

Ultrasonic CO₂ measurements during
quiet breathing with a portable
spirometer may potentially diagnose
airway obstruction

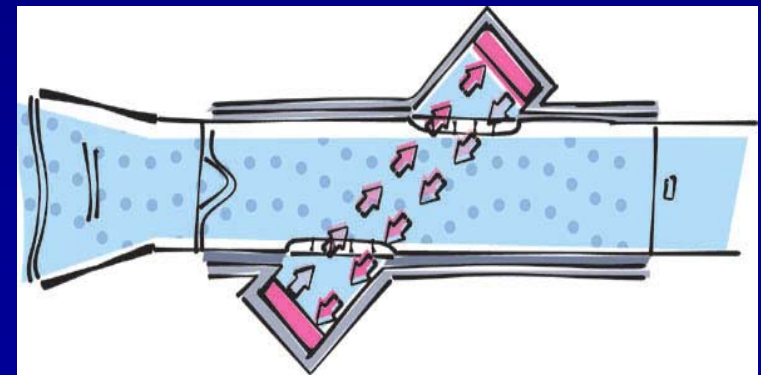
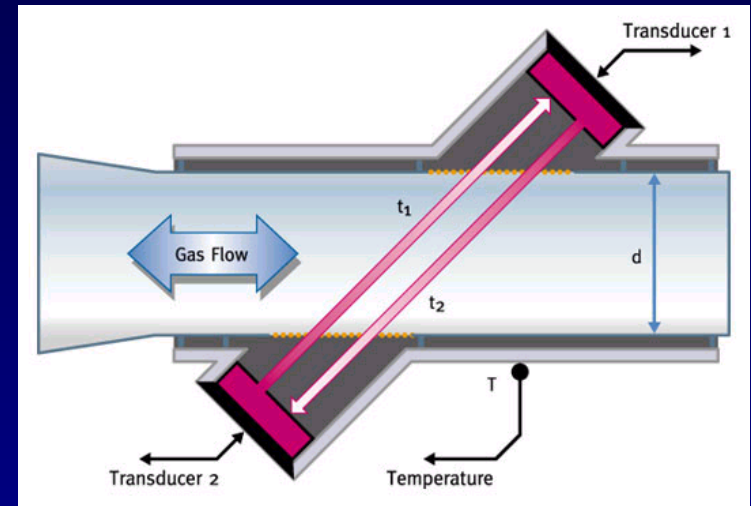
Robert Jensen, Ph.D.

Christian Buess, Ph.D.

Robert Crapo, M.D.

Ultrasound Transit Time Flow Measurement

- Transit time differences between upstream and downstream ultrasound pulses are used to measure gas flow velocity
- The bigger the difference in transit times, the faster the velocity (cm/sec)
- Velocity (cm/sec) x cross-sectional area (cm²) gives flow (cm³/sec) or (ml/sec)



Ultrasound Molar Mass Measurement

- The speed of sound in a gas is dependent upon the molar mass of the gas mixture. Although, temperature alters the speed of sound within a gas mixture it can be compensated for in the calculations.
- Mean molar mass of a mixture of n gases is determined as:

$$\text{Sum}_{(i=1 \text{ to } n)} [\text{Molecular Weight}_{[\text{gas}(i)]} \times \text{Concentration}_{[\text{gas}(i)]}]$$

Examples: Molar Mass Calculations

Room Air			
Gas	Concentration	Molecular Weight [g/mol]	Fract. Molar Mass [g/mol]
Nitrogen	0.781	28	21.8680
Oxygen	0.2093	31.99	6.6955
Carbon Dioxide	0.0003	44	0.0132
Argon	0.0094	39.95	0.3755
	1		
Mean Molar mass of Air at 0% Humidity			28.95
End Tidal Gas From The Lungs			
Gas	Concentration	Molecular Weight [g/mol]	Fract. Molar Mass [g/mol]
Nitrogen	0.77998	28	21.8394
Oxygen	0.14	31.99	4.4786
Carbon Dioxide	0.07	44	3.0800
Argon	0.0094	39.95	0.3755
Water	0.00062	18	0.0112
	1		
Mean Molar mass of End Tidal Gas			29.78

