

Sputum rheology as a tool for treatment evaluation and monitoring in Cystic Fibrosis

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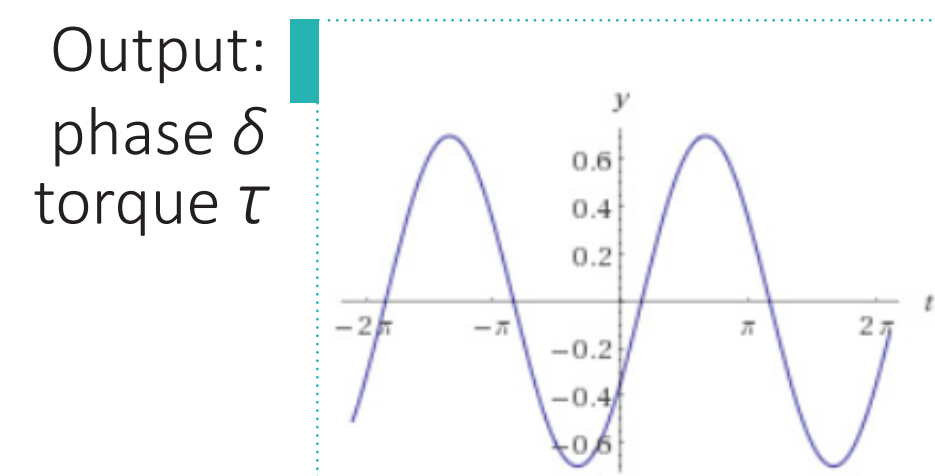
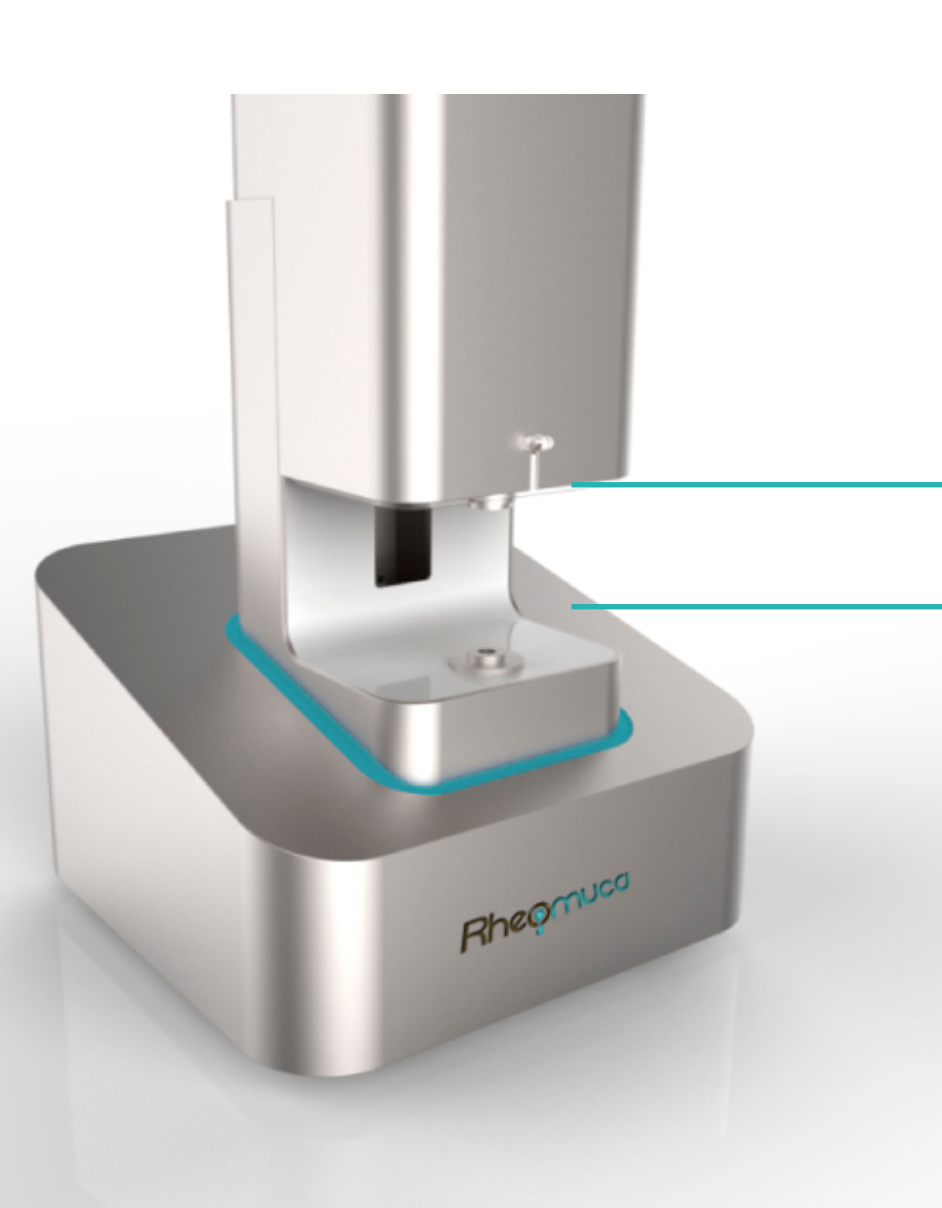
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Issue

