



## EFFICACY OF HYALURONIDASE INJECTION IN MINIMAL ASSOCIATED PATHOLOGICAL LESIONS OF VOCAL FOLDS

Mohamed Kamal Mobashir<sup>1</sup>, Amal Saeed Quriba<sup>1</sup>, Elham Magdy  
Hassan<sup>1</sup>, Sara El-Kilany Abd-elmonem Tantawy<sup>2\*</sup>

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### ABSTRACT

Voice is the most important factor in our day-to-day lives; it is the primary means by which humans and countless other animals communicate with one another to share information and ideas. Voice disorders can be caused by structural & /or functional alterations in the larynx, which prevent the voice from being able to fulfill the functional requirements of the speaker. This condition affects approximately thirty percent of the population at some point in their lives. Vibratory trauma appears to be the primary cause of minimum associated pathological lesions at the present time. Phonosurgery, pharmacology, technical equipment, and behavior modification voice treatment are the four primary approaches that can be taken to treat vocal issues. Phonosurgery is the most common approach. Vocal fold injection, also known as VFI, is a method that is considered to be minimally invasive that administers a variety of medications or materials into the tissues of the larynx. Because of developments in material science & endoscopic technology, this method has made a comeback, & its application in the field of laryngology has been brought to the forefront. The extracellular matrix protein known as hyaluronic acid has a significant role in the biomechanics of the vocal fold's movement. In certain circumstances, the overproduction of HA and the retention of HA in the superficial lamina propria of the vocal folds (SLP) can lead to the placement of the HA into the SLP, which can result in a decrease in the quality of the voice. By enzymatically cleaving HA, the HAase enzyme, also known as hyaluronidase, is able to breakdown HA. Both the permeability of connective tissues and the amounts of HA are decreased as a result of HAase-mediated breakdown.

**Key words:** MAPLs, Hyalornidase enzyme, VFI

**1** phoniatic unit, Department of ENT, Faculty of Medicine, Zagazig University

**2** Resident of phoniatics Zagazig university Hospitals

\*Corresponding author: Sara El-Kilany Abd-elmonem Tantawy

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### INTRODUCTION

It has been found that a higher occurrence of MAPLs is connected with a high occupational voice demand as well as talkativeness. Certain behaviors in life, as smoking & drinking alcohol, as well as particular dietary choices, as increasing the amount of caffeine consumed or the number of spices used in meals, contribute to an elevated risk. It has been demonstrated that MAPLs are strongly associated with a number of chronic medical diseases, including Gastroesophageal Reflux Disease (GERD) [1]. With regard to the visualization of vocal fold (VF) vibrations, stroboscopy is considered to be the gold standard in clinical practice. It is utilized in the process of assessing normal laryngeal pictures; nevertheless, it has limits

when it comes to evaluating aperiodic glottic cycles. These limitations are dependent on the basic frequency recording & the level of knowledge of the evaluator to recognize an irregular VF vibratory pattern, which is typical in the majority of laryngeal diseases [2]. Phonosurgery, pharmacology, technical equipment, and behavior modification voice treatment are the four primary approaches that can be taken to treat voice issues [3]. Phonosurgery is the most common strategy. The enzymes known as hyaluronidases, also known as endoglucosidases, have the ability to depolymerise hyaluronic acid, which ultimately results in its breakdown [4]. This is accomplished by hydrolyzing the disaccharides at hexosaminidic beta (1-4) links [5].

The aim of this work was selection of the optimal dose of vocal fold injection of hyalurodinase in different lesions.

### **Minimal associated pathological lesions of the vocal folds (MAPLs)**

Voice disorders are deviations in voice quality, a natural auditory-perceptual phenomenon where a listener perceives a voice as unpleasant or inadequate compared to their perceived normality [6].

### **Etiological classification of voice disorders according to Kotby et al. [7]:**

Vocal illnesses can be broken down into several groups, including organic voice illnesses, non-organic vocal illnesses, minimal associated pathological lesions (MAPLs), & neuropsychiatric conditions. MAPLs, also known as benign vocal fold lesions, consist of a variety of lesions, such as polyps, laryngeal cysts, vocal fold nodules, Reinke's edema, polypoid degeneration, & contact granuloma. [8].

