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Effect of small airways and viscoelasticity on lung mechanics from expiratory occlusion

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Abstract:
Monitoring the decay rate of airflow in spirometry may be clinically useful. The decay rate is expected to represent a combination of lung elastance and airway resistance. However, the decay rate calculated using the single compartment lung model is not expected to account for slower lung mechanics, such as small airways resistance and tissue viscoelasticity. This study assesses whether the decay rate is affected by these lung mechanics. An exponentially decaying flow was created using a shutter to occlude airflow during passive expiration for 15 healthy subjects. To approximate small airways resistance and viscoelasticity, the gradient of pressure increase (relaxation gradient) during shutter closure was measured. The occlusion resistance, elastance, and decay rate were also calculated for these breaths. None of these mechanics were found to be correlated with the relaxation gradient. The relaxation gradient was also found to be independent of driving pressure. Conversely, the relaxation gradient was found to depend on lung volume. The results of this study suggest using lung mechanics and decay rate to monitor changes in lung condition over time may miss information about changes in the small airways and viscoelastic lung tissue. Thus, it is useful for monitoring large airways disease, but may be ineffective for small airways disease such as ARDS.

Keywords: Spirometry, Mathematical models, Lungs, Parameter identification, Respiratory mechanics

1. INTRODUCTION

Spirometry is the gold-standard for assessing respiratory health. However, it is not able to directly measure the underlying mechanics of the lungs without further, typically invasive testing (Ranu et al. (2011)). Lung mechanics are affected by obstructive and restrictive disease, and will change as disease progresses. Hence, obtaining lung mechanics measurements could give important new insight into lung condition.

Current research looks at using the decay rate of expiatory airflow to monitor lung mechanics in response to disease (van Drunen et al. (2013); Oh et al. (2017). The decay rate can be analysed using a single compartment lung model, which predicts the decay rate of flow to represent a mixture of the lung's elastic and the airways' resistive properties. However, this model is not expected to account for air redistribution withing the lung and viscoelastic effects of the lung tissue. Two-compartment models are more appropriate for this task.

Typically, decaying airflow has been measured during forced expiration or in mechanically ventilated patients in intensive care. In contrast, this study assesses the decay rate induced by the brief interruption of expiration during tidal breathing, with a specific focus on how the lung's viscoelastic properties affect the decay rate calculated from the single-compartment lung model.

2. METHODOLOGY

2.1 Linear two compartment lung model

When airflow is interrupted during passive expiration, an immediate, large pressure increase followed by a smaller gradual increase over time can measured at the mouth. This effect is shown in Figure 1. The large pressure increase can be attributed to pressure equalisation in the large proximal airways. The smaller gradual increase can be attributed to stress recovery, and gas redistribution within the lung (Bates et al. (1988)).

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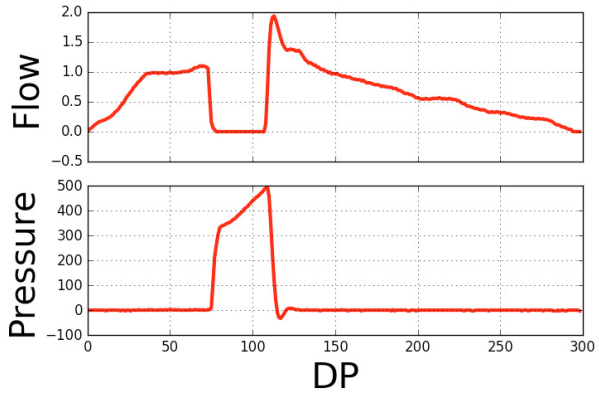

Fig. 1. Top: Flow (L/s) at each datapoint (DP) measured during shuttered tidal expiration. No airflow is measured when shutter occludes breath. Bottom: Pressure (Pa) measured at mouthpiece during shuttered tidal expiration. Note the rapid pressure increase followed by a slower increase sustained for entire shutter duration.