While sputum abnormal viscoelasticity is the main cause of the difficulties experienced by CF patients to have an efficient clearance, its physical quantification is currently impossible at the bedside. Today, those deficiencies are indirectly monitored through EFS measurements. We tested whether the Rheomuco device may quantify the rheological parameters of the sputum, and whether these parameters were sensitive to treatments.

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:

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

G' and G'' are function of γ and the frequency F

Out of phase contribution:

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

$\tan(\delta)$ Phase tangent

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

$\tan(\delta) < 1 \rightarrow$ Gel behavior
 $\tan(\delta) > 1 \rightarrow$ Viscous behavior

Clinical trial

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

10 CF patients, 10 healthy volunteers

Eligibility criteria:

- Adult CF patients with bronchial disorder, confirmed by Grenoble Reference Center.

Exclusion criteria:

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

Two visits 48 hours apart

First visit: Patients with CF have a spontaneous expectoration. Then all participants will have an induced expectoration with hypertonic saline solution (4.5%) during 10 minutes maximum. First incoming sputum in the following statistics.

Second visit: Patients with CF have a spontaneous expectoration followed by 20 minutes RhDNase nebulization and again a spontaneous expectoration 1 hour after.

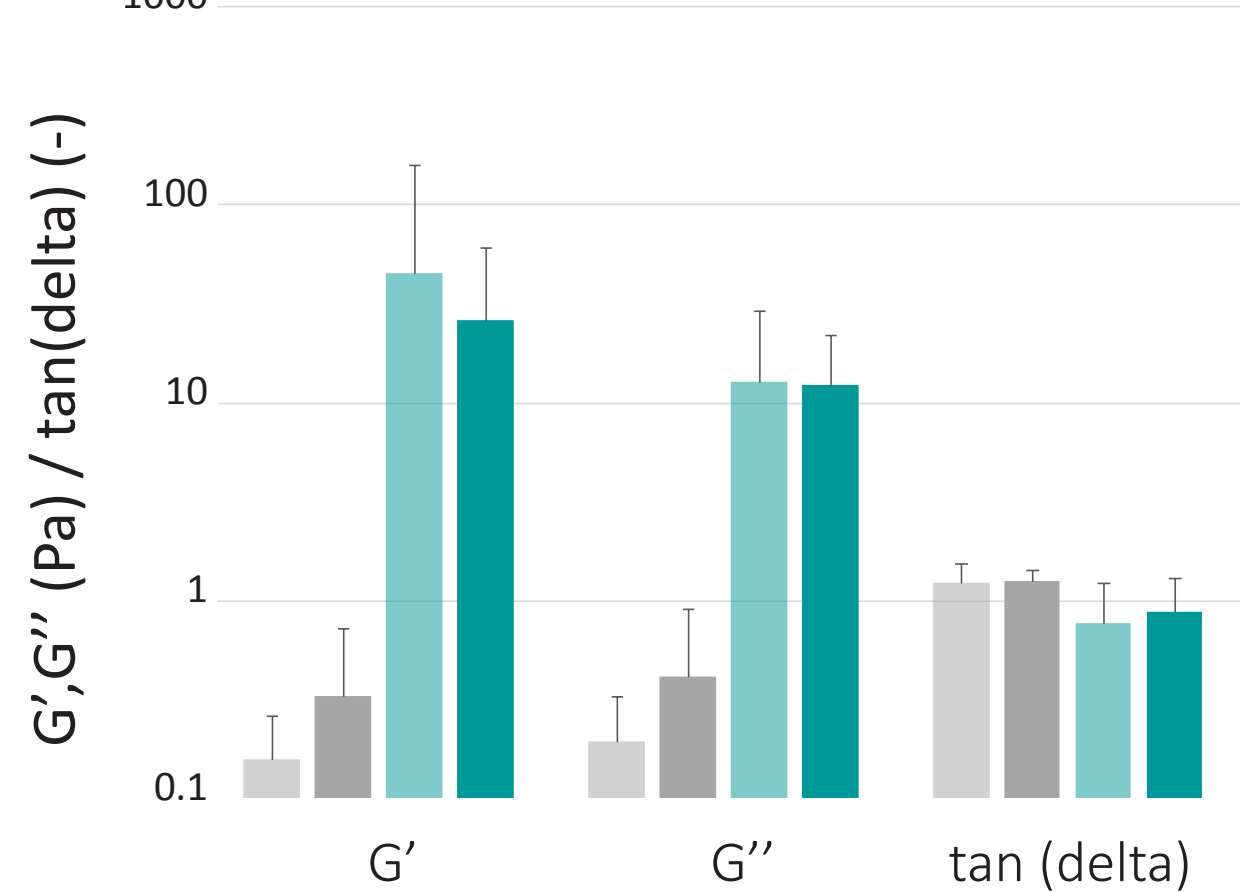
Expectoration were homogenized and Rheology measurements at 37°C are made on each of them on the Rheomuco device (Rheonova, France) dedicated to the measurement of rheological properties of sputum.

Results

Measurements for modulus G' and G'' are showed at a frequency $F=1$ Hz.