### **Vocal fold nodules (VFNs):**

Nodules situated near the margins of both vocal folds are considered to be benign lesions, vary in size from patient to patient and have a broad-based pointed shape [9].

### **Epidemiology:**

Males and females are the most likely to get vocal nodules. These kinds of people are usually always overdoers who are outspoken. When compared to profession, intrinsic talkativeness is more consistently associated with higher levels of talkativeness, unless the work is very demanding verbally [10]. There is a correlation between defects in glottic closure in the female larynx and the fact that nodules are seen more often in females [11].

### **Pathophysiology and Histopathology**

Due to the presence of arytenoid cartilages in the posterior third of the glottis opening, the membrane of the vocal folds is the sole component that contributes to vibration. Congestion & swelling of the blood vessels in a specific area are brought on by forceful vibration. Acute misuse or overuse may cause fluid to accumulate in the submucosa, which can result in submucosal swelling. This swelling is frequently referred to as incipient or early nodules [12].

### **Diagnosis:**

#### **History:**

Dysphonia, throat dryness or tightness, limited vocal range, & vocal tiredness are more

prevalent symptoms individuals with VFNs experience when they present themselves [13].

### **Laryngeal endoscopic Examination:**

Both the length of time that nodules have been present & the quantity of recent voice usage may have an effect on their size, shape, symmetry, & color. Even if one nodule could be bigger than the other, nodules do not appear in a unilateral fashion. [12].

### **Videostroboscopic examination:**

Stroboscopy reveals decreases in amplitude, hourglass glottal closure, & open phase dominance, as well as superficial swellings of the vocal folds (VFs) near the strike zone (the junction of the anterior & center regions of the VFs) [14].

### **Narrow band imaging (NBI):**

It might be challenging to identify the histopathologic features of vocal fold nodules using white light endoscopy, particularly when the lesion is very small. On the other hand, NBI is able to identify thickness of the basal membrane, fibrosis, & keratosis without further testing. These alterations seem to be a dispersed white region surrounding the lesion in the NBI pictures of vocal fold nodules which are being examined [15].

### **Management:**

**Medical:** It is important to ensure that the larynx is well lubricated by drink enough of water. The treatment of allergies & reflux should also be administered when they are present [12].

### **Behavioral:**

Because vocal abuse is the cause of vocal nodules, speech therapy (also known as voice therapy) occurs at the beginning of the process. In most cases, the nodules & the signs that are more evident tend to disappear, especially in cases when the patient is not a singer [12].

### **Vocal fold injection:**

Steroid injections can reduce capillary permeability, downregulate cytokines, and decrease collagen synthesis and fibroblast activity in the inflammatory stages, preventing scar or fibrosis formation [16].

### **Surgical:**

When the patient's voice continues to be significantly affected after an acceptable trial of treatment, which typically lasts for a minimum of three months, surgical removal becomes a possibility [12]. This is the case when nodules of any size continue to form. According to Kotby et al., the crucial size for VFNs is a base of 2.5 millimeters & a rise of 0.5 millimeters. If

the size is more than this, surgery may be regarded the main method of therapy available [7].

### **Vocal fold polyps (VFPs)**

Lesions that grow inside the superficial lamina propria (SLP) of the vocal fold are known as vocal fold polyps. These polyps are benign, exophytic, gelatinous, & include an atrophic epithelium. Typically, they are unilateral & localized at the mid-membranous vocal fold; nevertheless, it is possible to find lesions on both sides of the vocal fold. In addition to pedunculated, sessile, hemorrhagic, & non-hemorrhagic morphologies, there are a number of other potential formations [17].

### **Epidemiology:**

Around 85 percent of VFPs are seen in individuals who are younger or middle-aged, but they may also occur in people who are older, but less often. However, there is data that implies that males are more likely to have recurrences of VFPs than women. Studies have not proven a consistent predilection for VFPs depending on gender [17].