Two-compartment lung models have been used to describe airflow, accounting for the effect of stress recovery and air redistribution within the lung (Antonaglia et al. (1996)). Parallel and series lung models describe the lung as two separate compartments with unique resistance and elastance properties, allowing air to flow between the compartments. A viscoelactic lung model represents the lung as having a static elastic behaviour in parallel with a viscoelastic behaviour. All of these models describe the measured pressure by the same equation (Bates (2009)):

$$P(t) = A\ddot{V}(t) + B\dot{V}(t) + CV(t) + D\dot{P}(t) \quad (1)$$

where t is time, V is volume, and P is driving pressure. The shutter prevents airflow when closed. During this time, the pressure measured at the mouth is an approximation of the driving pressure. The parameters A, B, C, and D represent different combinations of underlying resistance and elastance for different two-compartment models. Due to this model ambiguity, with different properties of lung tissue and gas exchange able to be modeled by the same equation, the interrupter method is not able to say which property predominantly causes the slow increase in pressure during occlusion.

Total lung volume remains constant during occlusion, with parameter C creating a constant effect on pressure during his time. Parameters A and B depend on the airflow between lung compartments, which cannot be measured by interrupter technique Parameter D depends on the rate of change of measured pressure.

For the three two-compartment models described, parameter D is a combination of all model-specific viscoelastic or small airways lung mechanics Bates (2009), representing the time constant of small lung compartments or viscoelastic responses. The effect of parameters A and B on measured pressure are assumed to be dominated by parameter D, as all subjects in this study were healthy with minimal expected levels of air redistribution due to lung homogeneity. Equation 1 can thus be simplified to:

$$P(t) = P_0 + D\dot{P}(t) \quad (2)$$

To approximate the underlying lung mechanics, parameter D was measured from the average rate of change of pressure from 30 ms after shutter closure until 30 ms before the peak pressure is measured. This time frame was chosen to maximise the data used, while minimising the effect of pressure change caused by the shutter opening and closing.

2.2 Mechanics identification

A shutter built into a plethysmograph was used in this study to induce a decay rate in flow during tidal expiration. Subjects in this study were asked to pant into the plethysmograph's mouthpiece. The shutter closed after peak flow in expiration for 200-250 ms, and was activated 5 times with a minimum of 5 normal breaths between each shutter activation. This test was repeated twice for each subject, with a several minute rest between each test.

For each shuttered breath, the decay rate of the airflow caused by the shutter reopening was calculated. Adaptive filtering was used to separate the airflow due to respiratory muscles from the airflow due to the shutter. The average flow-rate of the tidal breaths preceding the shuttered breath was calculated. This value was then subtracted from the airflow measured during shuttering to leave an estimate of the airflow caused by the shutter. The decay rate was calculated from this data according to the single compartment lung model (van Drunen et al. (2013)).

The lung mechanics calculated were occlusion resistance (ROCC), and end-occlusion elastance. ROCC was calculated as per standard method (Eric Yat-Tung Chan (2007); Panagou et al. (2004)). The gradient of pressure from 30-75 ms after shutter was closed was extrapolated backwards to 15 ms before closure. This value was divided by the airflow recorded at that time to produce an estimate for airway resistance. Elastance was calculated as the pressure measured 30 ms before the shutter reopened divided by the measured volume of air in the lung during shuttering.

2.3 Data

Fifteen healthy subjects were enrolled in this study (6 Female, 9 Male, Age 27±4, BMI 24.5±3.8, 3 Smokers). All data used in this study was recorded by a Ganshorn PowerCube Body plethysmograph using LFX 1.8 Respiratory Diagnostic Software. Shuttering was controlled using the LFX software's ROCC manual activation mode. Table 1 shows specific details for each subject.

2.4 Ethics

The University of Canterbury Human Ethics Committee granted approval for this study, and the collection and use of the clinical data analysed in this study. Written, informed consent was given by all subjects prior to participation in this study.

3. RESULTS

The pressure gradient measured between 30 ms after shutter closure and 30 ms before peak pressure is referred to as "relaxation gradient". This relaxation gradient was compared to volume and pressure measurements reflecting

Table 1. Subject data. Smokers were included in this study.

