



POSITION PAPER

Optical coherence tomography in the laryngeal arytenoid mucosa for documentation of pharmacological treatments and genetic aspects: a protocol

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Abstract

Background: Optical coherence tomography (OCT) is an imaging technology that provides cross-sectional images of subsurface tissue structures in the larynx without biopsy. Focus has until now been on the vocal folds. Since many kinds of mucosal disorders can be defined in the arytenoid regions behind the vocal folds, and not on the vocal folds, we focus on this area in this protocol.

Objective: A superficial oedema, grading 1–5 of the arytenoid regions, can be made with high-speed films of 4,000 pictures/sec. A supplementary larynx set up with a clinical probe for OCT with cross-sectional measures can be made with a description of the levels of oedema and other parameters.

Design: Adult patients with subjective complaints of hoarseness or a problem in the larynx related to voice and swallowing for more than 6 weeks participated in a randomised-controlled study.

Perspective and conclusion: With this new OCT probe for the larynx arytenoid region, compared with high-speed films, we will be able to define pathological areas in the arytenoid mucosa as a future documentation of pharmacological treatment and genetics-related lifestyle advice.

Keywords: *nanometric diagnostic; reflux; mucosal function; mucosal diagnostics; upper airways; voice.*

In Context

Optical coherence Tomography is a very promising way of looking down into tissue with no need of a biopsy. It has been used extensively in eye and skin disorders. For the last 10 years the focus has also been on the throat, especially in cancer patients and on the vocal folds. Due to our experience with high speed films of the vocal folds (4000 pictures per second) has shown not only the vocal fold, but the region behind the vocal folds. An area where voice, respiration and swallowing meets. This protocol intends to propagate development of a probe to look at the tissue in the throat, including behind the vocal folds. Especially pharmacological treatment effects and genetic differences are of interest. Development of the probe for clinical use seems to be difficult, but it is possible together with engineers who already developed probes for other areas of the human body.

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Optical coherence tomography (OCT) is an imaging technology that provides cross-sectional images without biopsy of subsurface tissue structure at approximately 10- μ m resolution to a depth of 1.5 mm using backscattered light. OCT has shown promise in imaging normal vocal folds as well as various laryngeal disorders (1). The use of OCT to image the larynx during diagnosis and treatment of a vast array of laryngeal disorders continues to develop along with innovative surgical techniques. Monitoring the benign cellular and molecular events resulting in arytenoid oedema is of great

interest. There is a need to understand the normal histology of the arytenoid region compared with disorders causing arytenoid oedema at the inflammatory process level. The interesting thing is to find out whether it is related to infection, acid reflux, or allergy. A long-range OCT using Doppler OCT is providing useful clinical applications for diagnostic and therapeutic laryngeal procedures on the vocal folds (1).

Background

In a prospective cohort study, partial cure for dystonia was found, where the mode of treatment was antihistamine,

fexofenadine tablets, and local cortisone (budesonide) inhaler in the larynx with reduction of oedema of the arytenoid region as an objective finding (2, 3). Further, in a randomised-controlled trial of lifestyle change related to acid provocation, food and sleep habits were essential in laryngopharyngeal reflux with hoarseness (LPR) treatment, where treatment effect objectively was related to reduced oedema of the arytenoid regions (4), based on two Cochrane reviews showing lack of treatment evidence until now (5, 6).

The advanced high-speed film is one new tool which captures exact pictures of the moving larynx, including the arytenoid region, and another could be OCT, and they both should be used together in future randomised-controlled trials.

The swallowing process of the tissue in the upper oesophagus does affect voice control, especially for the nuanced registers stabilisation of the vocal fold function. The adductor muscles between the arytenoid cartilages cannot function efficiently, resulting in hoarseness, especially in the upper register.

It can be shown on OCT how the layers of the vocal folds develop, possibly corresponding to hormonal and paediatric development (7, 8). The arytenoid area layers in the larynx have not been investigated with OCT in pathology. The combined high-speed films and OCT will certainly give much more information on the pathology of the layers during voicing and swallowing. To date, we have only had high-speed films to look at the superficial arytenoid regions with 4,000 pictures/sec. Of course, we have many evidence-based measures hereof that also could be compared with OCT (9, 10). Sectional presentations of the arytenoid mucosa with OCT will in the future have enhanced value for diagnosis and treatment.

Objective

The aim was to determine, based on the literature and our studies of high-speed films, whether OCT with a laryngeal probe (1) is clinically feasible for evaluating oedema of the arytenoid region, in a stable way, or which kind of work should be made to improve the OCT probe before this is possible. Furthermore, if this method is applicable, it would be interesting to see if the visual arytenoid oedema grading system (1–5) could be the basis for further clinical quantified research of mucosal barriers in the upper airways, as it is done in dermatologic and eye disorders with great success (1).

Design

Criteria for considering patients for the study

Types of participants

Adults (aged 18 years or older) with hoarseness and complaints of swallowing for more than 6 weeks (dysphonia and laryngopharyngeal reflux). Patients who had

the symptoms for at least 6 weeks were included, irrespective of a definitive diagnosis or not. All patients should have undergone high-speed video laryngoscopy to exclude other identifiable causes of hoarseness, including malignancy, and vocal fold paralysis. A prospective randomisation is accomplished with supplementary OCT in one half of the patient group that includes at least 40 patients based on a power calculation of 5% difference of diagnosis evidence.

