Artificial Larynx, Mith or Reality?

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Abstract. Even now total laryngectomy remains the primary treatment for advanced laryngeal cancers. Recently tracheoesophageal prostheses proved effective in restoring voice after surgery. Microbial-derived rhamnolipids show promise in inhibiting biofilm formation that is the major limitation to the lifespan of voice prostheses. Despite attempts, larynx transplantation and artificial larynx construction face challenges, with tracheoesophageal voice prostheses being the most effective option. The work focuses on advancements in understanding the larynx, exploring laryngeal simulators, and developing an artificial larynx. Researchers aim to replicate mechanical properties and functions of the larynx. Laryngeal simulators with artificial vocal folds help diagnose pathologies, while progress in soft robotics is promising for creating implantable artificial larynges, potentially improving the quality of life for patients who underwent laryngectomy.

Keywords: *artificial larynx, vocal fold, voice, total laryngectomy, soft robotics*

Introduction

One hundred fifty years ago, Billroth performed the first total laryngectomy. Since then it became the treatment of choice for malignant tumors of the larynx. In the following decades several conservative treatments have been proposed for more limited laryngeal cancers and more recently not surgical treatments have been proposed in order to preserve the larynx that represents a fundamental organ in order to allow a good quality of life. The larynx is a very complex organ allowing us to communicate as it produces human voice, to eat as, through its sphincteric function, it allows us to assume food and liquids avoiding inhalation, and to breathe allowing us to live.

Although several procedures have been proposed and performed, total laryngectomy still represents the treatment of choice for advanced (most of T3 and most of T4) laryngeal cancers.

Quite recently very effective voice prosthesis have been produced (Provox valve, Blom-Singer valve, Groningen valve) that need to be implanted during or after total laryngectomy and which allow total laryngectomyzed patients to communicate. Through such prosthesis the air column produced by the lungs passes into the oesophagus and can be modulated by the residual vocal tract resulting in a voice that seems to be of far better quality if compared to the esophageal voice and to the one produced by the electrolarynx which represented for many years the only way to communicate for laryngectomized patients. The prevention and control of microbial biofilm formation are crucial elements for the prolongation of the lifespan of voice prostheses and the maintenance of health status. Studies conducted by Università del Piemonte Orientale and Politecnico di Torino in collaboration with ATOS Medical have recently demonstrated the applicative potential of microbial-derived rhamnolipids as next-generation anti-biofilm agents for the treatment of silicone for voice prostheses. Specifically, by the use of new nanotechnological approaches related to the functionalization strategies of silicone materials with rhamnolipids, the in vitro formation of Candida albicans and Staphylococcus aureus biofilms was significantly inhibited for periods of 29 and 63 days, respectively (Allegrone G. et al., 2022; Ceresa C. et al., 2019; Ciardelli G., 2022; Ciardelli G. et al., 2021; Fracchia L., 2022; Fracchia L., 2021).

On the other hand transplantation of the larynx, after several preclinical studies (Work et al.,1965; Boles et al., 1966; Ogura et al., 1966; Silver et al., 1967; Strome et al., 1992) has been also proposed by several authors (Krishnan et al., 2017; Farwell et al., 2013; Strome et al., 2001; Duque et al, 2007; Tintinago et al., 2005), but in the few reported cases the transplanted larynx did not function properly and at the end was rejected.

Also the attempts to build and implant an artificial larynx resulted to be ineffective (Debry et al., 2014) and until today the only functioning device is the tracheoesophageal voice prosthesis

Since several years we are working on a project that tends to build an artificial larynx together with the whole voice producing system (trachea and vocal tract) basing on the advances in soft robotic materials hoping that in the future a real help could be given to laryngectomized patients.