Subject	Sex	Age	Height (cm)	Weight (kg)	Smoker
1	M	30	190	100	n
2	M	38	175	100	n
3	M	32	187	87	n
4	M	29	183	95	n
5	F	24	173	80	y
6	M	29	183	78	n
7	M	23	185	73	y
8	M	23	184	71	n
9	M	27	178	90	n
10	F	29	168	62	n
11	F	22	167	53	n
12	F	29	161	53	y
13	F	23	164	64	n
14	F	25	172	70	n
15	M	31	181	114	n

initial and final conditions of the lung during shuttering, and to the lung mechanics calculated. R^2 values were calculated on these linear regressions separately for each subject, and for all subjects combined to give an overall trend. The R^2 values and overall gradients of the regression lines are shown in Tables 2 and 3, respectively.

3.1 Volume

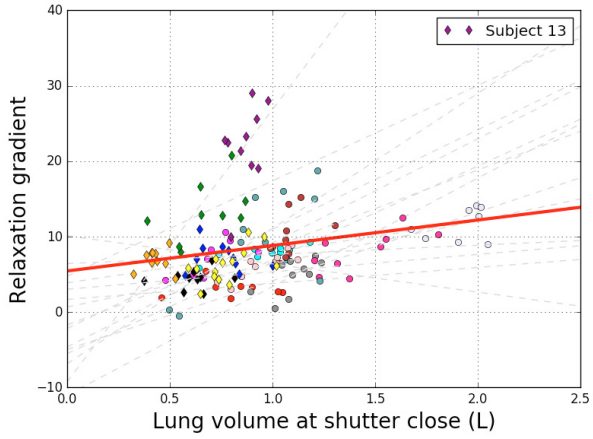

Fig. 2. Regression lines calculated between relaxation gradient and lung volume at shutter closure for each subject are shown in grey. Positive overall regression is shown in red.

A linear regression of relaxation gradient and volume was calculated for each individual in this study. For 14/15 subjects, the relaxation gradient was positively correlated with lung volume. A positive overall regression for all 148 shuttered breaths was calculated, and is shown in red in Figure 2. The R^2 of this regression was low at 0.05. However, excluding the outlier Subject 13 raised the R^2 value to 0.13 without significantly affecting the gradient of the regression line (see Table 3).

3.2 Pressure

Pressure measured at both 30 ms after shutter closure and at 30 ms before peak pressure was positively correlated to relaxation gradient, as shown in Figures 3 and 4, respectively. As shown in Tables 2 and 3, the regression

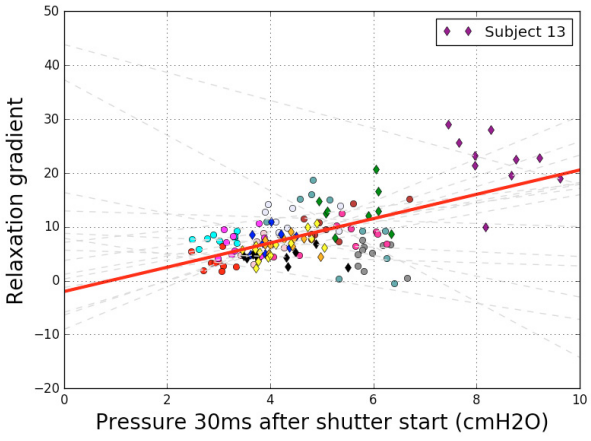

Fig. 3. Regression lines calculated for each subject between relaxation gradient and pressure measured 30 ms after shutter closure are shown in grey. Positive overall regression is shown in red.

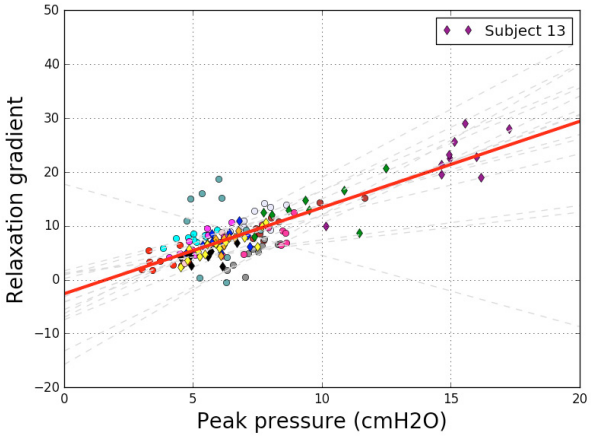

Fig. 4. Regression lines calculated for each subject between relaxation gradient and pressure measured 30 ms before peak shuttered pressure are shown in grey. Positive overall regression is shown in red.

calculated at shutter closure was highly dependent on Subject 13. The R^2 value decreased from 0.37 to 0.08 and gradient reduced from 2.25 to 0.99 when Subject 13 was removed from the overall regression line. The changes

Table 2. R^2 on regression line between relaxation gradient and measured data. Values were calculated separately for each subject, all subjects combined, and all subjects combined excluding subject 13.

