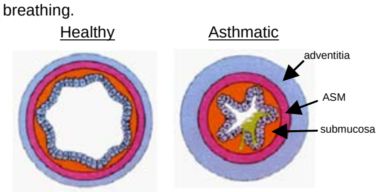
An Isolated Airway System to Study Airway Wall Properties

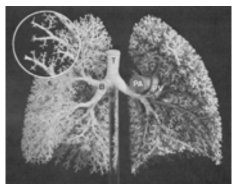
A.S. LaPrad, D.A. Affonce, and K.R. Lutchen
Department of Biomedical Engineering, Boston University

INTRODUCTION

Airways and Asthma

- The airway tree is a complex, asymmetric, 3-D structure.
- Asthma is an airway disease characterized by inflammation, thickening of the airway walls, and luminal secretions.
- Asthmatic airways are hyperresponsive and nonspecific provocation causes excessive airway smooth muscle (ASM) contraction and airway narrowing. This decreases the compliance of the airway wall and the cross-sectional area of the airway.
- Recent studies indicate that the contractile forces of ASM depend on its dynamic, pressure-controlled environment.[1,2]
- Hence, understanding airway hyperreactivity will require measuring how the ASM and airway wall interact before and after ASM stimulation, both with and without dynamic, normal breathing.



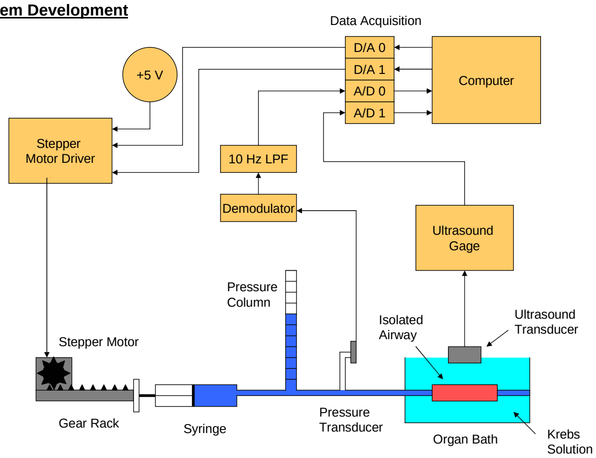


GOALS

- Design and develop an integrated hardware-software system to:
  - Deliver *in-vivo*-like pressure oscillations to isolated airways
  - Measure transmural pressure and airway radius changes in real-time
- Apply system on isolated airways from calf lungs to:
  - Measure static and dynamic pressure-area relationships before and after ASM stimulation
  - Measure airway wall compliance before and after ASM stimulation

METHODS

System Development



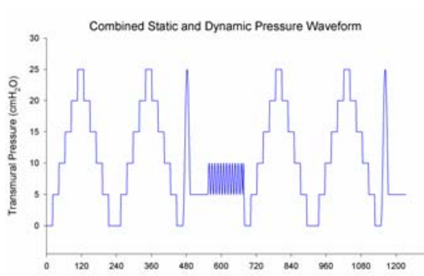
The system functions as follows:

1) A computer-controlled stepper motor system oscillates a fluid-filled syringe pump.
2) The syringe pump, in unison with a pressure column, establish appropriate pressures that are delivered to the isolated airway.
3) The amount of steps the motor takes determines the height of the pressure column and the pressure that is acting on the isolated airway.
4) Pressure and radius changes are measured by a pressure transducer and an ultrasound transducer, respectively.

Experiments with Isolated Airways

Protocol:

1) First and second generation airways were excised from calf lungs.
2) Each airway was mounted in the organ bath and tested for leaks.
3) The system control software outputted pressure waveforms to deliver to the airway.
4) Radius and pressure data were collected in real-time.
5) The ASM was stimulated with methacholine (MCh) and the pressure waveform was repeated.



RESULTS

Static Testing: 12 airways, 5.10 +/- 0.68 mm outer diameter, 1.11 +/- 0.24 mm wall thickness

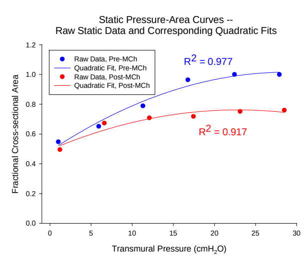


Figure 1: Representative raw static pressure-area (P-A) data and the corresponding quadratic fits used to obtain static P-A curves.