Types of intervention

Systematic treatment approach: laryngopharyngeal reflux

- 1) Pharmacological treatment, proton pump inhibitors (PPI)
- 2) Lifestyle modification and patient education

Allergy treatment

- 1) Removal of provocations of upper airways
- 2) Fexofenadine 180 mg tablets 1–2 a day and budesonide inhaler

Infections in the larynx

- 1) Erythromycin (Azithromycin) 500 mg a day for 6 days
- 2) Secondary antibiotics based on swabs with medical micro-pathological advice

The following outcomes will be assessed:

Subjective complaints

Hoarseness in singing and speaking, or other problems with your voice; lack of high notes (hoarseness); clearing your throat/excess throat mucus or postnasal drip; difficulty swallowing food, liquids, or pills (dysphagia); coughing after you eat or after lying down; troublesome or annoying cough; breathing difficulties; choking episodes (larynx hiccups); and sensations of something sticking in your throat or a lump in your throat (globules).

High-speed films of the larynx

Visual scores (1–5) of the oedema in the arytenoid regions (see Fig. 1) with kymograms, glottal openings quotients, electroglottograms, and segmentations (4, 9, 10).

Optical coherence tomography

Objective findings of laryngeal appearance on OCT images including histology related to cytoplasm in the superficial epithelium enables visualising of large and irregular glands as well as oedema and expanding blood vessels. A disorganised architecture of the epithelium can be presented together with an increased nuclear to cytoplasm ratio.

Arytenoid oedema is presented in Fig. 1

In our Cochrane review of laryngopharyngeal reflux, considerations were made of the function of the arytenoid

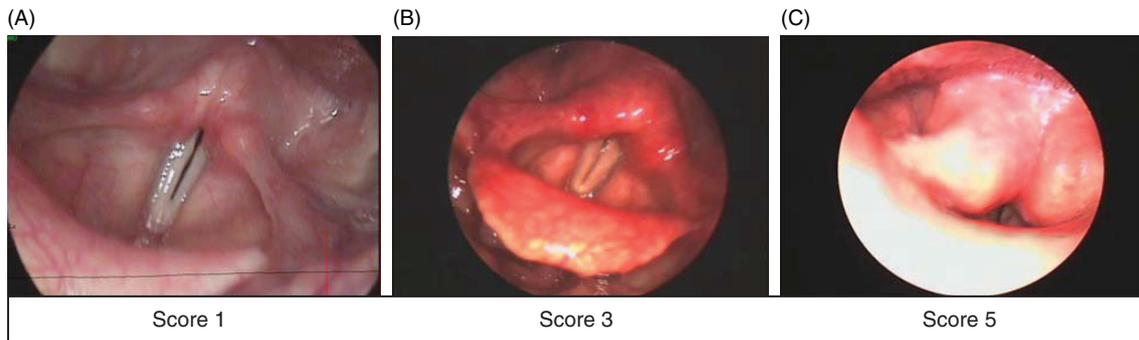


Fig. 1. High-speed film scores with 4,000 pictures/sec of the larynx including the arytenoid regions. Score 1 indicates a normal arytenoid region and normal vocal folds. Score 3 indicates a moderate oedema of the arytenoid region and normal vocal folds. Score 5 indicates almost total closure of the larynx due to arytenoid oedema (4).

region, and in our randomized controlled trial (RCT) these visual scores were valid (4, 6): visual scores (1–5) of the oedema, compared with symptom complaints.

Discussion

As with other new methods, the development evaluation includes apparatus development – in this case a probe for the larynx – as well as documentation of clinical use at best in randomised prospective clinical trials. OCT images of the vocal folds are well-known. A recent study has a detailed presentation of OCT of the vocal folds. To date, we have had no biopsies of the arytenoid regions because they have not been focused upon, even in this study. Focus has been on the vocal folds with OCT and the difficult construction of a probe for the larynx (1). In laryngology, the mucosa also has other areas of interest than the vocal folds. When it comes to treatment, especially in benign voice and swallowing disorders in the upper airways, especially in singers, laryngologists have an interest in documentation of diagnosis and treatment effect (11). As a routine, lactose intolerance, gluten intolerance, and mannose binding lectin is checked. These factors are known to affect the mucosal function in the entire body and may be the reason for the difference between laryngopharyngeal reflux and gastroesophageal reflux. To date, this has only been possible for the surface of the larynx with high-speed films with 4,000 pictures/sec as the true measure of vocal folds and arytenoid region surface (Fig. 1). Objective findings of laryngeal appearance on OCT images include histology related to cytoplasm, with cellular and molecular events resulting in arytenoid oedema in the superficial epithelium. OCT also enables visualising of large and irregular glands as well as expanding blood vessels. A disorganised architecture of the epithelium can be presented together with an increased nuclear to cytoplasm ratio. Since treatment of many disorders in the larynx are until now documented with only high-speed films and subjective complaints – the aspect of – as a minimum – to describe oedema and

the disappearance hereof with OCT would be a great step forward. Differences of the arytenoid area with OCT between various disorders is expected, especially of the dramatic effect of laryngeal treatment with fexofenadine and local budesonide inhaler in dystonia patients (2).

Conclusion

The OCT evaluation of tissue without biopsy has come to stay. It is invaluable in ocular and dermatological diagnosis and treatment (1). We have previously made a poster with an overview of most clinical upper airway areas (12). In laryngology, the focus has been on the vocal folds (1). Based on 10 years of experience in the development of high-speed films, OCT of the larynx arytenoid region, not only the vocal folds, will be of great significance in the diagnosis and treatment of laryngological disorders.

Conflict of interest and funding

The authors have not received any funding or benefits from industry or elsewhere to conduct this study. There is no conflicts of interests.

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