CF sputum properties correlate with pulmonary function

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Background

Mucus is a barrier to airway water loss and microbial invasion and maintains homeostasis in the airway. In patients with cystic fibrosis (CF), the sputum is tenacious, leading to abnormal mucus clearance. We have conducted a longitudinal study to examine changes in the biophysical properties of CF sputum over time in relation to disease status.

Objectives

1. To evaluate if changes in viscoelastic properties of CF sputum correlate with changes in pulmonary function over time
2. To evaluate if viscoelastic properties of CF sputum change with therapy

Methods

Sputum:
CF sputa were collected from 8 subjects (4 male; 6 adolescents, 2 adults) during pulmonary function testing at each clinical encounter over 5 years. Sputa were frozen at -80^{0}C until analyzed.

Dynamic rheology:
Dynamic rheology was measured using an AR1500ex rheometer (TA Instruments) in oscillatory mode over the linear portion of the stress/strain curve from 0.1 to 1000 rad/s.
The elastic G' and viscous moduli G", are given in Pa-sec.

Pulmonary function testing (PFT):
PFT was performed during outpatient clinic visits and met ATS criteria for reproducibility and expiratory time. The results are reported using NHANES III reference values.

Table 1:
Clinical and demographic characteristics of CF subjects (n=8). All subjects were on dornase alfa as mucolytic therapy.

Age (yr)	Sex	Sputum Pathogen(s)
17	M	MR *S. aureus, P. aeruginosa*
15	F	*P. aeruginosa, A. fumigatus*
15	M	MS *S. aureus*
14	M	MR *S. aureus, A. fumigatus*
52	F	*P. aeruginosa*
34	M	*P. aeruginosa*
13	F	MR *S. aureus, P. aeruginosa, A. fumigatus*
12	F	MR *S. aureus*

Results

Fig 1a. Mean Elastic Modulus G' stratified by FEV1 % predicted. Elasticity increased as FEV1 decreased (N=8 subjects). There were significant differences in G' between FEV1 strata (Kruskal-Wallis one-way ANOVA, p = 0.0007).

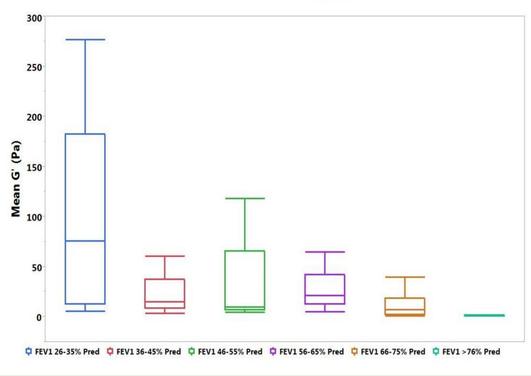


Fig 1b. Mean Viscous Modulus G" stratified by FEV1 % predicted. Viscosity increased as FEV1 decreased (N=8 subjects). There were significant differences in G" between FEV1 strata (Kruskal-Wallis one-way ANOVA, p = 0.0002).

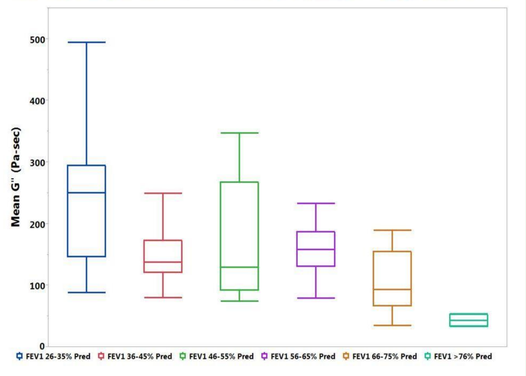


Fig 2a. Graphs of CF sputum G' plotted against FEV1 %Predicted for 8 subjects with CF. As the elastic modulus at 100 rad/s increases, there is a dramatic decrease in FEV1 %Predicted. The linear regression model is $G' = 103.9 - 1.36FEV1$, R^2=0.20.

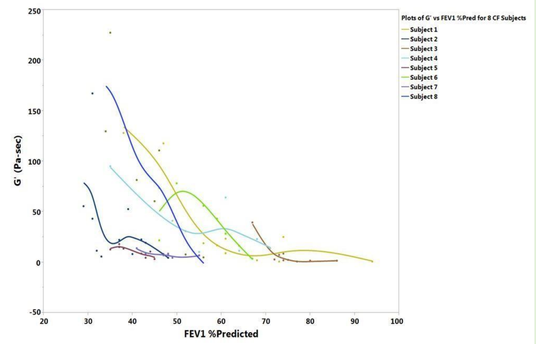


Fig 2b. Graphs of CF sputum G" plotted against FEV1 %Predicted for 8 subjects with CF. As the viscous modulus at 100 rad/s increases, there is a dramatic decrease in FEV1 %Predicted. The linear regression model is $G'' = 300 - 2.794FEV1$, R^2=0.26.

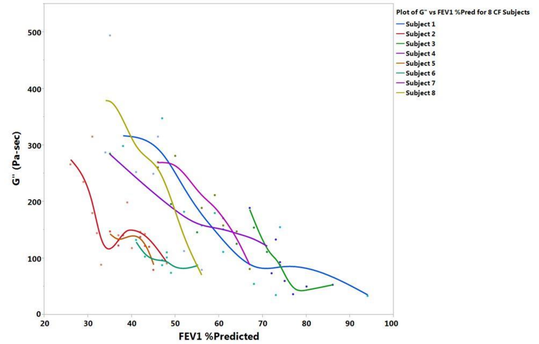
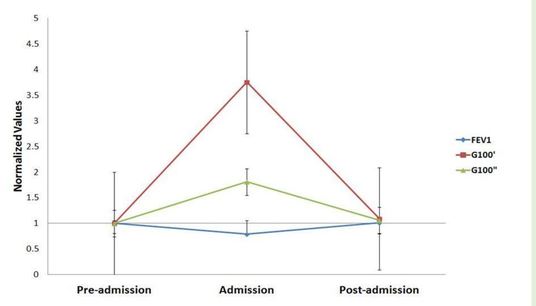


Fig 3. Normalized curves showing the relative values of pre-admission ("stable"), admission and post-admission (recovery) FEV1, G', and G"; from 8 subjects over 11 hospital admissions.



Discussion

The changes in viscoelastic properties correlate with changes in lung function as demonstrated by FEV1 %Predicted and the slope of this correlation was similar for all subjects.

During an exacerbation of CF lung disease requiring antibiotic therapy there is decreased FEV1 while G' and G" both increase. As FEV1 returns to baseline after therapy both G' and G" return to pre-exacerbation values.

Conclusions

The viscoelastic properties of CF sputum change in response to disease severity.

We speculate that changes in viscoelastic properties of CF sputum are due to changes in mucin and DNA polymer structure during the course of illness.

Sputum rheology may serve as a biomarker for CF disease surveillance and response to therapy.

References

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3. Kater A, Henke MO, Rubin BK. The role of DNA and actin polymers on the polymer structure and rheology of cystic fibrosis sputum and depolymerization by gelsolin or thymosin Beta 4. Ann N Y Acad Sci. 2007;1112:140-53.