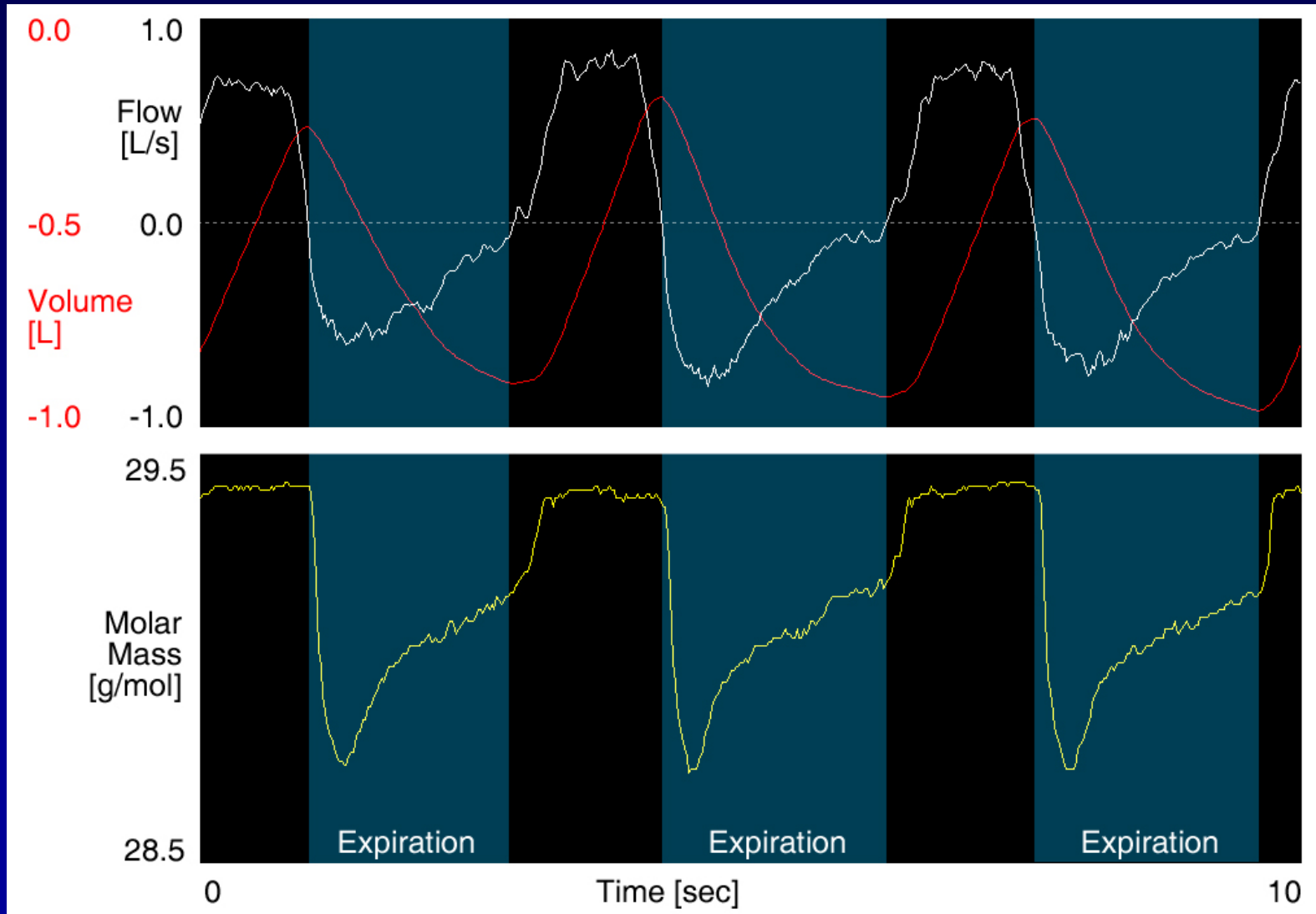
Accuracy of Measurements

Molar mass resolution of ultrasonic flow meter
= 0.01 g/mol

Average Molar Mass = 29.4 g/mol

$$100\% \times (0.01 / 29.4) = 0.034\%$$

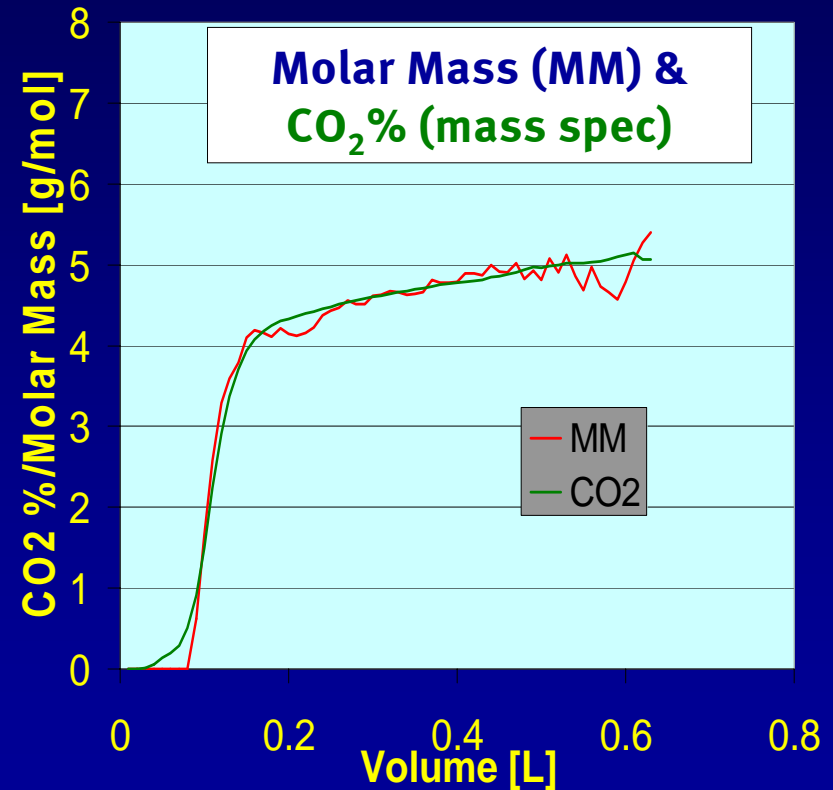
Molar Mass, Flow, and Volume Changes During Quiet Breathing



Application to Pulmonary Function Testing

Molar Mass (MM) is a Potential Surrogate for CO₂

- The sensor can simultaneously measure the molar mass of the exhaled gas using same transit time signals used to measure air flow.
- Eliminates problems associated with common analyzers
 - Time alignment
 - Calibration
 - Response time



Study Objectives

- Compare Molar Mass signals to CO₂ signals measured simultaneously with a mass spectrometer
- Extract similar parameters from both CO₂ and Molar Mass signals and compare them
- Evaluate the possibility of categorizing clinical patients with Molar Mass signal parameters into categories of obstruction

Study Design

Patients and healthy volunteers at the pulmonary function laboratory at LDS Hospital in Salt Lake City, Utah, USA

N=40 (21 Men, 19 Women)

Mean Age: 50.2 (range 22 to 75)

Measurements:

- Spirometry (FVC, FEV₁, PEF and FEV₁/FVC ratio)

- DLCO (only in scheduled patients)

- Mass spectrometer (%CO₂ Measurements)

