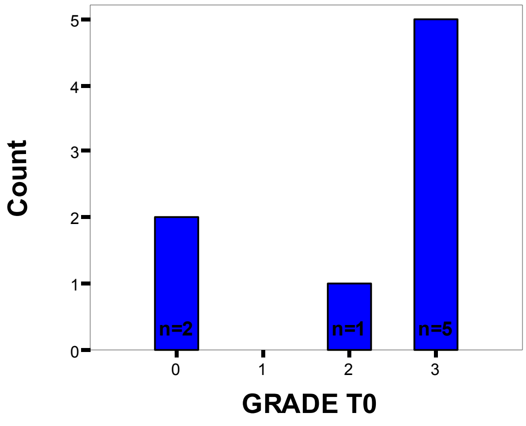
3.4.3. Perceptual analysis (GRBAS score)

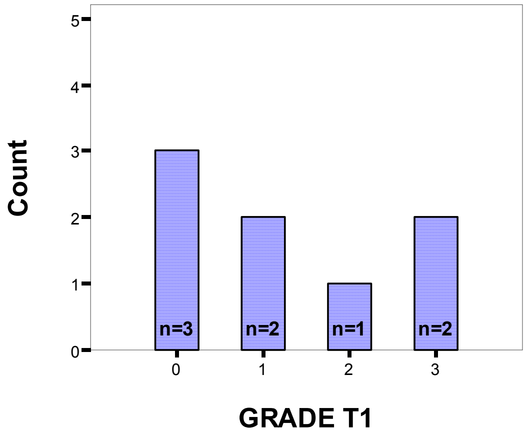
Group A

Compared to the GRBAS of T0, the grade improved in 5 cases (63%) and remained unchanged in 3 patients (p=0.034). Postoperatively, all 8 patients achieved a normal or mildly disturbed judgement of the *grade*.

The judgment of *roughness* improved in 2 cases, remained unchanged in 5 patients and worsened in 1 case; 7 patients achieved a normal result.

Both *breathiness* and *asthenia* improved in T1 in 4 cases and remained unchanged in 4 cases; 6 subjects achieved a normal *breathiness* (p=0.059), 4 a normal *asthenia*.





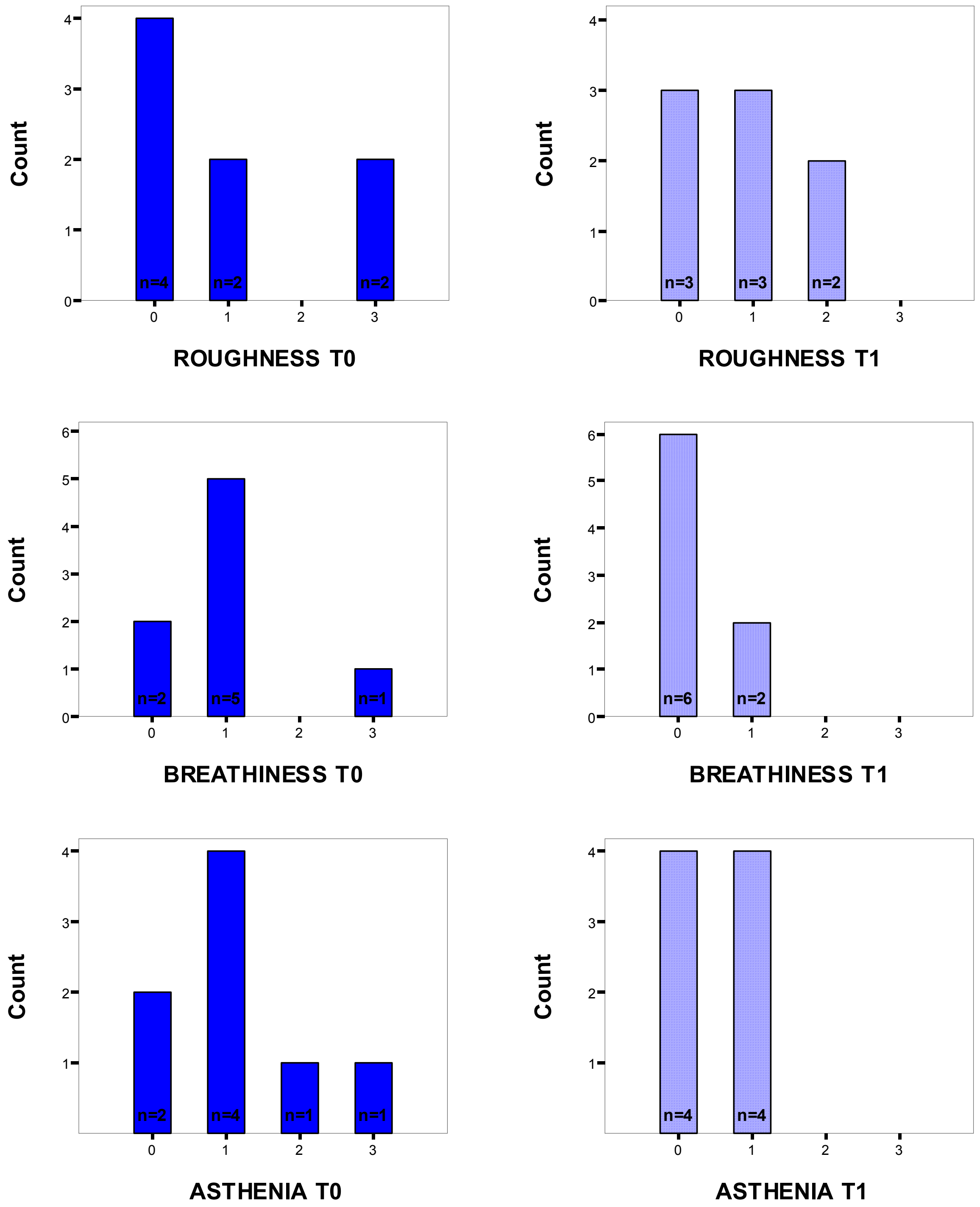


Fig 17. Group A, GRBAS Perceptual Voice Assessment T0-T1; *Grade, Roughness, Breathiness* and *Asthenia* judges on a scale 0-3; (n= 8 subjects/group)