Subject	Volume	Start pressure	End pressure	Decay rate	Elastance	Rocc
1	0.53	0.23	0.66	0.08	0.15	0.16
2	0.07	0.06	0.06	0.09	0.06	0.02
3	0.78	0.26	0.81	0.86	0.01	0.06
4	0.54	0.06	0.73	0.13	0.02	0.23
5	0.21	0.52	0.83	0.18	0.57	0.21
6	0.40	0.07	0.64	0.44	0.02	0.13
7	0.13	0.01	0.42	0.31	0.12	0.04
8	0.50	0.22	0.44	0.01	0.01	0.13
9	0.49	0.40	0.03	nan	nan	0.10
10	0.06	0.08	0.23	0.42	0.48	0.07
11	0.27	0.02	0.35	0.10	0.01	0.10
12	0.04	0.02	0.12	0.06	0.00	0.00
13	0.22	0.11	0.68	0.57	0.35	0.01
14	0.00	0.01	0.46	0.01	0.10	0.00
15	0.32	0.47	0.74	0.03	0.27	0.02
overall	0.05	0.37	0.68	0.03	0.27	0.15
without S13	0.13	0.08	0.37	0.01	0.03	0.00

Table 3. Gradient of overall regression line between relaxation gradient and measured data. Regression calculated for all subjects combined, and all subjects combined excluding subject 13.

	Volume	Start pressure	End pressure	Decay rate	Elastance	Rocc
Overall	3.38	2.25	1.60	0.07	0.68	1.66
Without S13	3.68	0.99	1.36	0.03	0.18	-0.01

for peak pressure were much smaller, with R^2 reducing from 0.68 to 0.37 for R^2 and the regression line's gradient reducing from 1.60 to 1.36.

3.3 Decay rate

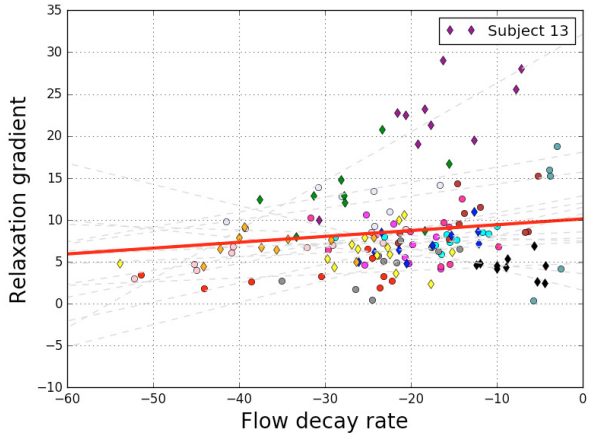

Fig. 5. Regression between relaxation gradient and the decay rate of flow caused by shutter reopening. Separate regression for each subject is shown in grey, and overall regression is shown in red.

No clear overall relationship was identified between relaxation gradient and flow decay rate, as shown in Figure 5. The R^2 value on regression with all 15 subjects was 0.03, with a gradient of 0.07. Both values reduced towards 0.0 when Subject 13 was excluded.