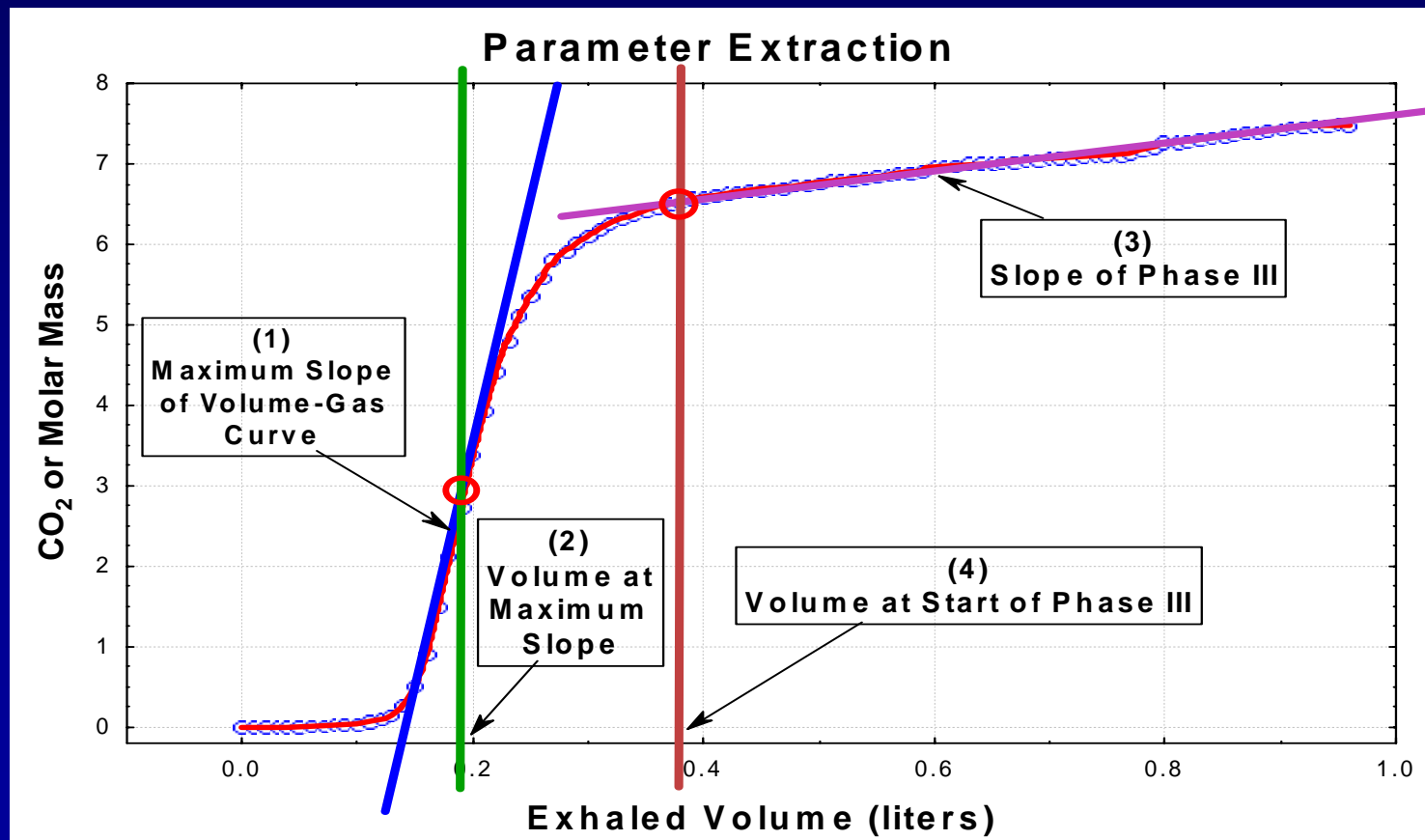
- Ultrasonic flow sensor (Flow, Molar Mass Measurements)

Data Collection

- Subject seated using nose clips
- Relaxed breathing for 5 minutes
- Slow vital capacity within first and last minutes of testing
- Mass spectrometer calibrated prior to each test
- Signals digitized at 200 samples/sec
- Tidal breaths combined for analysis into two composite curves (Volume vs CO₂ and Volume vs Molar Mass)

Parameters extracted from composite curves (for Volume-%CO₂ and Volume-Molar Mass curves):

1. Maximum slope of the volume-gas curve
2. Volume where the maximum slope occurs
3. Slope of phase III of the volume-gas curve
4. Volume at beginning of Phase III



Clinical Classifications From Spirometry, DLCO And Physician Diagnosis

- Normal (n=16)
- Mild Obstruction (4)
- Moderate Obstruction (6)
- Severe Obstruction (10)