TABLE 23. Group A T0-T1

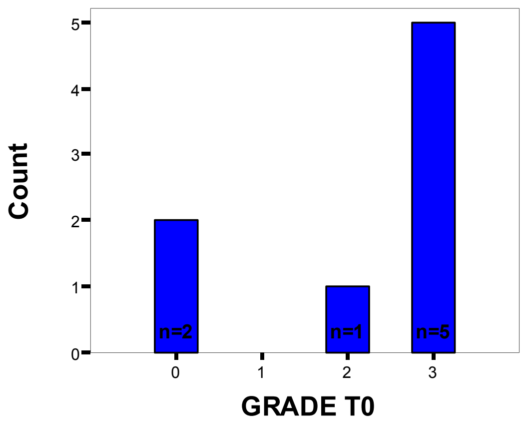
Wilcoxon Signed Ranks Test	grade T0 - grade T1	roughness T0 - roughnessT1	breathiness T0 - breathiness T1	asthenia T0 - asthenia T1
Z	-2,121(a)	-,816(a)	-1,890(a)	-1,633(a)
Significance	0,034	NS	NS (0,059)	NS

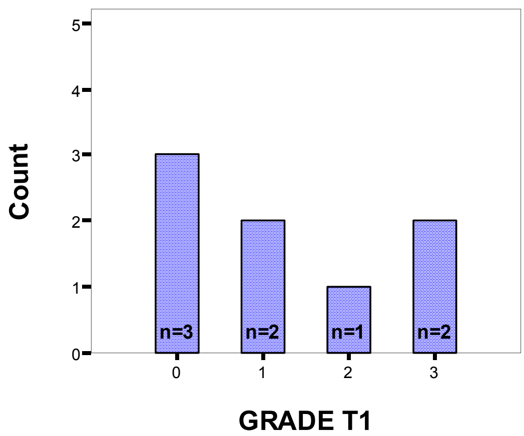
Group B

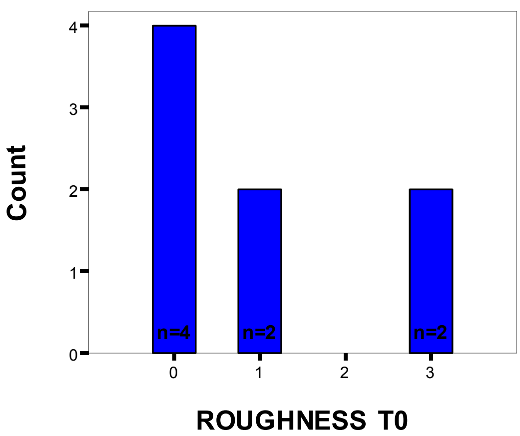
Comparing the *grade* T0 to T1, the *grade* improved in 4 patients and remained stable in 4 case (p=0.059).

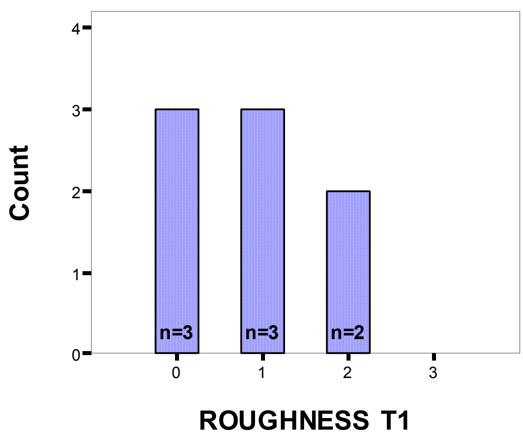
The *roughness* improved in 2 cases, remained unchanged in 4 patients and worsened in 2 cases.

Both *breathiness* and *asthenia* improved in 5 cases and remained unchanged in 3 patients; 7 patients achieved a normal or mildly disturbed *breathiness* (p=0.034) and *asthenia* (p=0.041). Only one patient presented a grade 3 in both *asthenia* and *breathiness*.