New technological approaches in artificial larynx development

The larynx is one of the smallest yet most complex organs in the human body. It performs three functions, two of which are vital: breathing, swallowing, and phonation. Anatomically, the larynx is a little box connected to the pharynx and esophagus and continuing into the trachea, composed of tissues, different for functions and consistencies as muscles, cartilages, nerves, vessels, and mucosa, ultra-specialized in some cases. A single horseshoe-shaped bone, called the hyoid bone, supports the larynx in the neck, connecting it to the jaw and the base tongue (Piazza et al., 2010). The larynx can perform movements in all directions of the three-dimensional space and, moreover, one of its components, (i.e., the vocal folds) can perform wave movements. The larynx is controlled by the autonomic, voluntary, and limbic nervous systems and the vascular network is just as complex.

In case of total laryngectomy, all the larynx functions are lacking. Currently, they are replaced with a tracheal stoma and a vocal prosthesis, which give many physical and social problems to the subject. In light of these premises, a total artificial larynx, intended as an implantable prosthesis able to replicate all the real mechanical properties of the biological organ, is still missing.

In the last 10 years, soft robotics has introduced a new way of thinking about robots, aiming at developing systems that are mostly composed of materials whose mechanical properties are in the range of soft biological matter. Intrinsic safety, adaptability, resilience, and conformability are among the major advantages brought by the use of soft and flexible robot bodies[1]. Following this research line, soft robotics technologies enabled the development of a new generation of implantable devices. The combination of elastomeric materials with tunable properties and muscle-like motions paved the way toward innovative soft active implants as an implantable artificial larynx.

[1] Zrinscak, D., Lorenzon, L., Maselli, M., & Cianchetti, M. (2023). Soft robotics for physical simulators, artificial organs and implantable assistive devices. Progress in Biomedical Engineering, 5(1), 012002. https://iopscience.iop.org/article/10.1088/2516-1091/acb57a

Nevertheless, the reproduction of such a complex organ needed a simplification, intended as the identification of the mucous membrane, cartilaginous, and muscular structures that are strictly necessary for the performance of the basic larynx functions.

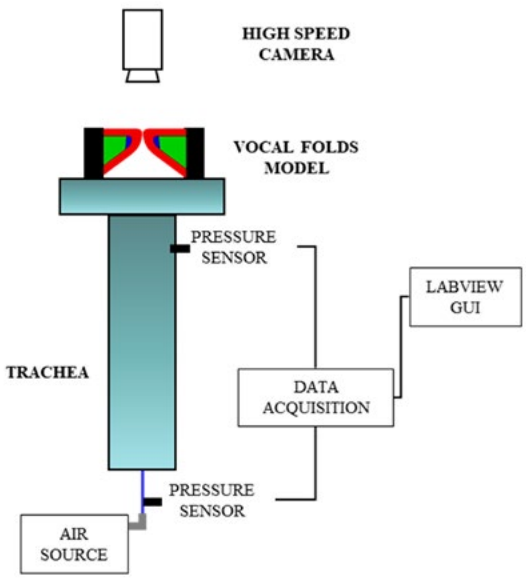

Figure 1: Full larynx configuration (Manti et al. 2015)

In order to reproduce a vocal signal like the human one, first studies were addressed to fabricate an artificial model of the vocal folds (VFs). VFs have a multilayer structure where each layer has different shape, thickness, and mechanical properties. According to the cover-body theory of Hirano the three layers are epithelium, lamina propria (superficial, intermediate and deep layer) and the vocal muscle (or thyroarytenoid muscle) (Hirano et al., 1985). The combination of morphology and mechanical properties defines the VFs oscillation. In order to fabricate an artificial model of VFs, Manti et al. (2014 and 2015) created a computational model of its geometry followed by the design. For the fabrication of the VFs prototype, the authors selected soft materials (silicones) with mechanical properties similar to the natural tissue in terms of viscoelasticity. The prototypes of VFs were arranged in a full-larynx configuration that is the phonatory configuration connected to a pressure air source, flowed to the glottic plane via a subglottal tube, obtaining an oscillation frequency and deformation mode closed to the physiologic ones (Fig. 1) (Manti et al., 2015).