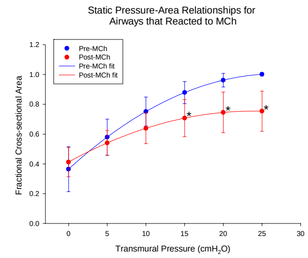


Figure 2: Mean static P-A curves before and after ASM stimulation for airways that reacted to MCh. Cross-sectional area decreased significantly after ASM stimulation. Six of the twelve airways tested showed a response to ASM stimulation.

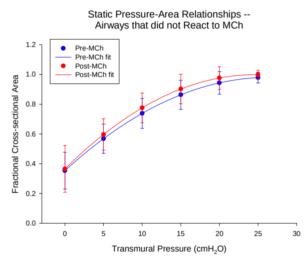


Figure 3: Mean static P-A curves before and after ASM stimulation for airways that did not react to MCh. There was no response to ASM stimulation for six of the twelve airways tested.

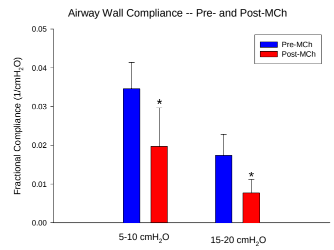


Figure 4: Airway wall compliance as a function of ASM stimulation, calculated from mean static P-A curves of reactive airways. The compliance of the airway decreased significantly after ASM stimulation.

Dynamic Testing

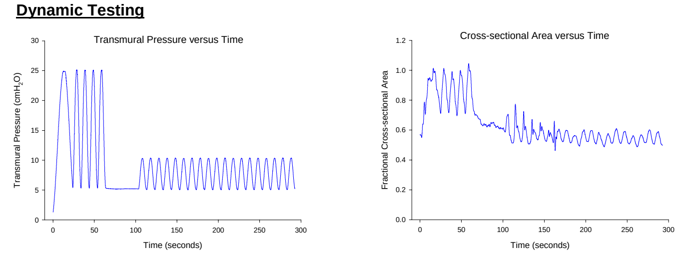


Figure 5: Cross-sectional area and transmural pressure versus time for a representative airway that underwent dynamic tests before ASM stimulation. Stress relaxation of the airway wall is present when the airway is held at 5cmH_2O. Also, the measured changes in cross-sectional area appear to decrease over time and then steady state. Thus, the change in compliance due to dynamic oscillations can be measured.

DISCUSSION

- Airway wall properties, including P-A relationships and airway wall compliance, can be quantified using the developed integrated system.
- Results indicate that ASM stimulation can significantly reduce the static compliance of isolated airways, which may have implications regarding deficiency in airway dilation in asthmatics.
- Lack of response to ASM stimulation (for 6 of the 12 airways tested) could be due to airway wall uncoupling, where the lumen of the airway narrows to a greater degree than the adventitia.[3]
- Future work includes:
  - Determining the effects of pressure oscillations before, during, and after ASM stimulation by calculating P-A curves and compliance for the steady state regions of dynamic tests
  - Measuring the dose response of isolated airways stimulated with MCh
  - Developing an endoscope system to measure both lumen and adventitia cross-sectional area

REFERENCES

(1) Gunst, S.J., and J.Q. Stropp, *Pressure-volume and length-stress relationships in canine bronchi in vitro*. American Physiological Society, 1988. 88: 2522-2531.
(2) Latourelle, J., B. Fabry, and J.J. Fredberg, *Dynamic equilibration of airway smooth muscle contraction during physiological loading*. J Appl Physiol, 2002. 92: 771-779.
(3) Mitchell, H.W., and P.R. Gray, *Uncoupling in the wall of the cartilaginous bronchus of the pig produced by smooth muscle contraction*. Pulmonary Pharmacology, 1996. 9: 29-34.

ACKNOWLEDGEMENTS

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