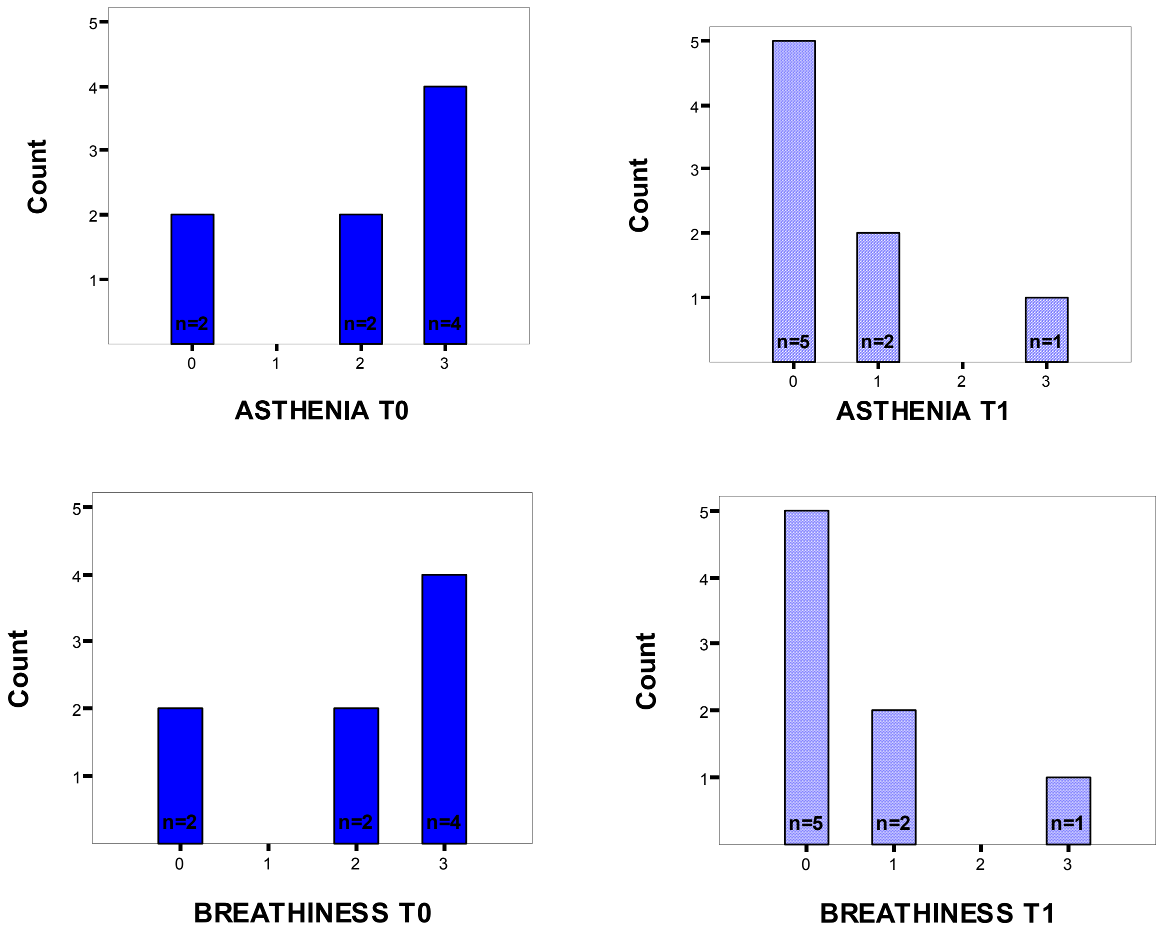


Fig 18. Group B, GRBAS Perceptual Voice Assessment T0-T1; Grade, Roughness, Breathiness and Asthenia judges on a scale 0-3; (n= 8 subjects/group)

TABLE 24. Group B T0-T1

Wilcoxon Signed Ranks Test	grade T0 – grade T1	roughness T0 - roughnessT1	breathiness T0 - breathiness T1	asthenia T0 - asthenia T1
Z	-1,890(a)	-,378(a)	-2,121(a)	-2,041(a)
Significance	NS (0,059)	NS	0,034	0,041

Group C

T0-T1

Compared to the GRBAS assessment of T0, the *grade* improved in 2 cases, remained unchanged in 5 patients and worsened in 1 case.

The *roughness* improved in 4 cases, remained unchanged in 3 patients and worsened in 1 case; 5 patients achieved a normal result.

Breathiness improved in 2 cases, remained unchanged in 5 case and worsened in 1 patient.

Asthenia improved in 3 cases, remained unchanged in 3 patients and worsened in 2 cases.

T1-T2

Comparing the results of T1 to T2, *grade* improved in 3 patients, remained unchanged in 1 case and worsened in 4 cases.

The *roughness* improved in 1 case, remained unchanged in 4 patients and worsened in 3 cases; 5 patients achieved a normal result.

Breathiness improved and remained unchanged in each case in 3 patients and worsened in 2 cases; 5 patients achieved a normal result.

Asthenia improved in 3 cases, remained unchanged in 1 and worsened in 4 patients.

T0-T2

Compared with the GRBAS of T0, the *grade* improved in T2 in 4 cases, remained unchanged in patients and worsened in in 2 cases.

The *roughness* improved in 3 cases, remained unchanged in 4 patients and worsened in 1 case; 5 patients achieved a normal result.

Both *breathiness* and *asthenia* improved in 5 cases, remained unchanged in 2 patients and worsened in 1 case; 5 patients achieved a normal *breathiness*.

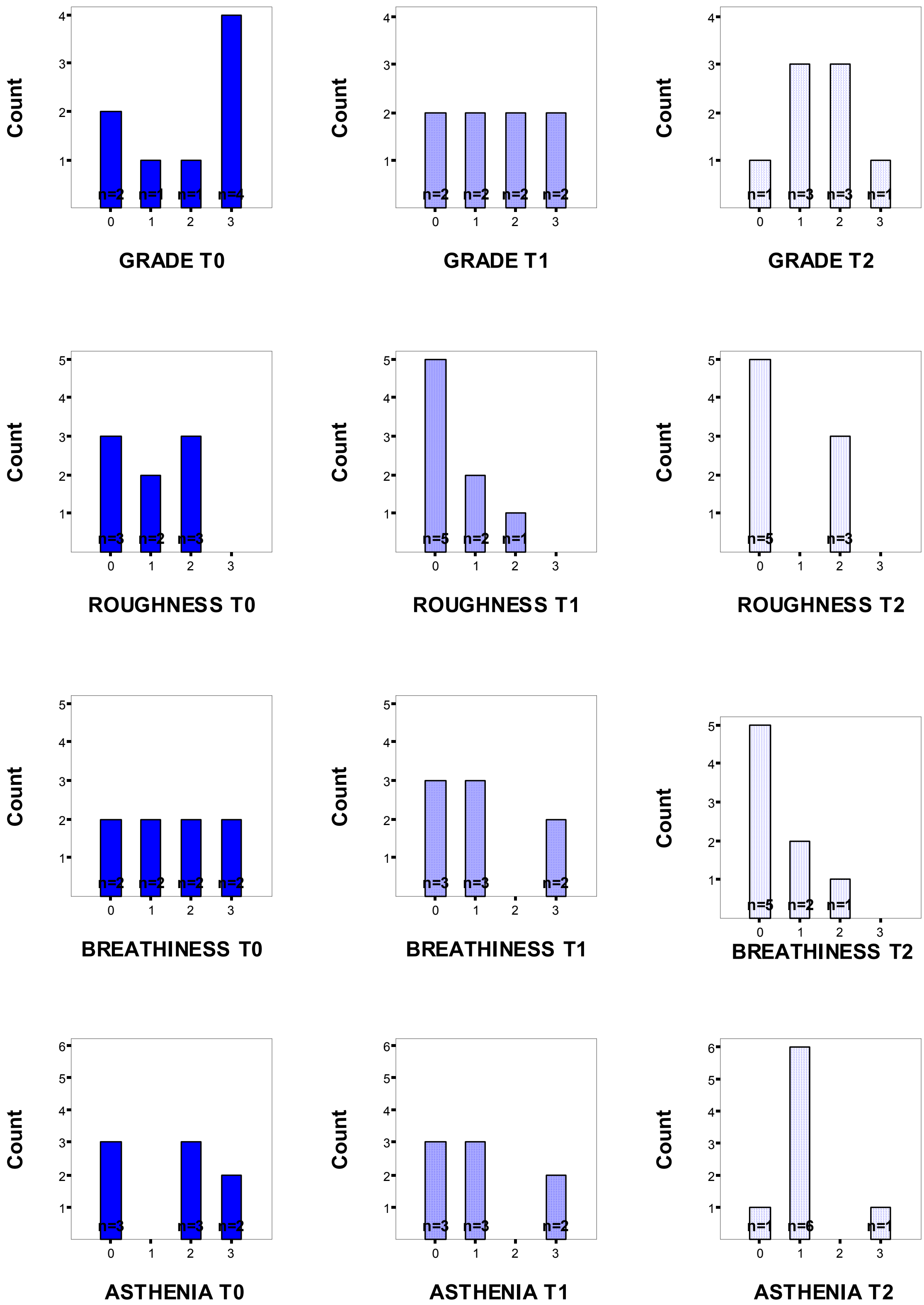


Fig 19. Group C, GRBAS perceptual voice assessment T0-T1-T2; Grade, Roughness, Breathiness and Asthenia judges on a scale 0-3; (n= 8 subjects/group)