Overall, the research studies required for the construction of an artificial model of the larynx offer the possibility to better understand the physiology underlying the voice production and the pathophysiology of dysphonia caused by different VFs diseases. The electroglottography (EGG) is a noninvasive tool to assess the vibratory motion of VFs during voice production, based on electrical impedance variations which occur on the VFs themselves during their vibration. Previous studies demonstrated the EGG allows to distinguish healthy subjects from pathological ones and organic from functional dysphonia by calculating a variability index (Zhang et al., 2004; Erath et al., 2012; Rauma et al., 2009).

Conte et al. (2021) described the results obtained from the realization of electrically conductive silicone VFs able to replicate an electroglottography (EGG) signal to provide a quantitative method for monitoring the VFs' vibratory characteristics (Fig. 2).

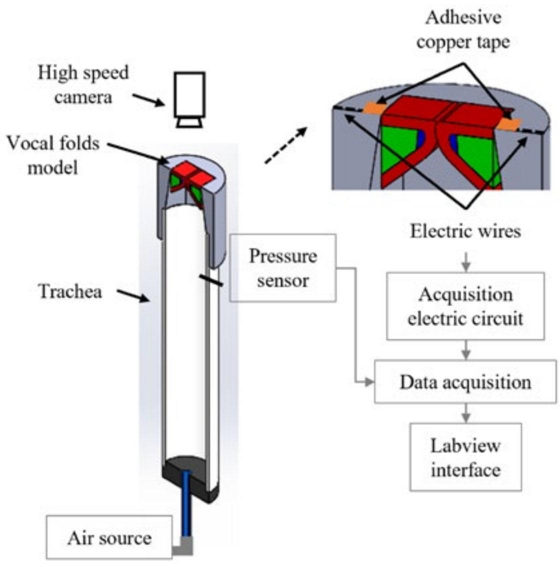

Figure 2: Experimental setup. Full larynx configuration scheme. (Conte et al. 2021)

The simulator showed similar oscillatory behavior to human VFs thanks to the materials used for their realization. Moreover, the prototype was able to reproduce an electrical signal comparable to a real EGG. This last result encouraged to test with the EGG the vibratory behavior of the artificial VFs in the presence of a VF lesion as polyp. Results showed that the simulator is able to replicate the vibratory characteristics of pathological VFs (Fig. 3).