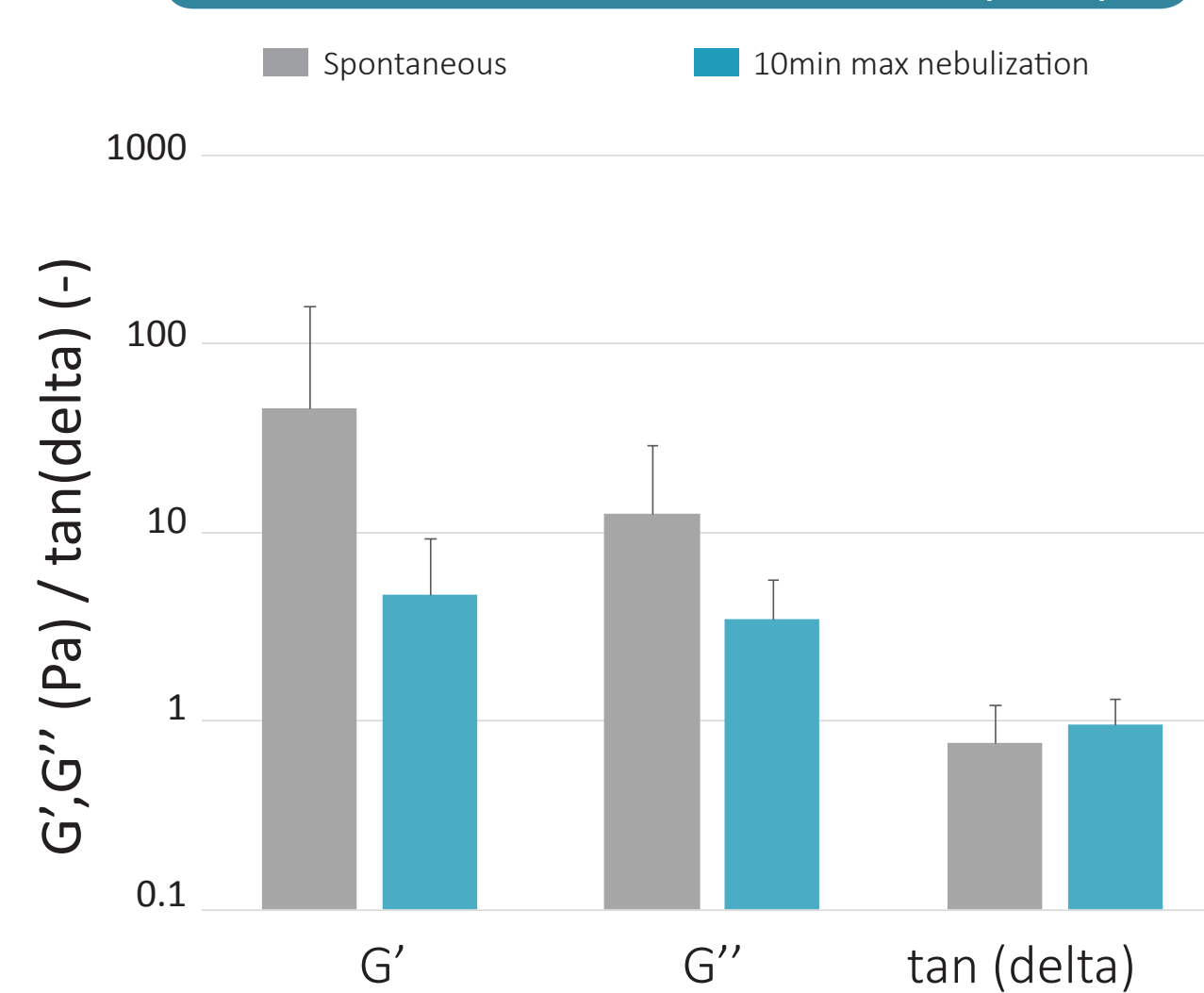
Statistical treatment of the data will be finalized for the end of the study which is scheduled for June 2017.

CF (n=10) vs Healthy (n=8)



