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Introduction

Sputum abnormal viscoelasticity is related to the difficulties experienced by some COPD patients to have an efficient clearance^{1,2}. Meanwhile the COPD early-diagnosis is still a major challenge. The study aims to find out whether rheology can be used in a clinical context to diagnose COPD and to assess the efficiency of treatments. Rheomuco device provides the classical and new rheological parameters of the sputum. These parameters were used to compared COPD patients and asthmatic patient from healthy volunteers, and to test the sensitivity of nebulization.

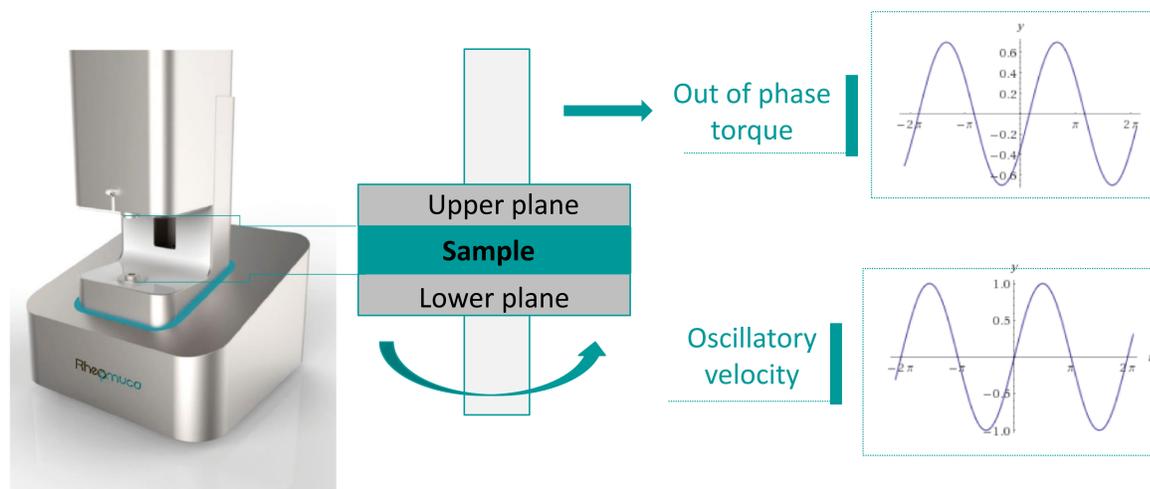
Methods

Rheology is the study of the flow of matter that exhibits a combination of elastic, viscous and plastic behavior. Elasticity, viscosity and plasticity are measured with a rheometer. The Rheomuco device was used to measure the viscoelastic properties in a clinical study (NCT02682290) called "Assessment of Rheological Parameters of Human Sputum". Three properties are mainly extracted: elastic modulus G' , viscous modulus G'' and the damping ratio $\tan\delta$. Viscale™ score is a combination of those rheological properties. The study was led by and in the Grenoble University Hospital (France) with 3 groups: 10 COPD, 10 asthmatics and 10 healthy volunteers. The eligibility criteria are COPD and asthmatic patients with bronchial disorder, confirmed by Grenoble University Hospital. The exclusion criteria are :

- FEV1 \leq 40%, PaO2 < 60 mmHg at rest
- Acute exacerbation during the last month
- contraindications for spirometry

Two visits V1 and V2 were performed 48 hours apart. Patients with COPD have a spontaneous expectoration. Patients with Asthma and healthy volunteers need an induced expectoration with hypertonic saline solution (4.5%) during 10 minutes to generate a sputum. Then, patients with COPD have an induced expectoration with hypertonic saline solution (4.5%) during 10 minutes maximum. First sputum out are taken for analysis.

Expectoration were homogenized and Rheology measurements at 37°C are made on each of them on the Rheomuco device (Rheonova, France) dedicated to the measurement of rheological properties of sputum.



Results

Measurements for moduli G' , G'' , $\tan\delta$ are showed at a frequency $F=1\text{Hz}$ inside the linear viscoelastic region ($\gamma \sim 3\%$). Moduli are significantly higher ($p < 0.05$) in COPD patients compared to healthy volunteers (Figure 2). Viscale™ is a score in logarithmic scale with discriminate both group. The asthmatic group is not significantly different from healthy group. All sputum have a gel like behavior with $\tan\delta < 1$. Nebulization makes G' and G'' sink: Viscale™ score rises and expectoration abilities may be improved. Nebulization induces only a small variation of $\tan\delta$: no change in sputum structure is observed, only dilution effect is present.

