ISSN: 2637-4927

Annals of Biotechnology

Open Access | Review Article

Optical Coherence Tomography *in Vivo* in Laryngology Clinics, an Overview

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Received: Feb 10, 2022

Accepted: Feb 28, 2022

Published Online: Mar, 04, 2022

Journal: Annals of Biotechnology

Publisher: MedDocs Publishers LLC

Online edition: http://meddocsonline.org/

Keywords: Laryngology; Optical coherence; Tomography (OCT); Cowork.

Abstract

The aim of this review is to show the distance between the technical side of OCT and the understanding and needs of the laryngologists. In updated scientific research on OCT in laryngology, especially of the vocal folds, there are some obstacles of the techniques before the clinicians can use optical coherence tomography routinely.

This dialog between technicians and clinicians must be refined. If this had been the case earlier it is possible that basic pathology demands could have been met by the technicians, e.g. edema of the larynx was studied already studied in 2005.

Examples of development of instrumentation is presented hand in hand with diagnostics in the upper airways with OCT, lately technology of ultra-high resolution could even show cellular differences in laryngology.

The combination of optical coherence tomography with deep learning is a clinical application possibility for future very necessary evidence-based studies for clinical use.

Introduction

The use of Optical Coherence Tomography (OCT) can solve some problems of diagnostics and therapy in clinical routine work. Till now, focus of the sparse literature has been on classification especially in malignancy and differentiation hereof. The diagnostic use started in anesthetized patients, but focus is now on *in vivo* setups. With photonics development, the literature includes many examples of OCT equipment [1]. We have earlier suggested a design for a prospective randomized study of what we think is most important for OCT in clinical use, namely pharmacological treatment of hoarseness due to infections and allergy, and also laryngopharyngeal reflux with lifestyle change. In the dialog with the developers time changes quickly and their focus is now on ultra-high resolution OCT for detecting tissue abnormalities in the larynx [1,2].

The aim of the study is to optimize the discussion between developers and laryngologists in the clinic. In the clinic, we could use the equipment already on the market because the demands are very basic: diagnosis and documentation of edema eventual with grading of treatment of infections, allergies and reflux in prospective randomized studies of OCT, in co-work with developers. Some technical equipments are presented [3].

Cite this article: Pedersen M, Larsen C. Optical Coherence Tomography *in Vivo* in Laryngology Clinics, an Overview. Ann Biotechnol. 2022; 5(1): 1024.

The vocal folds have several layers as extensively discussed by Woo [4]. For many developers the knowledge of the relatively simple layers of the vocal folds is unknown. With OCT, the parts of the vocal folds can be specified. As referred to by Brian Wong et al, edema of the larynx can be seen - so it can also be seen when it disappears. This is enough for randomized control studies.

Some technical aspects discussed in the literature

In 2006 Lohscheller et al defined out vocal vibratory vocal fold edges with a flowrate of 98 frames per second. They suggested that hoarseness could be due to monolateral as well as bilateral incongruence during movement [5]. Since then, many technical systems have been developed. Out of 6 systems of OCT for vocal fold images, the systems SS-OCT117 seemed to be the best as evaluated by Pham et al [6].

Coughlan et al discuss a full field high-speed and long range OCT of awake patients with vertical cavity surface imaging laser source OCT, with a frame rate of 200 Hz. They have a large discussion of earlier works and description of the normal layers of the vocal folds in normal subjects [7]. No pathology is discussed.

Since most laryngologists use stroboscopy and not high-speed videos (mostly of 2.000 - 4.000 frames per second) for evaluating vocal folds, Maguluri et al tried to use stroboscopy of OCT on ex vivo in an excited larynx. This is a possibility also *in vivo* [8]. Sharma et al present office-based high-speed endoscopic images of OCT with correction of motion of the probe and focus artefacts with a sampling rate 250 Hz. As late as 2021 they only present normal subjects but do not take pathology into account [9].

Ultra-high-resolution technique is resulting in a single cell solution possibility also documented in skin on basal cell carcinoma as discussed by Israelsen et al, it is noted that this is a research project in dermatology where new techniques are tested in pathology [10]. The use of ultra-high resolution OCT is described in the skin in details by Israelsen et al. the same equipment could be used in laryngology if the cooperation could be updated between the clinical workers and developers [11].