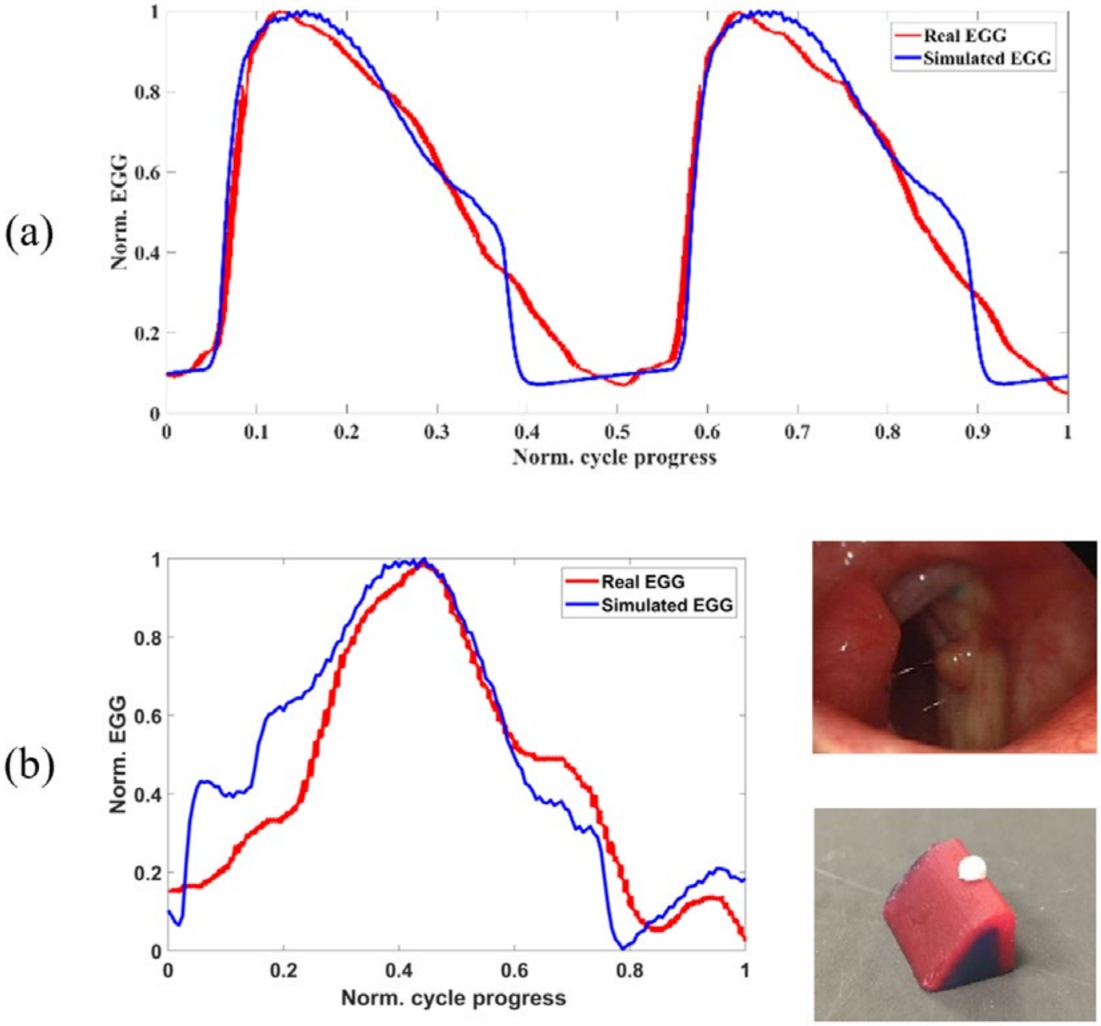

Figure 3: Clinical EGG signal (red) and simulated EGG signal (blue) of physiological (a) and pathological (b) condition. (Conte et al. 2021)

Nevertheless, the necessary condition to obtain an artificial vocal signal as close as possible to the human one, is the integration of the VFs in a more complex simulator that should include the VFs and the sub- (i.e., trachea) and supra-glottic (i.e., vocal tract) structures to obtain a complex pneumo-phono-articulatory apparatus. The development of larynx simulators as platforms for clinical investigations will represent a powerful tool to characterize and cluster different vocal folds pathologies, which can lead to a significant improvement of prevention programs and an early diagnosis for laryngeal diseases. In addition, the simulation of the larynx with materials similar to the natural counterpart represents an innovative approach for studying new prostheses for use in laryngectomized patients. This allows the development of artificial larynx increasingly similar to its anatomical counterparts, replicating mechanical characteristics and functionality. However, a total artificial implantable larynx, able to replace the current vocal prosthesis, is still at research level. In this regard, Pozzi et al. recently (2023) analyzed the larynx of different animal classes, to find basic structures and movements. They found that two cartilages (i.e., the cricoid and the arytenoids) and three muscles (i.e., the posterior cricoarytenoid, the lateral cricoarytenoid, and the thyroarytenoid) are common to all the studied species. Starting from the cartilages, a prototype of larynx must have a ring-shaped cricoid cartilage to keep the airways open. It is present in all studied species, even in those without a high vocalization complexity. On the other hand, the opening and closing movements of the VFs are ensured by the three muscles cited above: the posterior cricoarytenoid, which opens the vocal folds; the lateral cricoarytenoid, which closes the vocal folds without stretching them; and the thyroarytenoid, which stretches the vocal folds. The opening and closure of the glottis allow the air to pass through the airways from one side and the vocal folds to vibrate to the other. The tension of the vocal folds guarantees a tight closure of the glottis during swallowing. Different tensions of the vocal folds guarantee different voice tones. Without this modulation, the voice would be a monotonic voice, but at the early stage of this work, it may be acceptable. Pozzi et al. (2023) provided a preliminary and simplified schematization created as a CAD (computer-aided design) model in SOLIDWORKS® software that reproduces the layout of the VFs connected to the arytenoids and that shows their movements driven by the three selected muscles (Fig. 4). The future challenge is the selection and development of the most suitable actuation technology to replicate the double and opposed motion of the VFs that provides, at rest, the open status for breathing, the closing for the phonation, and the tension for the modulation of the voice.