### **Pathophysiology and Histopathology:**

Vocal fold phono-trauma, a form of vocal abuse, is more common in professions requiring extensive voice use. VFPs show minimal thickening of basement membrane zones, fibronectin deposition, and cellular connections that have become more expansive as a result of fluid penetration & loss of adhesion [17].

### **Diagnosis:**

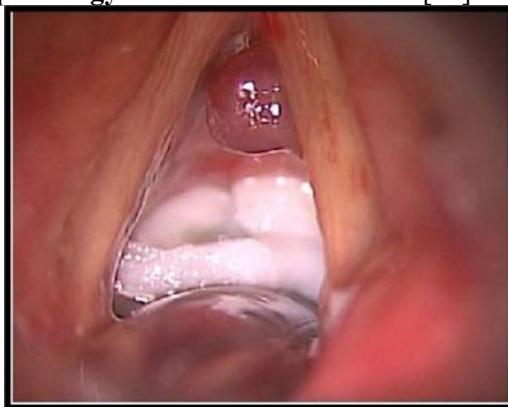
#### **History:**

Hoarseness & changes in voice are signs that occur most often. There is a possibility that large polyps may induce respiratory symptoms, as asthma & blockage of the respiratory system [18].

#### **Laryngeal endoscopic Examination:**

The laryngoscope allows for the direct visualization & evaluation of a lesion, including its size, morphology, & the effect it has on the motility of the vocal folds [17].

It is possible for hemorrhagic polyps to lose their vascular look & become pedunculated. This means that they move in and out of the glottis with inspiration & expiration, & they may also be displaced during phonation activities [12].



Vocal fold polyp [19].

### **Videostroboscopic examination:**

On the other hand, videostroboscopy reveals that minor polyps have normal to little lowered amplitude & mucosal wave, but bigger polyps typically suppress vibratory characteristics. Depending on the bulk & stiffness of the lesion, mucosal wave phase asymmetry may be present in individuals [17].

### **Narrow band imaging:**

As a result of its capacity to detect aberrant vascular topologies that are present in the lesions, narrow band imaging is able to observe tiny laryngeal structures. Utilizing wavelengths of light that match to the body's ability to absorb hemoglobin makes it easier to see the architecture of the cardiovascular system.[17].

### **Management:**

**Medical:** It is important to ensure that the larynx is well lubricated by drink enough of water. The treatment of allergies & reflux should also be administered when they are present [12].

#### **Behavioral:**

A brief voice therapy course is recommended to teach voice care. The vocal fold is normally required to undergo surgical excision in order to restore it to its natural look & function. However, small hemorrhagic polyps may be reabsorbed using conservative methods [12].

#### **Vocal fold injection:**

Injections of subepithelial steroid into the vocal folds could be an alternate therapeutic option for VFPs [17]. Hyaluronidase Injection: An

elevated hyaluronic acid (HA) is noted in cases of polyps [20].

**Surgical:**

Phon microsurgery is still considered the therapy of choice for VFPs. Several studies have demonstrated that phon microsurgery for VFPs is effective in the restoration of vocal quality & function in both professional & nonprofessional voice users when performed under the supervision of a qualified surgeon [17].

**Other lines of treatment:**

One of the relatively new therapeutic modalities for laryngeal papilloma, photoangiolytic laser treatment of laryngeal lesions was introduced by Mcmillan [21].

**Vocal fold cyst**

The vocal fold cyst is an ovoid structure which appears within the substance of the vocal fold (underneath the mucosa within the superficial lamina propria), lined by mucous membrane and contains either mucous or keratin flakes [22].

**Epidemiology:**

In terms of epidemiologic findings, the most notable one is a history of excessive use of the

voice [12]. Patients are usually adults (both male and female) [22]. Mainly in Third – Fifth decade [7].

**Pathophysiology and Histopathology:**

Intracordal cysts can be categorized as either mucous retention or epidermal inclusion kinds, depending on their characteristics.