TABLE 25. Group C TO-T1

Wilcoxon Signed Ranks Test	grade T0 - grade T1	roughness T0 - roughnessT1	breathiness T0 - breathiness T1	asthenia T0 - asthenia T1
Z	-1,089(a)	-1,414(a)	-1,089(a)	-,966(a)
Significance	NS	NS	NS	NS

TABLE 26. Revision T2-T3

Wilcoxon Signed Ranks Test	grade T1 - grade T2	roughness T1 – roughness T2	breathiness T1- breathiness T2	asthenia T1- asthenia T2
Z	-,215(a)	-,846(a)	-,649(a)	-,087(a)
Significance	NS	NS	NS	NS

TABLE 27. Revision TO-T2

Wilcoxon Signed Ranks Test	grade T0 - grade T2	roughness T0 – roughness T2	breathiness T0 - breathiness T2	asthenia T0 - asthenia T2
Z	-,750(a)	-,557(a)	-1,807(a)	-1,000(a)
Significance	NS	NS	NS (0,071)	NS

3.4.4. VHI-self assessment

Group C self assessed their voice after the last intervention with the VHI-10 and 5 supplement questions concerning their voice. (Annex 3: Questionnaire, “Autoévaluation vocale”).

Six out of 8 patients confirm, that they have moderate difficulties with their voice (grade 2 on a scale 0-4 (4=highest degree of confirmation)). 6 out of 8 patients do not wish further treatments with a speech-pathologist. 3 of the patients do not want another surgical intervention and only one of the 8 patients is demanding another surgery. 6 out of 8 patients deny, that T1 was not without effect. 5 out of 8 patients negate, that the second intervention was ineffective.

4. DISCUSSION

This study compares the pre- and postoperative results of medialization of unilateral vocal fold paralysis, using two common techniques, fat injection and medialization thyroplasty. A total of 24 selected patients who had undergone medialization are analyzed. 8 of them are treated with a fat injection, 8 with medialization thyroplasty and 8 underwent a revision of a fat injection.

There are two therapeutic goals of medialization: The first is to restore normal phonatory function, the second to improve swallowing. This is especially important in patients exhibiting aspiration. Several surgical techniques are known to treat UVFP. The surgery is usually following a therapy with a speech pathologist, that did not lead to a satisfactory result. Fat injection and medialization thyroplasty are the most common surgical techniques used in Europe.

However, the question which one of the common procedures is the appropriate approach to treat UVFP remains difficult to answer. The indications for each treatment are not well defined. Choosing the right technique is important in a time of evidence based medicine, both for the patients' satisfaction and the reduction of health-care costs by avoiding revision surgery.

There were two major aims of this study: The first was to analyze if a more precise indication for fat injection or medialization thyroplasty could achieve better results for patients with UVFP. This could help reducing the rate of patients needing a revision. The second objective was to analyze when a revision is justified and recommendable. This question is important to avoid unnecessary revision, that are leading to no amelioration and in some cases even aggravation of the results.

4.1. Population

4.1.1. Age and sex

The frequency of UVFP increases with the patients‘ age. The increased incidence of cancer and neurological disorders may likely be a reason (81, 82). In this study, the number of patients is relatively high in the 4th, 5th and 6th decade of both male and female patients. This young average can be explained by the high percentage of paralyses caused by thyroid cancer and thyroid surgery (82). At the same time the young average age can explain the low percentage of other cancer malignancies, which are more common in elderly patients (Table 3). Another explication for the young average is the different demand for surgery in different age groups: Younger patients are probably more dependent of their voice in their professional life then elderly. This may lead to an elevated demand for surgery. The increased risk of surgery in elderly patients may inhibit some to undergo this non vitally important procedure.

The three analyzed groups are different in terms of sex and age (Table 2). In the group A, 7 out of 8 patients are female and the population is younger than group B. This is probably due to the high number of thyroid etiologies in this group. The mean age in group C is lower than the age of the mean population (Table 2). As is explained above, the demand for a revision due to bad results is probably more frequently seen in younger patients.

4.1.2. Paralysis

Paralysis and side of UVFP

Of the 24 patients with UVFP, 14 are paralyzed on the left side and 10 on the right side; among the population studied, the incidence of left laryngeal paralysis is 58%, and 42% of paralysis on the right side. This correlates with the recurrently described fact in literature, that the left side is more frequently involved in paralyzes than the right side. Among other causes, this is due of the longer and more exposed course of the left RLN (53).

Etiology of UVFP

The etiology of UVFP is dominated by thyroid and parathyroid causes (42%), followed by lung cancer (5/24). 71% of the analyzed paralyses were the consequence of surgery; in 15 out of 17 cases, the RLN or the Xth nerve were sacrificed or traumatized in the course of a cancer surgery nearby the nerves. This rate of post surgical paralysis is higher than it is reported in the literature (6, 53). A comparison with other studies remains however difficult, because in this study, all vocal fold immobilities which resulted from a mechanical fixation of the vocal fold itself (e.g. cricoarytenoid ankylosis) were excluded.

In literature, tumoral causes of RLN paralysis is described for 17% to 40%, (6, 53, 75, 81, 82). In this series, 71% of the RLN paralyses are the consequence of a surgery.

Idiopathic RLN paralysis, defined as failure to detect causes of paralysis, occurs at a significant frequency in the literature, accounting for 11% to 41.3% (75, 81). In contrast, a rate of 8% was numbered in this present study. Yumoto et al point out the high variation's rate of idiopathic RLN paralysis. He quotes a range from 1.5%

to 14% in the English literature and a range from 25.9% to 41.3% in the Japanese reports (82).