Figure 1 : Healthy (n=10) vs COPD (n=10) vs Asthma (n=10)

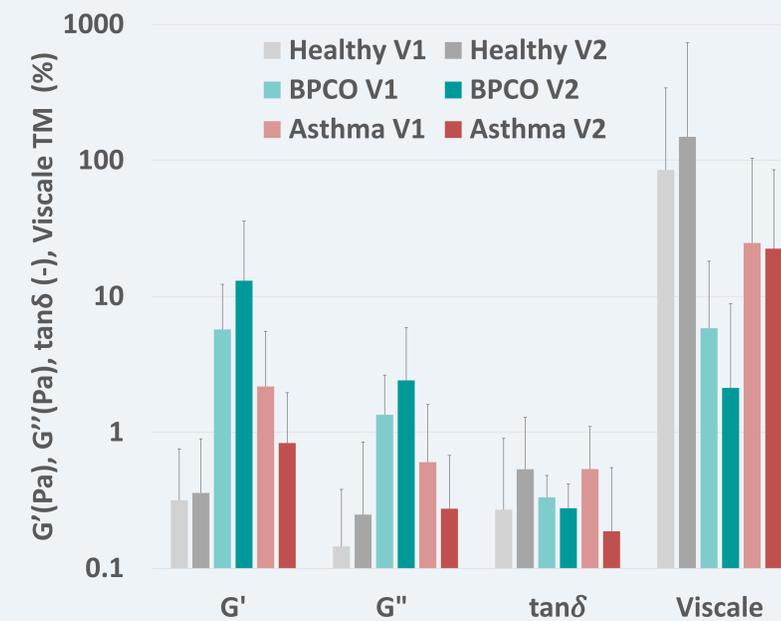
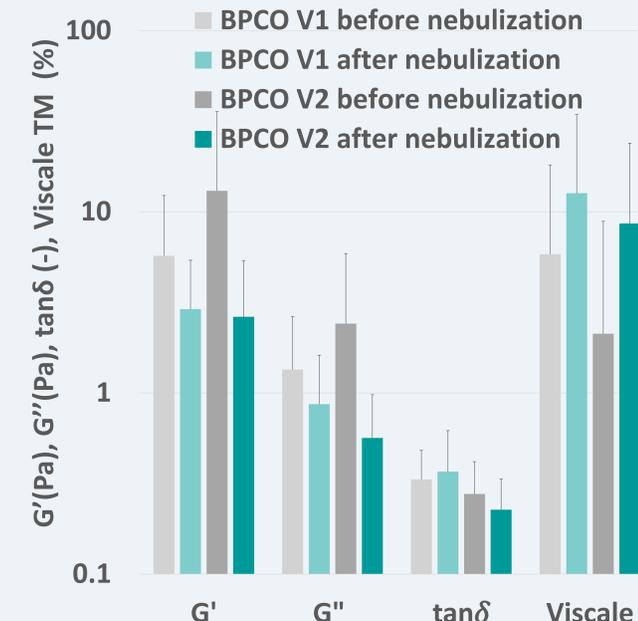


Figure 2 : Effect of nebulization on COPD (n=8)



Conclusions

COPD patients sputum without exacerbation exhibit over 1 decades more viscoelastic properties (elastic and viscous) than healthy volunteers sputum, as well as the viscale™ score.

Viscoelastic parameters for COPD drastically decrease following nebulization ($G'/2$ and $G''/1.5$). As $\tan\delta$ is not affected by nebulization, the drop of viscoelastic properties is only due to dilution effect.

Sputum viscoelastic properties do not discriminate asthma from healthy volunteer in this first analysis. More mechanical properties regarding asthma will be analyzed in the forthcoming full analysis.

The next step is to evaluate the potential of the technique to monitor treatments in COPD patients, and to establish the prognosis of exacerbations. The other potential is to use the technical has an early-diagnosis criteria, for sputum with a viscale™ score under 50%.

Bibliography

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