3.4 Lung elastance and airway resistance

With Subject 13 included, elastance appeared to be correlated with the relaxation gradient, as shown in Figure 6,

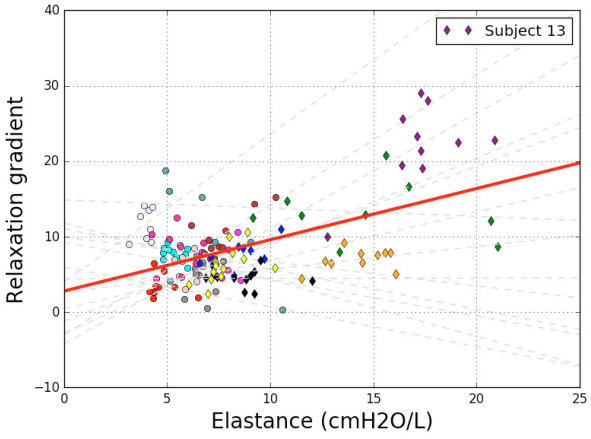

Fig. 6. Regression between relaxation gradient and elastance calculated at shutter opening. Separate regression for each subject is shown in grey, and overall regression is shown in red.

with R^2 value of 0.27 and gradient 0.68. However, when Subject 13 was removed the R^2 value dropped to 0.03, and gradient also reduced significantly to 0.18.

Similar to elastance results, no clear relationship was identified between occlusion resistance (ROCC) and relaxation gradient. R^2 of the regression for 14/15 subjects was 0.00, with gradient -0.01 as shown in Tables 2 and 3. The R^2 value and gradient changed significantly with Subject 13 added to the regression.

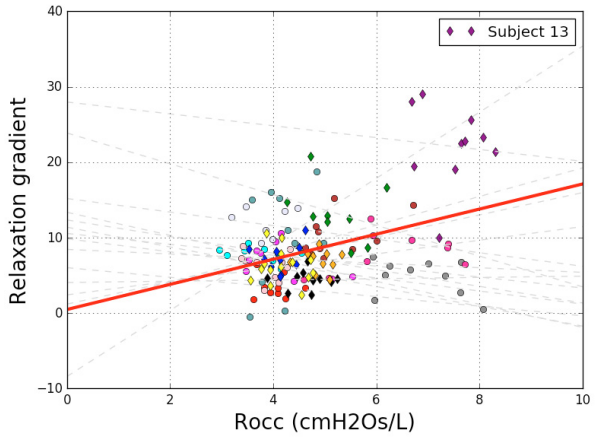

Fig. 7. Regression between relaxation gradient and occlusion resistance calculated at shutter closing. Separate regression for each subject is shown in grey, and overall regression is shown in red.

4. DISCUSSION

4.1 Subject 13

Data from Subject 13 significantly influenced the overall regressions calculated in this study. This influence was due to many of their metrics being significantly higher than all other subjects. They had the highest measured ROCC, relaxation gradient, pressure, and average elastance, with normal flow decay rate and lung volume at shutter closure. These metrics mean this subject is visible as a clear outlier in every regression figure in this study.

No other subjects were found to significantly alter overall results when removed from the regression.

4.2 Initial conditions

The results of this study suggest relaxation gradient is affected by lung volume. Linear regression to volume measurements were stable, even after the removal of the outlier data from Subject 13, as shown in Tables 2 and 3. Conversely, it is not clear whether the relaxation gradient is affected by the pressure measured at shutter close.

As lung volume reduces during expiration, airway resistance will increase as airway diameter reduces. The reduction in diameter slows the rate air can redistribute in the lung, and consequentially the rate of pressure increase at the mouth. Additionally, some portions of the lung may no longer be recruited, trapping air in the lungs. Trapped air would not contribute to the pressure increase seen at the mouth due to air redistribution.

Pressure measured at shutter closure is created by two main mechanics: The natural recoil from the lung and chest wall, and additional external pressure from muscular breathing effort. The pressure generated by lung recoil increases proportional to the volume of air in the lung, $P = EV$. This relationship with volume, which does affect the relaxation gradient, may explain the positive correlation seen between relaxation gradient and pressure. Peak pressure has a stronger correlation than at shutter closure due to pressure at the mouth increasing according to the relaxation gradient during shuttering.

Changes in muscular breathing effort during shuttering significantly affect the measured pressure, obscuring the contribution of air redistribution and viscoelasticity. Because subjects were asked to pant, there may be additional active muscular elastance on top of viscoelastic effect.

4.3 Lung mechanics

Figure 4 suggests peak pressure measured during shuttering is correlated with the pressure gradient. However, the elastance calculated from end shutter pressure, which typically equaled the peak pressure, did not show this trend. This result supports the hypothesis that the relaxation gradient of healthy lungs is not significantly affected by driving pressures of tidal breathing (Freezer et al. (1993)).