TABLE 28. Selection of the major etiologies of Unilateral recurrent nerve paralysis

Study (n)	Year	Tumor %	Surgery %	Idiopathic %	Others %
Study population n=24	**2008**	**13**	**63**	**8**	**16**
Group A		**12,5**	**62,5**	**25**	
Group B			**62,5**		**37,5**
Group C		**25**	**62,5**		**12,5**
Laccourreye et al (n=325)(43)	2003	8,6	75	12	4,4
Yumoto et al (n=422)(82)	2002	19	33	22	26
Havas et al (n=108)(22)	1999	14	40	33	13
Benninger et al (n=280)(6)	1998	25	24	20	11
Terris et al (n=84)(75)	1992	40,5	34,5	10,7	14,3
Yamadas et al (n=564)(81)	1983	17	12	41	30

Paralysis onset -T1, posttreatment evaluation and follow-up period

There is a bias in this study inherent to a retrospective review: Paralysis onset-T1 (months) ranges from 5 to 137 months, with a mean of 27 months; the timing of posttreatment evaluation ranges from 1 to 64 months (mean 10 months) and the follow-up period ranges from 3 to 79 months (mean 25 months).

This wide range could be a potential source of confounding data. On the other hand, all the three groups have the same widespread time range. This decreases the bias on these criteria. Based on the preceding arguments, I believe that the time range has a minimal confounding effect on this study.

4.2. Pre-and postoperative characteristics, T0-T1 comparison

In this study, different ways of assessments are used: fibroscopy, objective acoustic and aerodynamic parameters, perceptual analysis of the voice using the GRBAS score and a postoperative VHI self-assessment of the patients. It was a aim of the study to figure out if those parameters are appropriate and meaningful to make a differentiation between the three groups before the first treatment was done. A judgment about the two treatments fat injection and medialization thyroplasty can be made by analyzing and comparing the results of T0-T1 (see below).

4.2.1. Fibroscopic assessment

T0: The parameters of *larynx rotation* and *false vocal fold* show statistically significant differences between the groups. In contrast, the rating parameter *glottic closure* is not an appropriate assessment element to distinguish the three groups.

Group A can be differentiated from Group B and C assessing the *larynx rotation*: Only one patient in this group shows a moderate *larynx rotation*, while 7 of 8 patients present no or only a mild rotation.

Group C can be distinguished by the parameter of *false vocal fold*: No patient of the revision group shows an important false vocal fold, 7 of 8 cases present no or only mild false vocal fold.

T1: The only statistically postoperative difference between the groups presents the *larynx rotation* between group A and group C. This difference is the same as preoperative.

T0-T1: The posttreatment score of the groups A and B demonstrate both improvements in the three evaluated parameters. The group C demonstrates an improvement of the *larynx rotation*, but not of the other evaluated fibroscopic parameters.

4.2.2. Acoustic and aerodynamic parameters

T0: The acoustic and aerodynamic parameters are good parameters to distinguish the groups A and B. It is a bias of this study, since patients selected for fat injection have usually less severe disturbance in acoustic and aerodynamic parameters than patients selected for medialization thyroplasty. Knowing this point of view the result is not astonishing. Group C demonstrates varying results in the measurements of *glottic gap*, *MPT* and *expiratory volume*. The results of *MPT* and *expiratory volume* lie between them of group A and B. The results of *glottic gap* are probably falsified by two measurements: patient 18, with a result of 20.43 cc/dB/sec, and patient 24, with a result of 26.42 cc/dB/sec. These results are impractically high for a *glottic gap* measurement. This shows the weakness of the acoustic and aerodynamic parameters: The manner how to measure the parameter influences enormously the results and have a potential to falsify the results. Most suitable but more or less impracticable is when the examination is continuously made by the same person. In contrast to the posttreatment scores, the comparison of all the acustic pretreatment scores between the injection and the medialization groups were significantly different.

T1: In the posttreatment scores, only the results of the *expiratory volume* show a postoperative difference between group B and A, and between group B and C. The *expiratory volume* of group B is already in T0 significantly more elevated than in group A and C.

T0-T1: The fat-injection group has a significant amelioration of the *expiratory volume, MPT* and *glottic closure* show positive tendencies. In group B the parameter *expiratory volume* is the only rating parameter in T1 that is not changing statistically- but it has a positive tendency. That explains why the *expiratory volume* of group B is more elevated than in the other groups. The revision group can only demonstrate positive tendencies in both procedures.

4.2.3. Perceptual analysis (GRBAS score)

The GRBAS score shows pre- and postoperatively no significant differences between the groups. Nevertheless, the groups show tendencies: While group A shows better and group B worse results in the GRBAS score than the population mean, group C cannot be classified. In this group the judgements are evenly spread over the grades 0 to 3.

Comparing the T0 and T1, Group A improves the parameter *grade* statistically significant, while group B improves *breathiness* and *asthenia*. Group C improves none of these parameters, neither in comparison of T0-T1, nor in T1-T2 and T0-T2 comparison.

Several research groups observe that the GRBAS score is reliable across all parameters except of the parameter *strain* (78). They report that the parameter *grade* has the highest reliability of the GRBAS score, and that the parameter *strain* the least (14, 78). The parameter *strain* was identified only in one patient's voice. This is explainable by the observation that *strain* represents normally a psycho-acoustic impression of unsuccessful speech production during phonation, a state that is usually not present in UVFP.

4.3. Revisions

A major aim of this study was to analyze whether it is justified or not to make a revision of a fat injection that led in the first time to an unsatisfactory result. And if yes, what kind of procedure (fat reinjection versus thyroplasty) should be recommended to the surgeon and his patients.

Comparing the result T0-T1, the group C shows less satisfactory results than group A and B. While group A and B improve their results in all judgments statistically significant, group C improves only in the parameter *larynx rotation*. In the acoustic and aerodynamic parameters, the group C improves in *glottic closure*, *MPT* and *expiratory volume* from T0 to T1. But only the *MPT* result is statistically significant. In the perceptual analysis the group C did not improve statistically significant in any parameter. These postoperative results can easily explain the patients‘ demand for a second surgery.

It is very interesting to analyze the changes from T1-T2. Because in this case, neither the fibroscopic, nor the acoustic and the aerodynamic analysis show statistically significant improvements.

Nevertheless, comparing the fibroscopic analysis of T0-T2, both *larynx rotation* and *glottic closure* improves. At T2, 8 of 8 patients show normal or mildly disturbed *glottic closure*. This is the same result as group A and B. The parameter *false vocal* fold turns out to be a very constant criterion; it does not change neither from T1-T2, nor from T0-T1. The acoustic and aerodynamic parameters improve in *glottic gap*, and slightly in *MPT* and *expiratory volume*. Only half of the patients finally improves their *grade* from T0-T1.