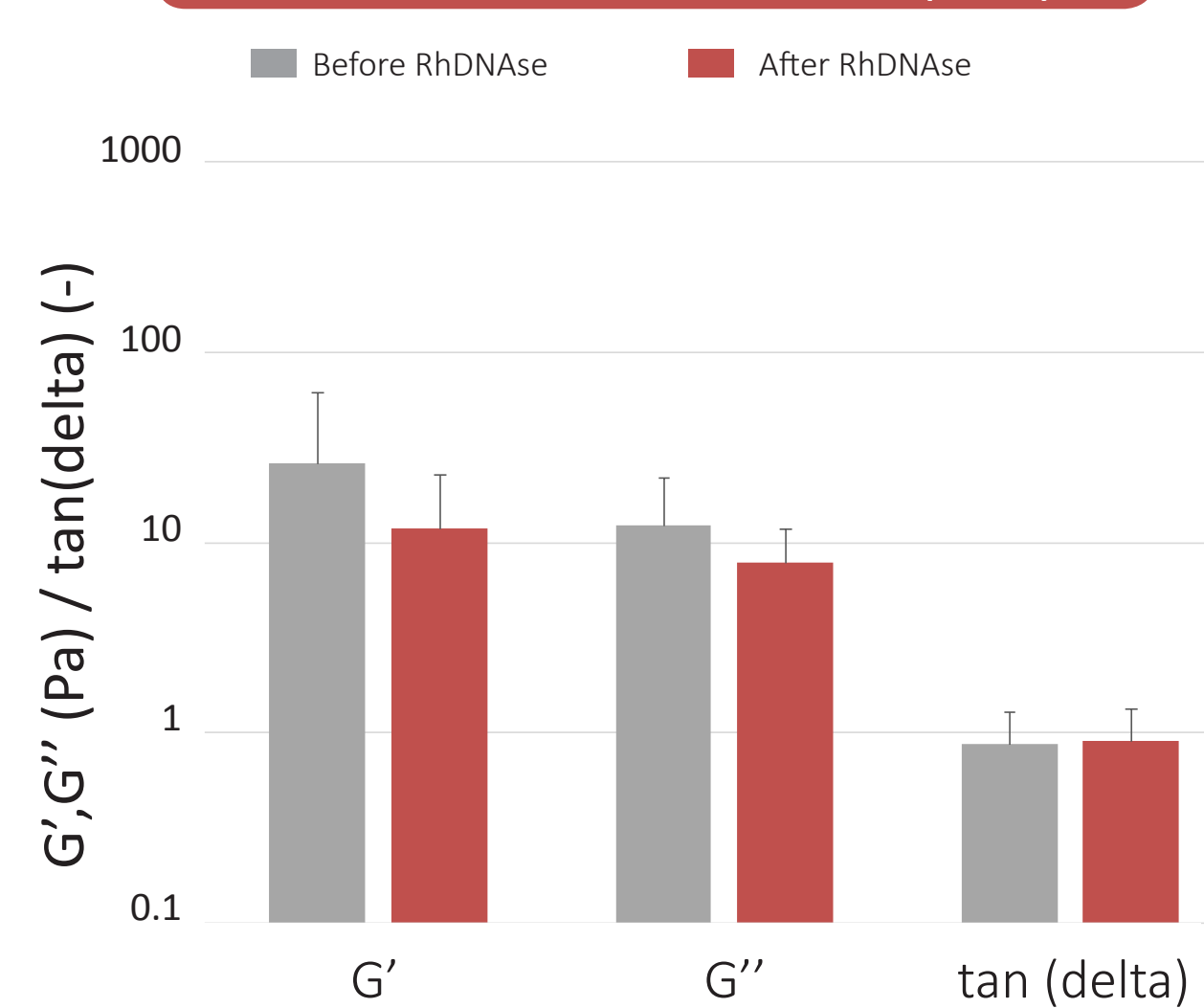
Elastic and viscous modulus G' , G'' are both several times higher in CF patients.
Healthy $\tan(\delta) < 1$: Normal Gel like sputum
CF $\tan(\delta) > 1$: Viscous sputum (sticky)

Effect of nebulization on CF (n=6)



Nebulization reduces makes G' and G'' sink: Drop of consistency
Small variation of $\tan \delta$:
No change in behavior with CF $\tan(\delta) > 1$

Effect of RhDNase on CF (n=5)



RhDNase reduces G' by 35 % and viscous modulus G'' by 50 %.
Change in behavior with CF $\tan(\delta) < 1$:
Same behavior as Healthy volunteer

perspectives

Conclusion

- CF patients sputum exhibit 2 decades more viscoelastic properties (elastic and viscous) than healthy volunteers sputum.
- These parameters drastically decrease following nebulization ($G'/4$ and $G''/10$), less due to RhDNase ($G'/1.5$ and $G''/2$).
- Contrary to nebulization, RhDNase changes the behavior CF sputum ($\tan(\delta) > 1$) into the healthy behavior ($\tan(\delta) < 1$).

The next step is to evaluate the potential of the technique to monitor treatments in CF patients, and to establish the prognosis of exacerbations, through more clinical trials.

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