At the same time that epidermal cysts contain accumulated keratin, mucous retention cysts, also known as ductal cysts, are formed when the duct of a mucous gland becomes clogged & retains glandular secretions[12].

**Diagnosis:**

**History:**

An individual who has epidermal cysts exhibits many of the same symptoms & characteristics that are associated with voice abuse as a patient who has nodules. Dysphonia in 69- 96% of patients, or phonasthenia [7].

**Laryngeal endoscopic Examination:**

This lesion is usually small, lentil-sized and sometimes multiple. The size varies from 1-10 mm [22]. Cysts are more common to be unilateral than bilateral [7].



Left vocal fold cyst [22]

**Videostroboscopic examination:**

As a result of the displacement of the lamina propria, the mucosal wave along the side of the cyst may be diminished or nonexistent [23].

**Narrow band imaging (NBI):**

These lesions are distinguished by the presence of a capsula that is filled with a semisolid substance and is located underneath the epithelium of the vocal fold. With the use of NBI, it is possible to detect with greater precision both the absence of vessels in the region around the cyst as well as the specific

vessel configuration in the region surrounding the cyst [24].

**Management:**

**Medical:**

General supportive measures, such as hydration and potential acid reflux management, may be helpful but will not resolve this problem [12].

**Surgical:**

Because the lesions do not normally improve with conservative therapy alone, it is recommended that the lesion be surgically removed using microflap excision to remove it [25].

### **Vocal process granuloma**

It is a benign lobulated growth swelling, may be unilateral or bilateral and caused by irritation or trauma. It is formed at a characteristic location in the vicinity of the posterior vocal fold over the vocal process which lies just underneath the membrane covering the larynx (Karkos et al., 2014).

#### **Epidemiology:**

Affect mainly males of fourth –fifth decade of life [7].

#### **Pathophysiology and Histopathology**

The thin mucosa & perichondrium that cover the cartilaginous glottis become inflamed. This may occur as a consequence of the arytenoids being apposed (slamming together) with excessive force at the beginning of the vocalization process (also known as a glottal stroke), or when the throat is cleared frequently or persistently. Inflammation of the vocal process area can also be exacerbated by acid reflux; the affected region may develop ulcers or a granuloma that is grouped together [12].

#### **Diagnosis:**

##### **History:**

presented mainly by Phonasthenia and may cause high pitched voice or sometimes vocal fry [7].

##### **Laryngeal endoscopic Examination:**

Erythema is also usually apparent on the vocal process and coming upward on the medial surface of the arytenoid cartilage [26].

##### **Stroboscopic signs:**

When a big granuloma is present, it may prevent the mucosal wave and glottic closure from occurring normally [27].

##### **Management:**

##### **Medical:**

Individuals who do not exhibit signs of reflux should still begin an anti-reflux treatment on the basis of empirical evidence [12].

##### **Behavioral:**

Accent method of voice therapy which usually improves the contact granuloma but, after prolonged program [7].

##### **Vocal fold injection:**

Indirect injection of a depot corticosteroid directly into the lesion & the area surrounding its base can result in a reduction in the size of visible lesions [12].

##### **Surgical:**

Surgery should be a last resort, not only because of the expectation of maturation and spontaneous detachment but also because

postoperative recurrence of the ulcer or granuloma is predictable [12].

### **Reinke's edema (RE) of vocal folds**

An buildup of edematous mucoid gelatinous fluid in the superficial layer of the lamina propria (reinke's space) of the membranous component of both vocal folds over their whole length is the cause of fusiform swellings, which are characterized by the presence of fusiform swellings [28].

#### **Epidemiology:**

Tobacco usage, voice abuse & overuse, & infections in the upper respiratory tract are the primary causes of this condition [29].

Affect both sexes equally with female predilection than male as they lead to harsh voice which is not accepted by female and leading them to ask the specialist [21].