Analyzing these results must lead to the conclusion that the results of a revision of a UVFP treated with a fat injection are even more unpredictable than the first treatment. The results are varying, and even when there are individual improvements, the entire result is not satisfactory.

4.4. Conclusion

Initially, this study wanted to answer the following questions:

- Which clinical factors influence anatomic and functional results?
- What are the reasons for unsuccessful treatment of UVFP?
- Can a more precise indication for fat injection or medialization thyroplasty achieve better functional results for patients with UVFP?
- Is a revision of a fat injection justified?

UVFP is not the result of a complete muscle denervation. Some groups demonstrates high synkinetic reinnervation rates in animal experiments (66% to 88% of all paralysis); it is probably that human beings show comparable results (19, 70). The entire glottal configuration, including *larynx rotation* and *false vocal folds*, are the results of a sophisticated denervation process. The laryngoscopic appearance of a paralyzed vocal fold does not reliably reflect the type of lesion and prognosis (73). Crumley describes the huge range of larynx presentation after initial paralysis and following synkinesis (11). This variety makes the choice of the treatment of UVFP so challenging and often kind of unpredictable.

In this study the parameters *larynx rotation* and *false vocal folds* show statistically significant differences between the three analyzed groups. On the other hand, the rating parameter *glottic closure* seems to be not an appropriate assessment element to distinguish the three groups. Furthermore, this study demonstrates that patients with *false vocal folds* present better postoperative results. This might be due to the patients‘ ability of glottal compensation.

There are numerous reason for unsuccessful surgery: individual anatomy, different patients‘ demands and varying surgical training are some of them. But the treatment of UVFP has even more challenging aspects: Basically, UVFP is both a neurologic and a mechanical problem. Both treatments, fat injection and medialization thyroplasty, are only mechanical solutions. The natural creation of synkinesis following vocal fold paralyzes has very variable clinical characteristics. Both offered and analyzed treatments will always be limited in their result and indicate a reason for unsuccessful and unpredictable treatment. Until now, no satisfying solution interacting with the neurological cause of the paralysis was found. The variability of the synkinesis is another reason for the unpredictable outcome of the rehabilitation.

Analyzing the patient’s results, we can come to the following conclusion about choosing precise indications: Those patients without any *false vocal folds* should be treated in T1 with a more intervening treatment. Under this aspect the today‘s standard is the medialization thyroplasty. Patients without visible *larynx rotation* should be treated in T1 with a less aggressive surgery as fat injection. In case of an unsatisfactory result, a revision should be discussed in any case with the patient. To figure out if another choice of the indication for fat injection or /and medialization thyroplasty achieves better postoperative results should be studied in further studies.

The study tries to answer the question, whether a revision of a fat injection is justified or not. The results show, that the outcome of a revision is even more unpredictable than the results of the initial treatment. This result indicates, that the wrong indication of the initial medialization treatment influences not only the first, but also the final result. Both medialization thyroplasty and fat injection are surgical procedures that injure the vocal folds. Once the vocal fold is injured, every following treatment is done under the influence of the first one. Umeno et al point out that the additional injection laryngoplasty after framework surgery can be an effective treatment for patients who still have a important glottal gap after surgery (77). Analyzing the results of this study, the indication for a revision surgery are very limited. A revision is justified after an initial fat injection only in two cases: First when the patient's voice did not change or became worse after the first injection and second when the patient is very demanding.

The data in the present study describe a significant difference of pre- and postoperative results and improvement in fibroscopic assessment, acoustic and aerodynamic parameters and voice quality. Nevertheless further studies with a larger number of patients and randomized groups are needed to precise whether the proposed indication for fat injection and medialization thyroplasty in UVFP are effective.

5. ZUSAMMENFASSUNG

Das klinische Bild von Patienten mit einseitiger Stimmbandparese ist sehr variabel. Diese Vielfalt macht die klinische Klassifizierung schwierig. Dies führt zu abweichenden Behandlungsstrategien. Zur Indikationspräzisierung für wurden drei verschiedene Patientengruppen analysiert.

Die Arbeit analysiert eine Serie von 24 Patienten deren einseitige Stimmbandparese entweder mit autologer Fettinjektion oder einer Medialisierungs Thyroplastie behandelt wurde (insgesamt 36 Operationen). Acht Patienten wurden aufgrund eines unbefriedigenden Ergebnis mehr als einmal behandelt. Jeder Patient, der eine Revision der Behandlung erforderte, bekam einen Patienten zugewiesen der mit einer einmaligen Fettinjektion oder Thyroplastie behandelt wurde. Fibroskopische Aufnahmen, objektive akustische und aerodynamische Parameter der Stimme, der GRBAS-Test und eine Self-assessment Test zur Stimmbeurteilung wurden beurteilt und verglichen die drei Gruppen.

Die Ergebnisse zeigen einen signifikanten Verbesserung der Prä- und Postoperativen Ergebnisse der Fibroskopischen Beurteilung und der akustische und aerodynamische Parameter der Stimme. Präoperativ zeigen sich in der fibroskopischen Bewertung von Larynx Rotation und Falsche Stimmlippen Unterschiede zwischen den drei Gruppen. Postoperativ haben sich die Ergebnisse angeglichen. Alle drei Gruppen verbessern sich postoperativ. Auch in den akustischen und aerodynamischen Parametern sind die präoperativen Ergebnisse der Fettinjektionsgruppe und der Thyroplastiegruppe unterschiedlich. Der GRBAS Score verändert sich prä- und postoperativ nicht signifikant. Die Revisionsgruppe profitiert weder in der Fibroskopischen Bewertung, als auch in den akustisch- und aerodynamischen Parametern von einer Verbesserung in der zweiten Operation. Nichtsdestotrotz sind die Ergebnisse der Larynxrotation und Glottischer Schluss im Vergleich zum präoperativen Zustand verbessert.

Die Arbeit empfiehlt eine Behandlung mit einer Thyroplastie für Patienten, die präoperativ keine Falschen Stimmlippen in der Fibroskopie zeigen. Patienten ohne Larynx Rotation sollten mit einer Fettinjektion behandelt werden.

