

# The impact of phonomimetic vibration on vocal fold inflammation

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## Introduction:

To date there is no ultimate recommendation on how long patients should rest their voice after an acute injury. Orientating on other medical fields, where a rapid mobilisation after surgery is aimed at in order to achieve an earliest possible recovery. In the past years, there has been a tendency in decreasing the interval of voice rest after phono-microsurgery. The impact of mechanical forces on the lamina propria has been addressed by several papers, knowing that it plays an important role in phonation. [1][2][3][4][5][6]

This *in vitro* study aims to reveal the impact of mechanical stress by means of vibrational forces on vocal fold fibroblasts (VFF), the most abundant cells in the lamina propria, during an acute inflammatory reaction by putting an emphasis on the molecular and cellular level. [7]

## Materials and Methods:

After an inflammatory stimulus, 144.000 human VFF per well were exposed to vibrational forces for three days in order to imitate a physiologic vocal strain. [8] Mechanical stimulation was applied for four hours over a period of 72 hours. An acute inflammatory reaction was simulated by adding 5ng/mL IL1b as well as the same concentration of TGFb1. Consequently, each experiment was carried out in four different settings: static as well as dynamic, both with and without cytokines.

Subsequently the differences in mRNA expression as well as the concentrations of proteins, being responsible for the extracellular matrix (ECM) composition of the lamina propria, and of proteins, which are known to play an important role in inflammatory reactions, were investigated and compared amongst the different groups. All experiments were repeated four times.

## Results:

Cytokine treatment induced a change in the expression of ECM- as well as inflammation-related genes.

The pro-inflammatory cytokine IL11, as well as the myofibroblast marker alpha smooth muscle actin ( $\alpha$ -SMA) were significantly reduced when additional vibration was applied. Hyaluronic acid (HA) concentration was significantly increased due to the cytokines, however mechanical stimuli did not show any effect on HA metabolism.

## Discussion:

The upregulation of certain genes and proteins by the cytokine treatment was in line with other *in vivo* experiments. It therefore reflects the applicability of our *in vitro* inflammatory model. IL11 belongs to the IL6-family and appears to be an essential part in the down-streaming pathway of TGFb1. It therefore plays an important role in pro-fibrotic reactions. [9]

During fibrogenesis VFF transform to myofibroblast, leading to a wound contraction in order to facilitate healing. However, simultaneously, they may impair oscillatory properties of the vocal folds and consequently cause hoarseness. [10]  $\alpha$ -SMA is a well-established myofibroblast marker.[8][11] Elevated concentrations of these two proteins as well as the absence of changes in the desirable anti-fibrotic ECM component HA due to vibration, suggests a beneficial effect of mechanical stimulation following inflammation. These findings corroborate clinical studies which recommend early voice activation following an acute event. [5][12][13]

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