# SPUTUM RHEOLOGY AS A TOOL TO ASSESS COPD DIAGNOSIS COMPARED TO ASTHMA DIAGNOSIS, AND TO EVALUATE THE EFFICIENCY OF TREATMENTS

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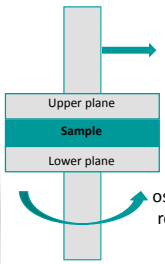
## Issue

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 patients from healthy volunteers, and to test the sensitivity of nebulization.

## Rheometry

Rheology is the study of the flow of matter that exhibits a combination of elastic, viscous and plastic behavior by properly combining elasticity and fluid mechanics. Elasticity, viscosity and plasticity are measured with a rheometer.




In phase contribution:
- G' elastic modulus

$$G' = \frac{\tau}{\gamma}\cos\delta$$

Out of phase contribution:
- G'' viscous modulus

$$G'' = \frac{\tau}{\gamma}\sin\delta$$

- tan$\delta$ Phase tangent

$$\tan\delta = \frac{G''}{G'}$$

G' and G'' are measured for different $\gamma$ and frequency F. If they are too high, epithelial cilia may be blocked.

tan$\delta$ is used to characterize the microstructure of the sputum: its modification means a modification of the sputum molecular structure.

tan$\delta$<1 → Gel behavior
Mucus stands on the epithelium.
tan$\delta$>1 → Viscous behavior
Mucus flows down in the lung.

## Clinical trial

Assessment of Rheological Parameters of Human Sputum [Rheomuco, NCT02682290]

**10 COPD patients, 10 Asthmatic patients and 10 healthy volunteers**

**Eligibility criteria:**
- COPD and asthmatic patients with bronchial disorder, confirmed by Grenoble University Hospital

**Exclusion criteria:**
- FEV1 ≤ 40% ; PaO2<60 mmHg at rest
- Acute exacerbation during the last month
- Contraindications for spirometry

**Two visits V1 and V2, 48 hours apart**

On each visit:
Patients with COPD have a spontaneous expectoration.
Then they have an induced expectoration with hypertonic saline solution (4.5%) during 10 minutes.

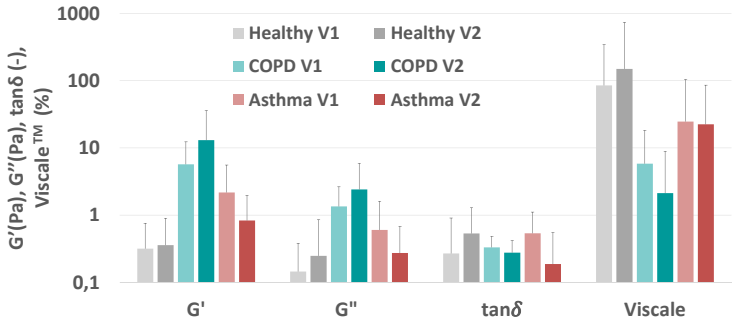
Patients with Asthma and healthy volunteers need an induced expectoration with hypertonic saline solution (4.5%) during 10 minutes to generate a sputum.

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

## Results

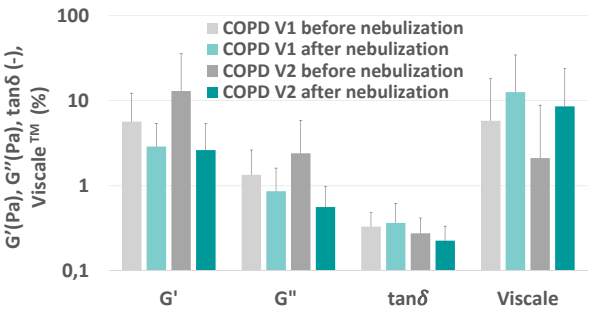
First sputum out are taken for analysis. Measurements for moduli G', G'', tan$\delta$ are showed at a frequency F=1Hz inside the linear viscoelastic domaine ($\gamma$~3%). Viscale™ , a score in logarithmic scale, is a combination of the rheological properties above. All statistical treatment of the data will be finalized for the end of the study which is scheduled for october 2017.

**Healthy (n=8) vs COPD (n=10) vs Asthma (n=10)**




Elastic and viscous moduli are significantly higher (p<0.05) in **COPD patients compared to healthy volunteers**. Viscale™ score discrimates both groups. The asthmatic group is not significantly different from healthy group. All sputum have a **gel like behavior** with **tan$\delta$<1.**

**Effect of nebulization on COPD (n=8)**




Nebulization makes G' and G'' sink: **Viscale™ score is improved.** Small variation of tan$\delta$: **no change in sputum structure**, only dilution effect is present.

## Conclusion

1. COPD patients sputum without exacerbation exhibit over 1 decade more viscoelastic properties (elastic and viscous) than healthy volunteers sputum, as well as the viscale™ score.
2. These 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.
3. Sputum viscoelastic properties do not discriminate asthma from heathy 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%.

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**Serisier** D.J. et al. **2009**. "Macrorheology of Cystic Fibrosis, Chronic Obstructive Pulmonary Disease & Normal Sputum." Respiratory Research 10

**Tomaiuolo** G. et al. **2014**. "A New Method to Improve the Clinical Evaluation of Cystic Fibrosis Patients by Mucus Viscoelastic Properties." PloS One 9