Eine Revision sollte den Patienten nur in zwei Fällen durchgeführt werden: Wenn die Stimmqualität sich entweder verschlechtert oder nicht verändert hat. Und wenn der Patient sich eine Revision ausdrücklich wünscht.

Weitere Studien mit einem größere Patientengut und randomisierten Gruppen müssen durchgeführt werden um die Indikationen für Fettinjektion und Thyroplastie weiter zu präzisieren.

Summary

Patients with unilateral vocal fold paralysis (UVFP) exhibit a wide variability in phonatory, swallowing and airway dysfunction. This diversity makes a clinical classification difficult resulting in varying interpretation and treatment. In order to precise indications of medialization, different groups are analyzed: Patients, who improved with either autologous fat injection or medialization thyroplasty or both, and patients who did not improve after the procedure.The aim is to look for prognostic factors which may influence functional results.

This study reviews a series of 24 patients who underwent medialization of UVFP by medialization thyroplasty or autologous fat injection (36 procedures in total). For each patient who needed a revision of its treatment two correspondent patients who were treated with a single fat injection and a single thyroplasty were selected. There were three groups: single fat injection (n= 8), single thyroplasty (n=8) and fat injection+ revision (fat re-injection or thyroplasty) (n=8). Fibroscopy, objective acoustic and aerodynamic parameters, perceptual analysis of the voice and a VHI self-assessment are used as assessment.

The data in the present study describe a significant difference of pre- and postoperative results and improvement in fibroscopic assessment, acoustic and aerodynamic parameters and voice quality. Analyzing the pre-treatment fibroscopic assessment the judged parameters of *larynx rotation* and of *false vocal fold* show statistically significant differences between the groups. The posttreatment score does not show statistically differences between the groups, while both groups demonstrate improvements in the three evaluated parameters. The pre-treatment scores of the acoustic and aerodynamic parameters are in contrast to the post-treatment score significantly different between the injection and the medialization group. The GRBAS score shows pre- and postoperatively no significant differences between the groups. Analyzing the changes from T1-T2 of the revision group demonstrate that neither the fibroscopic, nor the acoustic and the aerodynamic parameters show statistically significant improvements. Nevertheless, comparing the fibroscopic analysis of T0-T2, both *larynx rotation* and *glottic closure* improved.

Those patients without any *false vocal folds* in the fibroscopic assessment should be treated in T1 with a medialization thyroplasty. Patients without visible *larynx rotation* should be treated in T1 with a fat injection. A revision should be discussed with the patient in any unsatisfactory case.

A revision after an initial fat injection is justified only in two cases: When the patient's voice did not change or became worse after the first injection and second when the patient is very demanding.

Further studies with a larger number of patients and randomized groups are needed to precise whether the proposed indication for fat injection and medialization thyroplasty in UVFP are effective.

6. Abkürzungsverzeichnis

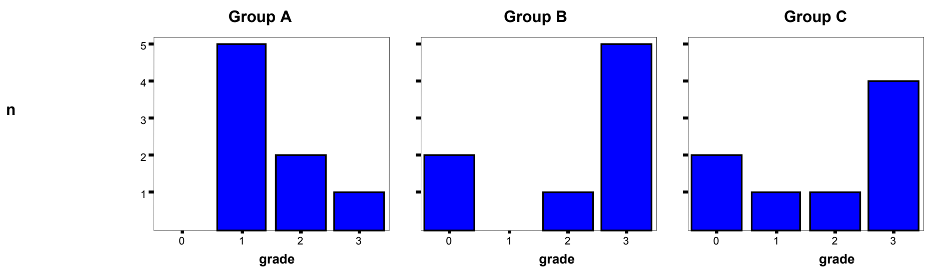
CT	Cricothyroid muscle
ELS	European Laryngological Survey
F	Female
GRBAS	Grade, Roughness, Breathisness, Asthenia, Strain
IA	Interarytenoid muscle
L	Left
LCA	Lateral cricoarytenoid muscle
M	Male
MPT	Maximum phonation time
PCA	Posterior cricoarytenoid muscle
R	Right
RLN	Recurrent laryngeal nerve
SLN	Superior laryngeal nerve
TA	Thyroarytenoid muscle
UVFP	Unilateral vocal fold paralysis
VHI	Voice Handicap Index
VOS	Voice Outcome survey
V-RQOL	Voice Related Quality Of Life
X	Xth cranial nerve

7. Anhang

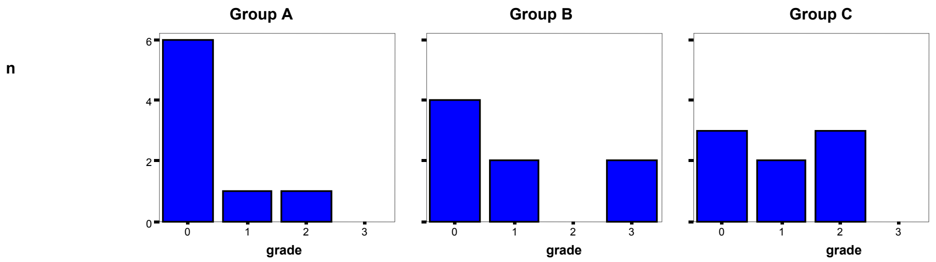
Annex 1: Perceptual GRBAS of preoperative voice recordings

GRBAS score, PRETREATMENT;

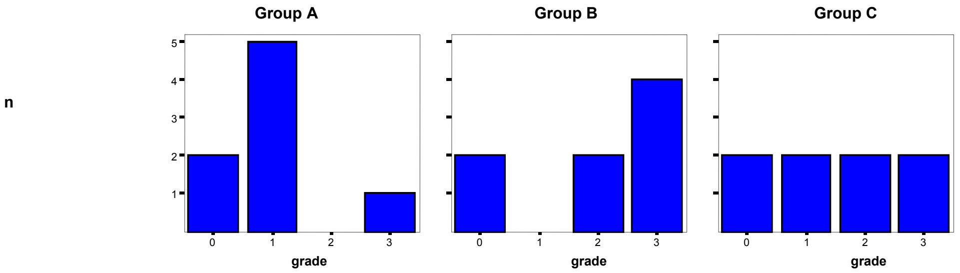
Group A (Fat Injection), Group B (Medialization thyroplasty), Group C (Revision)