#### **Pathophysiology and Histopathology:**

Elevated blood pressure, vascular congestion, & venous stasis are the outcomes of long-term smoking & voice misuse. Because of these situations, diffuse polypoid alterations occur, & they are permanent. However, the degree of edema or turgidity, as well as the voice disturbance that results from them, might fluctuate depending on how much voice is used [12].

Reinke's edema and polypoid degeneration affect the anterior two thirds of the vocal fold (membranous part). As this part is the most active during phonation [30].

#### **Diagnosis:**

##### **History:**

Present mainly with Dysphonia, low pitch voice in 97% of patients, phonasthenia or no complaint in males as deeper voice is accepted [7].

##### **Laryngeal endoscopic Examination:**

In most cases, a laryngeal examination will indicate the presence of pale, watery bags of fluid that are linked to the superior surface & the borders of the folds. Clusters of polyps may be observed in situations that are particularly severe [12].

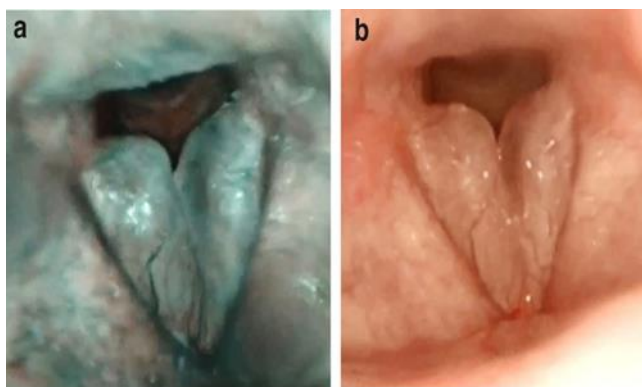
##### **Videostroboscopic examination:**

Reinke's edema is identified as having a statistically significant association with the normal mucosal wave pattern [23].

##### **Narrow band imaging:**

There is a fairly characteristic configuration for these lesions, & the conspicuous vessels that they include can already be recognized very clearly [24].





a, b Reinke's edema of both vocal folds in NBI (a) and WLE (b) modus [24].

### **Management:**

**Medical:** The patient with bilateral diffuse polyposis is encouraged to give up smoking. RE is not a lesion that is caused by inflammation; it does not improve with the typical anti-inflammatory treatments that are available, as the nonsteroidal anti-inflammatory drugs [29].

### **Behavioral:**

The study emphasized the limitations of voice therapy in reducing risk factors for RE by implementing effective voice counseling, restoring normal voice quality, and restoring VF functions post-treatment [29].

### **Vocal fold injection:**

The enzymatic breakdown of the excessive overexpressed HA in the lamina propria is the role that HAase plays in the treatment of Reinke's edema. This helps to achieve hydration in the Reinke's space & reduces the contour irregularities, which allows for the avoidance of surgical intervention [29].

### **Surgical:**

It has been reported that surgical lines are the primary method of treatment for RE treatment. In order to achieve the primary objective of the surgical lines, which is to enhance the quality of the voice while preserving the outlines of the glottal epithelium and the superficial lamina propria to the greatest extent possible [29]. The Reinke's space was drained of the edematous mucoid gelatinous fluid with the use of traditional surgical methods, which involved making a mucosal incision. This mucosal incision could be done using cold instruments in a procedure known as "cold steel" micro-laryngeal phono-surgery "MLP" [7] or by using microdebrider systems [31].

### **Other lines of treatment:**

"CO<sub>2</sub> laser" [14] was brought into the area of phonosurgery as a replacement for cold tools

used for mucosal incision. This was done in an effort to reduce the amount of blood that was released during the operation [7]. By targeting oxyhemoglobin in Reinke's space, which is responsible for vascular congestion in RE, photoangiolytic laser is utilized for the treatment of nonvascular phono-traumatic lesions in VFs, including RE. Regarding its efficacy in decreasing edema, however, there are still some questions [32].

### **Diagnostic tools of dysphonia**

#### **Patient interview:**

Full History taking focusing on Onset and duration of vocal symptoms. Auditory-perceptual examination, video stroboscopy, acoustics, aerodynamics, & subjective ratings generated by the individual are all components that are recommended by the European Laryngological Society as part of a thorough assessment of voice problems [33].