No clear relationship was identified between occlusion resistance and pressure gradient. This outcome was expected because occlusion resistance is calculated from the large pressure change as shutter is closed. This pressure change is attributed to the static lung resistance of the proximal airways. Additionally, the decay rate measured after shutter opening was not correlated with relaxation gradient. The lack of correlation suggests the decay rate depends only on static lung mechanics when measured by the single compartment lung model.

The results of this study indicate the lung mechanics measured with the interrupter technique do not represent mechanics of air redistribution and viscoelastic effects within the lung. As a result, mechanics measured from shuttering may not be able to be used to accurately monitor or detect conditions affecting small airways or tissue deep in the lungs, such as ARDS.

4.4 Limitations

This study analysed tidal breathing of healthy subjects. Hence, the results found may only be applicable to healthy lungs. Lung disease may affect the observed lung mechanics significantly, and the relationships analysed in this study. These results are also only applicable for low levels of lung volume and breathing effort. Mechanics measured during peak expiratory effort may be different.

Expiration during spontaneous tidal breathing is not entirely passive, Hence, decoupling the effect of respiratory muscles and viscoelasticity on the relaxation gradient is not possible without more invasive measures.

5. CONCLUSIONS

The decay rate and lung mechanics measured in this study were not found to be reflective of small airways resistance and lung viscoelasticity. As a result, using the decay rate to monitor changes in lung mechanics over time may miss information about changes in condition of small airways and lung tissue. Conversely, monitoring the relaxation gradient during shuttering may provide this information, as two-compartment lung models show it is highly dependent on small airways resistance and elasticity.

6. ACKNOWLEDGMENTS

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REFERENCES

Antonaglia, V., Beltrame, F., Lucangelo, U., and Grop, A. (1996). Assessment of the Viscoelastic Constants Using the Rapid Airway Occlusion Technique. In A. Gullo (ed.), *Anaesthesia, Pain, Intensive Care and Emergency Medicine — A.P.I.C.E.: Proceedings of the 10th Postgraduate Course in Critical Care Medicine Trieste, Italy — November 13–19, 1995*, 407–414. Springer Milan, Milano. doi:10.1007/978-88-470-2203-4_36.

Bates, J.H., Baconnier, P., and Milic-Emili, J. (1988). A theoretical analysis of interrupter technique for measuring respiratory mechanics. *Journal of Applied Physiology*, 64(5), 2204–2214. doi:10.1152/jappl.1988.64.5.2204.

Bates, J.H.T. (2009). *Lung Mechanics: an Inverse Modeling Approach.* Cambridge University Press, Leiden. OCLC: 609842956.

Eric Yat-Tung Chan (2007). Use of the interrupter technique in assessment of lung function. *Journal of Paediatric Respirology and Critical Care*, 3(4), 6–8.

Freezer, N.J., Nicholai, T., and Sly, P.D. (1993). Effect of volume history on measurements of respiratory mechanics using the interrupter technique. *Pediatric Research*, 33(3), 6.

Oh, A., Morris, T.A., Yoshii, I.T., and Morris, T.A. (2017). Flow Decay: A Novel Spirometric Index to Quantify Dynamic Airway Resistance. *Respiratory Care*, 62(7), 928–935. doi:10.4187/respcare.04850.

Panagou, P., Kottakis, I., Tzouvelekis, A., Anevlavis, S., and Bouros, D. (2004). Use of interrupter technique in assessment of bronchial responsiveness in normal subjects. *BMC Pulmonary Medicine*, 4, 11. doi:10.1186/1471-2466-4-11.

Ranu, H., Wilde, M., and Madden, B. (2011). Pulmonary Function Tests. *The Ulster Medical Journal*, 80(2), 84–90.

van Drunen, E.J., Chiew, Y.S., Chase, J.G., Shaw, G.M., Lambermont, B., Janssen, N., Damanhuri, N.S., and Desaive, T. (2013). Expiratory model-based method to monitor ARDS disease state. *BioMedical Engineering OnLine*, 12(57).