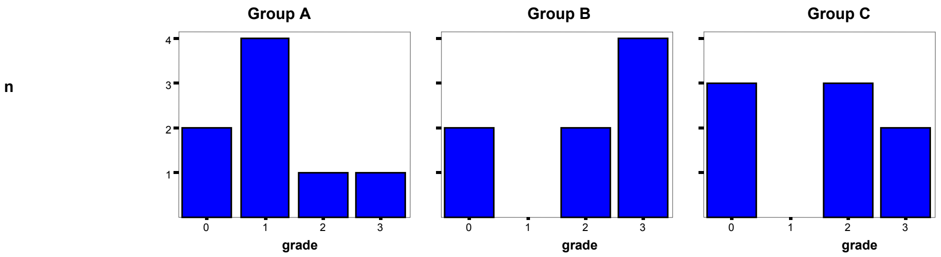
GRADE



ROUGHNESS



BREATHINESS



ASTHENIA

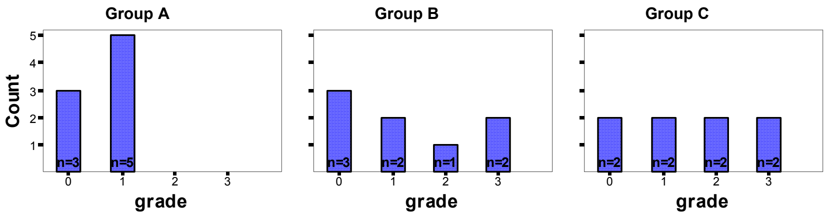
No statistically significant differences were found between the three groups among any of the judged quality of voice ($p>0.05$ in all cases)

Annex 1. Preoperative GRBAS Perceptual Voice Assessment; Grade, Roughness, Breathiness and Asthenia were judges on a scale 0-3. (n= 8 subjects/group)

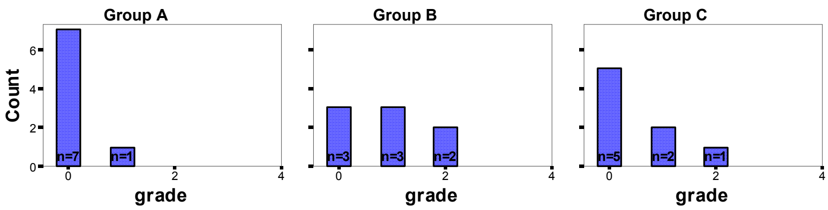
Annex 2: Perceptual GRBAS of postoperative voice recordings

GRBAS score, POSTTREATMENT;

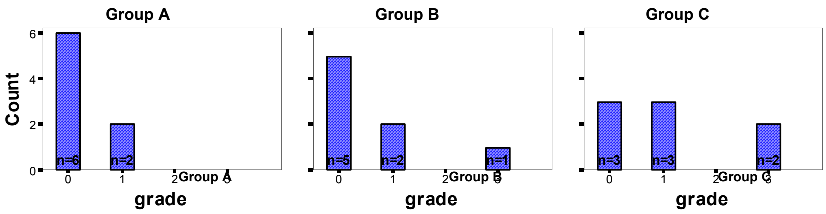
Group A (Fat Injection), Group B (Medialization thyroplasty), Group C (Revision)



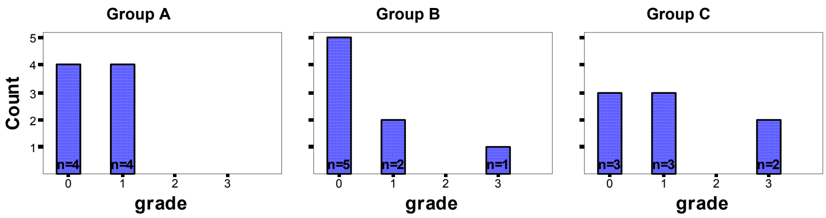
GRADE



ROUGHNESS



BREATHINESS



ASTHENIA

No statistically significant differences were found between the three groups among any of the judged quality of voice ($p>0.05$ in all cases)

Annex 2. Postoperative GRBAS Perceptual Voice Assessment; Grade, Roughness, Breathiness and Asthenia were judged on a scale 0-3 (n=8 subjects/group)

Annex 3: Questionnaire, “Autoévaluation vocale”

Autoévaluation vocale

Jamais (0); Presque jamais (1) ; parfois (2) ; presque toujours (3); toujours (4).

VHI-10 (« voice handicap index »)

On m’entend difficilement à cause de ma voix	0	1	2	3	4
On me comprend difficilement dans un milieu bruyant	0	1	2	3	4
Mes difficultés de voix limitent ma vie personnelle et sociale	0	1	2	3	4
Je me sens écarté(e) des conversations à cause de ma voix	0	1	2	3	4
Mes problèmes de voix entraînent des pertes de revenus	0	1	2	3	4
J’ai l’impression que je dois forcer pour « produire » de la voix	0	1	2	3	4
La clarté de ma voix est imprévisible	0	1	2	3	4
Mes problèmes de voix me perturbent	0	1	2	3	4
Je me sens handicapé(e) à cause de ma voix	0	1	2	3	4
On me demande : « Qu’est-ce qui ne va pas avec ta voix ? »	0	1	2	3	4

Annexe :

Je ne me sens pas à l’aise avec ma voix	0	1	2	3	4
Je voudrais bien avoir un autre traitement concernant ma voix. (Orthophoniste)	0	1	2	3	4
Je voudrais bien avoir un autre traitement chirurgical concernant ma voix :	0	1	2	3	4
J’ai l’impression que la première intervention n’a pas changé ma voix	0	1	2	3	4
J’ai l’impression que la deuxième intervention n’a pas changé ma voix :	0	1	2	3	4

NOM: ________________________________

Signature: ________________________________ Date: ____________________

Figures and Tables

8. Literaturverzeichnis

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9. Acknowledgment

I wish to express my sincere thanks to all those who have helped me to finish this dissertation.

To Prof. Dr. Frank Metternich, University Hamburg, for supporting the idea of a french-german cooperation and for providing the administrative part of this dissertation.

To Prof. Sophie Perié, University Paris VI, for the opportunity to work with her in a way that inspired the idea of my future profession.

To Prof. Jean Lacau St. Guily, University Paris VI, for the opportunity to train and work in his department and providing research facilities.

To Dr. Bernard Roubeau, Tenons Hospital, Paris, for introducing me to the field of speech pathology.

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