The first self-reported psychometric test that was designed to measure voice dysfunction was the Voice Handicap Index -30 [34].

In addition, a condensed version known as VHI-10 has been produced, which consists of ten elements chosen from the first thirty items [35].

**The Arabic version of VHI** It is well acknowledged as a self-assessment instrument that is both accurate and reliable for determining the severity of voice abnormalities among individuals who speak Arabi [36].

#### **Elementary diagnostic procedures:**

##### **Auditory perceptual assessment (APA):**

Utilizing a collection of terminology that reflect specific qualities of the voice & rating them on scales that measure the severity of every feature, perceptual evaluation of voice refers to the process of employing the human ear in a methodical manner to rate the quality of the voice [37].

The method has also been utilized for a long time as a tool for the first visit assessment of a individuals who is seeking assistance in a voice clinic. In this scenario, the objective is to acquire information that is pertinent to diagnosis & treatment [38].

The **GRBAS** system, which requires the utilization of five characteristics that were described by Hirano [39], is the oldest & most widely utilized system on a global scale: **grade (G)** indicates the total degree of hoarseness or vocal irregularity that the patient is experiencing. A psychoacoustic sense of the irregularity of vocal fold vibrations is represented by the descriptor "**rough**" (**R**). The irregular oscillations in the fundamental frequency or the amplitude of the glottal source sound are what it refers to that correlate to. A psychoacoustic perception of the amount of air that is leaking through the glottis is represented by the letter B, which stands for "breathy." In this context, turbulence is relevant. The asthenic (A) voice is characterized by a lack of power or frailty. A lack of higher harmonics or a weak strength of the glottal source sound are both factors that contribute to this phenomenon. A psychoacoustic impression of a hyperfunctional condition of phonation is that which is represented by the letter S.

#### **Clinical diagnostic aids:**

#### **Documentation of the glottic picture by laryngeal examination as follows:**

#### **The larynx can be examined in several ways:**

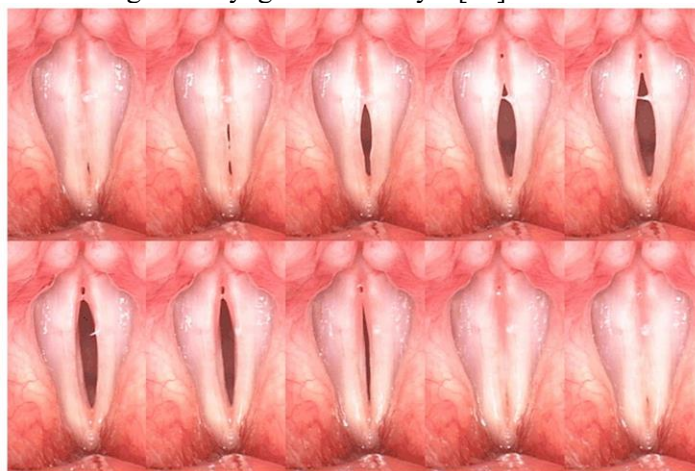
There is frequently poor visibility & no lasting image of the larynx while using the laryngeal

mirror, which is supposed to enable three-dimensional imaging & a high color resolution. In light of this, it is challenging to determine whether or not the treatment that was selected is effective. The fiberoptic naso-laryngoscope or a newer "chip-tip" video-endoscope is crucial for patients with unusual anatomy or exceptional gag reflex [12]. With the help of laryngeal imaging procedures like Videostroboscopy (VLS), Videokymography (VKG), & High-Speed Videoendoscopy (HSV), it is already possible to perform direct visual monitoring of the vibratory function of the vocal folds [40].

#### **Videostroboscopy (VLS)**

When it comes to the inspection of the vocal folds & the evaluation of individuals who have voice abnormalities, video laryngostroboscopy (VLS) is currently the procedure that is most generally employed. With the help of this valuable imaging tool, it is also possible to evaluate the results of treatment for laryngeal disorders or the functional outcome of phonosurgical procedures [23].

