STUDY OF VOCAL FOLD MECHANOBIOLOGY USING AN AIRFLOW-DRIVEN PHONATION BIOREACTOR

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Introduction

The vocal folds are located within the larynx. They are the main organ of voice production for human communication. During phonation, the vocal folds undergo periodic mechanical stresses as for other mechanically active organs, such as the heart, the lungs, tendons and muscles. During speech and singing, the vocal folds oscillate at frequencies ranging from 20 to 3 kHz and with peak amplitudes of a few millimetres.

Depending on pitch, level and dose, the biomechanical stresses involved in phonation can alter vocal fold cell activity and tissue structure in multiple ways. Excessive phonatory stress can damage tissue structure and induce cell-mediated inflammatory response, resulting in a pathological vocal fold lesion. On the other hand, a specific form of vocal fold oscillation, which involves small impact and large amplitude tissue mobilization, is prescribed therapeutically for patients with mildly injured vocal folds.

Although biomechanical forces clearly affect the physiology and pathology of the vocal folds, our current understanding of how mechanical forces regulate these processes at the cellular and molecular level is insufficient. Research on the vocal fold mechanobiology is warranted. Vocal fold bioreactors are currently developed to provide a biomimetic environment that allows the systematic manipulation of physical and biological factors on the cells of interest *in vitro.* Existing bioreactors are mechanically driven using electromagnetic voice coil actuators, in which cells may be agitated by unwanted mechanical or unwanted fluid perturbation.

In this study, we designed an airflow-induced and self-oscillated vocal fold bioreactor that mimics human vocal fold vibrations, in particular the presence of a mucosal wave.

Methods

An airflow-induced, self-oscillated vocal fold bioreactor was developed and used to apply mechanical loading to immortalized human vocal fold fibroblasts (Figure 1). The oscillation frequency, onset pressure, and pressure-versus-flow characteristics of the vocal fold replicas were in the range of human phonation. sCells were housed in hyaluronan-silicone composite synthetic vocal folds. Cytotoxicity test was carried out to test the toxicity of the synthetic vocal folds. Samples were imaged using a light microscope 24 hours post-culture.

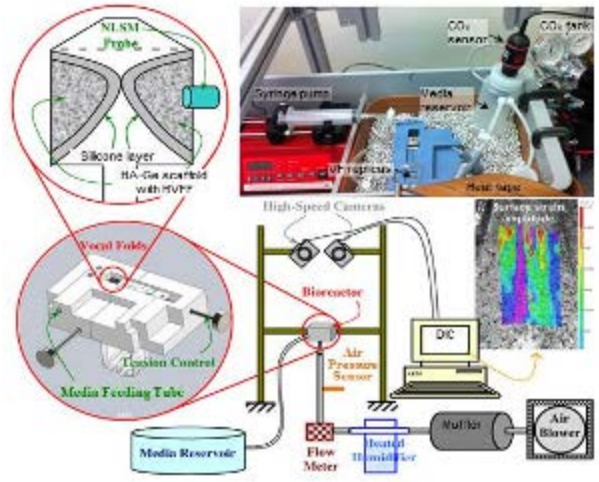

Figure 1. Vocal Fold Bioreactor. Synthetic vocal folds self-oscillate in response to air flow. The scaffold is heated and enclosed in a sterilized environment. Extracellular matrix components are imaged with nonlinear laser scanning microscope. Mechanical deformations were measured with digital image correlation. HVFF = human vocal fold fibroblasts

Results

Preliminary results indicated cells showed normal growth in the synthetic vocal folds at the 24-hour time point. Further cytotoxicity test will be performed for longer time points. In addition, the effects of different mechanical regimes on cell activity, such as extracellular matrix protein expression and alignment, will be available at the time of presentation.

Discussion

We investigate the influence of mechanical loads, function of pitch, amplitude and rest periods, on the distribution, concentration and orientation of extracellular matrix proteins measured with nonlinear scanning microscopy.