One of the new possibilities is to deduct tissue variabilities with Convolution Neural Network (CNN) in automatic segmentation with OCT, probably always with post processing filtering as presented by del Amor et al on skin. A dice coefficient of 0,83 +/- 0,06 on 270 human skin images was found. Again, this development into AI age is made by dermatologists and could as well be made by laryngologists [12]. Also in ophthalmology, deep learning is used for image classification and pattern recognition. They suggest standardization for ground truth and prospective validations [13]. Laryngology is left behind.

The vocal folds in detail

Epithelium and basement membrane

The epithelium surface consists of non-keratinized squamous epithelium. Elsewhere in the larynx ciliated columnar epithelium with goblet cells and mucus is found, the scarce vessels are orientated parallel to the vocal folds.

Under the epithelium the basement membrane is found that serves as the anchory layer for lamina propria.

Lamina propria

The superficial layer

Is relatively thick with extra cellular matrix of hyaluronic acid. It has loose fibrillar collagen that runs largely perpendicular from the deep layer to the basement membrane. Large extra cellular matrix of glycoproteins is also located here with a consistency of water/gelatin, resulting in viscous elastic properties, also called Reincke's space. It is thickest in the mid membranous portion of the vocal folds. This layer is primary responsible for the mucosal wave. The whole lamina propria is 1-1.5 mm thick in the mid membraneous portion as presented by Woo [4].

The intermediate layer

Is rich in elastic fibers with higher concentration in the anterior and posterior.

The deep layer

Is called the vocal ligament inserted anteriorly into the thyroid cartilage and posteriorly into the vocal process of the arytenoid cartilage, it includes dense parallel collagen fibers arranged horizontally in a wave pattern fixed to conus elasticus discussed by many authors [3,4].

Clinical aspects discussed with references

Some studies discuss tissue details and pathologies of the vocal folds and nearby organs. Classification of pathology and further possibility of diagnostics are also looked upon with OCT. Wittig et al discuss classification of tissue with OCT and make a combination with deep learning [14]. A quantitative evaluation of the human vocal fold extracellular matrix using multiphoton microscopy and optical coherence tomography was done by Benboujja and Hartnick, this is very interesting study but only in normals [15]. The same team has study maturation of the vocal folds [16].

It would be extremely helpful if it was possible to use the phenomena described in oral epithel, Stasio et al describe images of 28 healthy patients [17]. A study was made on wide-field and long-ranging-depth optical coherence tomography microangiography of human oral mucosa by Wei et al, who describe the structures that we would like to see in the daily clinic:

The structure characteristics of human tissue with OCT is shown during wound-healing as it appears with tissue inflammation, vascular capillary loop density and vessel morphological orientation, the qualitative evaluations reveal pathological underpinnings. Especially the progress of oral capillary angiogenesis is a symptom of healing, of invaluable help for the time course of therapy [18]. Another invaluable study was made on neck tissue where the authors were capable of differentiating nodules from fat [19].

In 2016 Volgger et al describes with OCT that it is possible to differentiate malignant lesions from early malignant and premalignant lesions with high sensitivity and specificity but they think that technical limits still hamper implementation into clinical routine [20].

In 2005 the perspectives of use of OCT in the clinic was already discussed by Klein et al, with a flexible OCT probe in vivo. It is the case for this team and as well as for Brian Wong and his team, that they have focused on further development of the techniques for OCT. It could have been optimal if they in a discussion with colleagues had defined the minimum expectations for the clinical use [21].

Discussion and conclusion

We have discussed some of the newer equipments of OCT and have presented the ongoing development. So the next problem will be to make randomized prospective studies for evaluating the usability in clinical connection. In the clinic many patients show infections, allergy and laryngopharyngeal reflux in the larynx as the reason for hoarseness and we do need documentation of treatment of these disorders as well as lifestyle changes.

Pathology of the larynx was evaluated with OCT during universal anesthesia and soon after with local anesthesia in vivo. Brian Wong et al discussed several benign disorders of 82 patients *in vivo* [3]. Another group was focusing on development during mutation [16]. In dermatology, Israelsen et al suggest high-resolution OCT, which can be used together with high-speed video pictures of the larynx [10]. Several studies focus on classification with deep learning. The equipment for OCT might make time ready for prospective randomized studies to document *in vivo* OCT in laryngeal pathology, in interdisciplinary co-operation between technicians and laryngologists.

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