It is possible to analyze the characteristics of stroboscopy in terms of the quality of mucosal pathology, the degree of involvement, the quantification of the stroboscopic examination, & the categorization of the lesion based on its location. A normal mucosal wave pattern has been shown to have a statistically significant link with nodule, palsy, & Reinke's edema. Additionally, a diminished or nonexistent mucosal wave can be noticed on the side of the cyst [23].



Montage of stroboscopic images obtained from successive points in several glottal cycles [41].

#### **High Speed Videoendoscopy (HSV)**

In order to examine the vibratory biomechanics of the vocal folds & to improve the accuracy of

voice assessment & treatment, HSV laryngeal imaging has become a more accessible & intriguing clinical & research tool than it was

in the past. With its enhanced temporal & spatial resolution, as well as its use of color, HSV is able to transcend the restrictions that were previously present [42].

An intrinsic shortcoming of stroboscopy in the visualisation of aperiodic vibrations was the impetus for the development of **videokymography** [43]. In contrast to the latter two approaches, which provide software-based reconstruction of kymographic images taken from high-speed laryngoscopy and laryngeal stroboscopy, respectively, the videokymographic system is capable of delivering kymographic images immediately and in real time upon a video screen. Videokymography & high-speed digital kymography are the only two methods that are helpful for imaging aperiodic vibrations of the vocal folds within the three approaches [43].

#### **Narrow-band imaging (NBI)**

A new optical imaging system uses two wavelengths of light, 415 nm and 540 nm, to detect hemoglobin in the superficial mucosa. The shorter wavelength, 415 nm, shows a brownish color, while the longer wavelength, 540 nm, visualizes deeper subepithelial vessels in a blue color [15].

#### **Acoustic analysis:**

Because of its noninvasive nature, low prices, & ease of application, the acoustic analysis of voice quality is a topic that is of significant interest to phoneticians & voice clinicians [44].

**Fundamental frequency** is the rate at which vocal folds vibrate each second & is denoted in Hertz (**Hz**) Fundamental frequency is a measure of musical pitch. Variations in the fundamental frequency are brought about by alterations in the mass, length, & tension of the vocal folds [45].

The cycle-to-cycle change in frequency & amplitude that occurs during phonation is what is referred to as **jitter and shimmer** at the same time. [44]. Vibration of the vocal folds is seen to exhibit a low amount of jitter in healthy speakers, but diseased voices are noted to exhibit higher levels of jitter.

**Harmonic-To-Noise Ratio (HNR)**, sometimes referred to as the signal-to-noise ratio, is a measurement that illustrates the degree of periodicity present in a signal [46]. This is an

estimation of the energy that is included within the harmonics of the speech signal as well as the noise energy that is present in the signal [47].

An additional measurement that corresponds to the degree of regularity and periodicity of the voice signal is called the **Cepstral Peak Prominence (CPP)**. [46].

It is an aerodynamic measure known as the **maximal phonation time (MPT)**, which is stated in seconds and represents the longest length of time that a vowel can be vocalized continuously. Phonation times that are fewer than ten seconds are generally thought to be abnormal. [48].

#### **Management of MAPLs**

Voice hygiene guidance & voice therapy are the primary components of **conservative treatments**, often known as behavior modification by voice therapy [49].

Voice therapy, also known as the Accent Method (AM), is a form of therapy that is considered to be either a mainstream or a complementary approach to treatment. It is in conjunction with medication or phonosurgery that the AM of voice therapy is most commonly utilized as a supplemental treatment that is used [50].

#### **Vocal fold injection (VFI)**

Vocal fold injection, also known as **VFI**, is a method that is considered to be minimally invasive and is used to provide a variety of medications or materials into the structures of the larynx. [51] This approach has reemerged as a result of advancements in material science & endoscopic technology, & its application in laryngology has been brought to the forefront. Due to the limits of injection materials & instruments, the original procedure for injecting the vocal folds was carried out utilizing a transoral method while the patient was under general anesthesia [52].