The grand challenge of all these research studies remains the creation of an implantable artificial larynx able to substitute the biological one after laryngectomy. As with all implantable materials, the problem remains the long-term biocompatibility. Currently, the voice prostheses are designed to be easily removed and replaced periodically without surgery, but this is hard to imagine for an artificial larynx. For this reason, it is of paramount importance the selection of materials in terms of resistance to biofilms and mechanical stress due to the never-still condition of this organ.

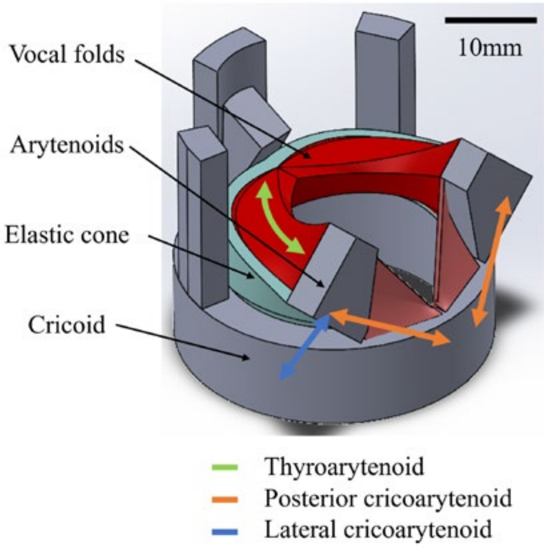

Figure 4: CAD design of the human artificial larynx. The vocal folds are in the scheme, integrated in the elastic cone. The actions of the three selected muscles are shown with arrows: the posterior cricoarytenoid muscle (in orange), opens the vocal folds; the lateral cricoarytenoid muscle (in blue) closes the vocal folds; the thyroarytenoid muscle stretches the vocal folds. (Pozzi et al. 2023)

Conclusions and future outlook

The purpose of this work is to provide some knowledge about the larynx and the current progress in the field of clinical and surgical investigation through the development of laryngeal simulators and an artificial larynx, able to reproduce all the mechanical properties and functions of the original organ.

The larynx with its three functions (breathing, swallowing, and phonation) is one of the most complex organs in the human body, and, therefore, still very much studied. In case of advanced laryngeal carcinoma, the gold standard is the surgical procedure, consisting on the complete removal of the organ. This implies many issues related to the quality of the patient's life. Hence, it is fundamental to try to restore all the lost functions. To achieve this goal, the researchers are moving in the direction of laryngeal simulators, replicating the mechanical properties of the real larynx, with integrated artificial vocal folds, able to reproduce their vibration. In addition, the use of a conductive materials in the simulator (Conte et al., 2021), made it possible to replicate an EGG signal under pathophysiological conditions from which quantitative parameters could be extracted. This approach will allow clinicians to perform early diagnosis of the vocal folds pathologies.

However, an artificial larynx, intended as an implantable prosthesis, able to reproduce all the laryngeal functions, is still missing. A first step was taken by Pozzi et al. (2023), in which a simplified primitive model of an artificial larynx, capable of restoring lost functions, is described. Thanks to developments in the field of soft robotics, it will be possible to obtain an artificial larynx composed of biocompatible materials with human-like behavior. In addition, the developed soft technologies will be able to be used to replicate muscle functionalities. The development of an artificial larynx will be an important solution that can dramatically change the laryngectomized patient's life conditions.

Aknowlegdments

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Conflict of interest statement

All authors declare that they have no conflicts of interest.

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