#### **Trans-cutaneous VFI:**

It is performed by 2 physicians; one is doing the injection and the other is scoping the patient for visualization. The needle may be inserted either through the cricothyroid membrane, or via the thyrohyoid membrane or trans-cartilaginous through the thyroid ala [16].





Trans-cutaneous approach; (A) cricothyroid approach, (B) transcartilaginous approach, (C) thyrohyoid approach [16].

To obtain adequate visualization & patient compliance in office-based VFI, it is necessary to administer the appropriate anesthetic. Although there is no agreement on the method of local anesthesia that should be used throughout the treatment, topical lidocaine continues to be the most common kind of local anesthesia for VFI. The laryngologist's preference determines both the application method & the amount of the lidocaine [51].

#### **Trans-nasal approach:**

A specially constructed disposable injection needle is used for the injection process. This needle has an outside sheath that measures 180 centimeters in length & has a diameter of 1.8 millimeters. Meanwhile, the inner needle is flexible & has a hard tip that measures 25 gauges. Endoscope working channel is where the needle is placed into the device [53].

#### **Micro laryngeal surgery**

It is dependent on a number of various aspects, including the experience of the surgeon, the severity of the dysphonia, the type of lesion, & the individual's vocal request, whether or not phonosurgical treatment is indicated for patients who have MAPLs. [54]. Anterior commissure resections have the potential to result in synechiae during surgical excisions. It is common for acquired anterior glottic web to develop following endoscopic resection of bilateral laryngeal lesions, which invariably leads to the presence of raw mucosal surfaces in close proximity [55]. When acquired glottic stenosis is present, breathing, voice production, & airway protection are all negatively impacted. Reconstructing the stenosed glottis is one of the most significant issues that laryngologists are having to deal with in this day and age [56].

#### **Hyaluronidase enzyme injection**

Typically, the duration of action for hyaluronidase is between 24 & 48 hours, & it has an instantaneous effect. Its half-life is two minutes. Hyaluronidase's first action may break

cross-links in the hyaluronic acid dermal filler, causing it to function in a manner similar to that of natural hyaluronic acid in the skin, which has a half-life of twenty-four hours [57].

#### **Indications for the use of hyaluronidase:**

##### **Vascular Occlusion**

It is anticipated that 0.001% of patients who receive dermal filler treatment would experience imminent necrosis, which is equivalent to one case in every 100,000. Hyaluronic acid filler injections should be handled as soon as possible because they can cause vascular impairment [58].

##### **Blindness**

The periocular embolism of hyaluronic acid causes instantaneous blindness, which is accompanied by terrible ocular discomfort. In order for the retina to survive, the circulation of the retina must be restored within sixty to ninety minutes [59].

##### **Tyndall Effect**

The term "Tyndall effect" refers to the scattering of light that can be observed in specific individuals following the injection of hyaluronic acid. This phenomenon causes the skin to take on a bluish hue, & it is most frequently observed in the sub ocular region. Hyaluronidase is a potential solution to the issue that has been presented [60].

##### **Unacceptable Cosmetic Outcome**

It is possible to properly treat overcorrection or misplacement of hyaluronic acid filler with hyaluronidase; however, this is typically the result of improper injection procedure or an incorrect selection of product for a specific application [61].

##### **Delayed Onset Nodules**

On the other hand, hyaluronidase might be able to treat lumps or nodules that show up several months after the original treatment [57].

##### **Allergic or Immunogenic Reaction to the Hyaluronic Acid Dermal Filler [57].**

##### **Complications:**

Following therapy, it is not uncommon to see bruising & swelling [4]. An allergic reaction is the most dangerous consequence that can occur after the administration of hyaluronidase. Various allergic reactions have been described, and these reactions vary depending on the location that is being treated. When high doses of hyaluronidase have been administered, as well as when the medication has been supplied intravenously, hypersensitivity reactions have been observed. [57].

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