Total Analyzed = 36

Statistical Analysis

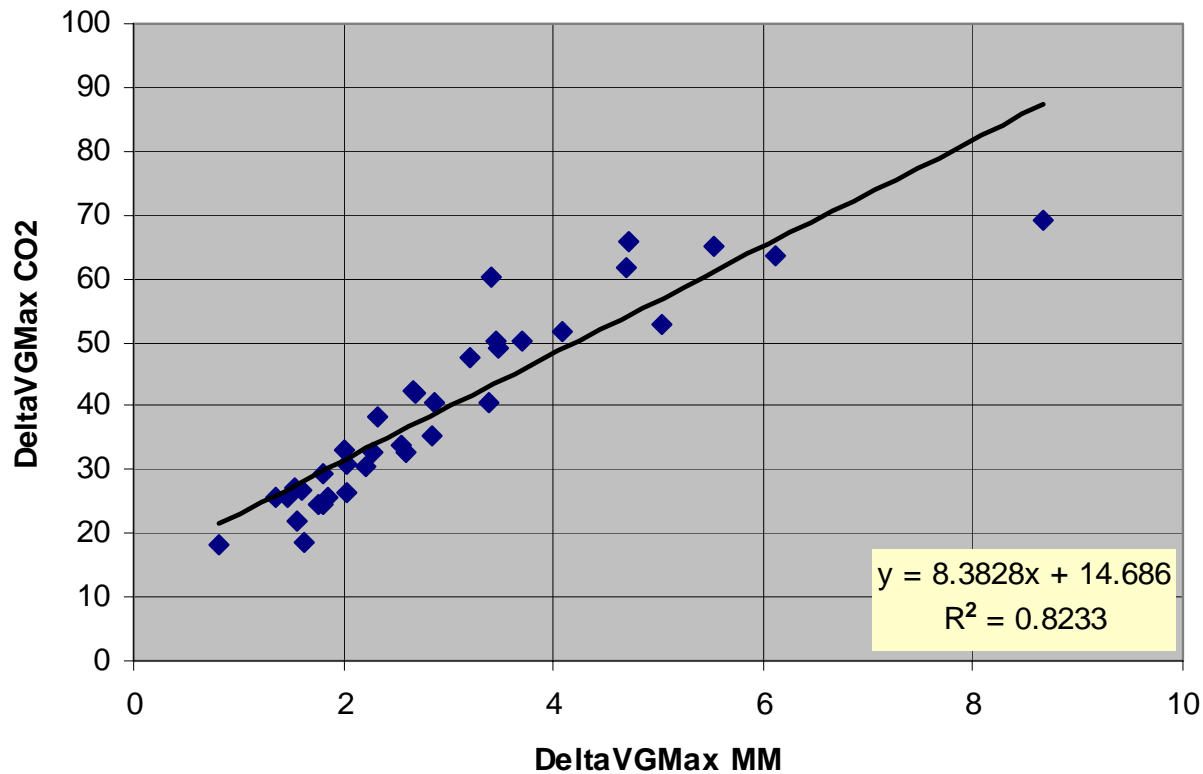
- Correlations between CO₂ and Molar Mass parameters
- Linear Discriminant Analysis
 - Compare % Classification using Volume-%CO₂ parameters vs. Volume-Molar Mass parameters to categorize subjects
 - Incorporate Age, Gender in addition to Molar Mass parameters to categorize subjects
 - Categorize to “Normal” or “Any Obstruction”

Mean Parameter Values

	Normal	Mild	Moderate	Severe
FEV1	3.11 ± 0.75	3.24 ± 0.84	1.91 ± 0.74	1.55 ± 0.55
FVC/FEV1	77.9 ± 8.6	66.3 ± 3.0	59.3 ± 6.6	46.4 ± 8.9
Max $\Delta\%CO_2/L$	3.54 ± 1.80	2.82 ± 1.36	3.37 ± 1.62	1.75 ± 0.48
Volume at Max $\Delta\%CO_2/L$	0.120 ± 0.031	0.172 ± .062	0.123 ± .021	0.141 ± .036
Slope Phase III	2.19 ± 1.45	4.82 ± 1.85	4.74 ± 3.33	4.90 ± 2.23
Volume at Phase III	0.450 ±	0.443 ± .015	0.435 ± .037	0.450 ±

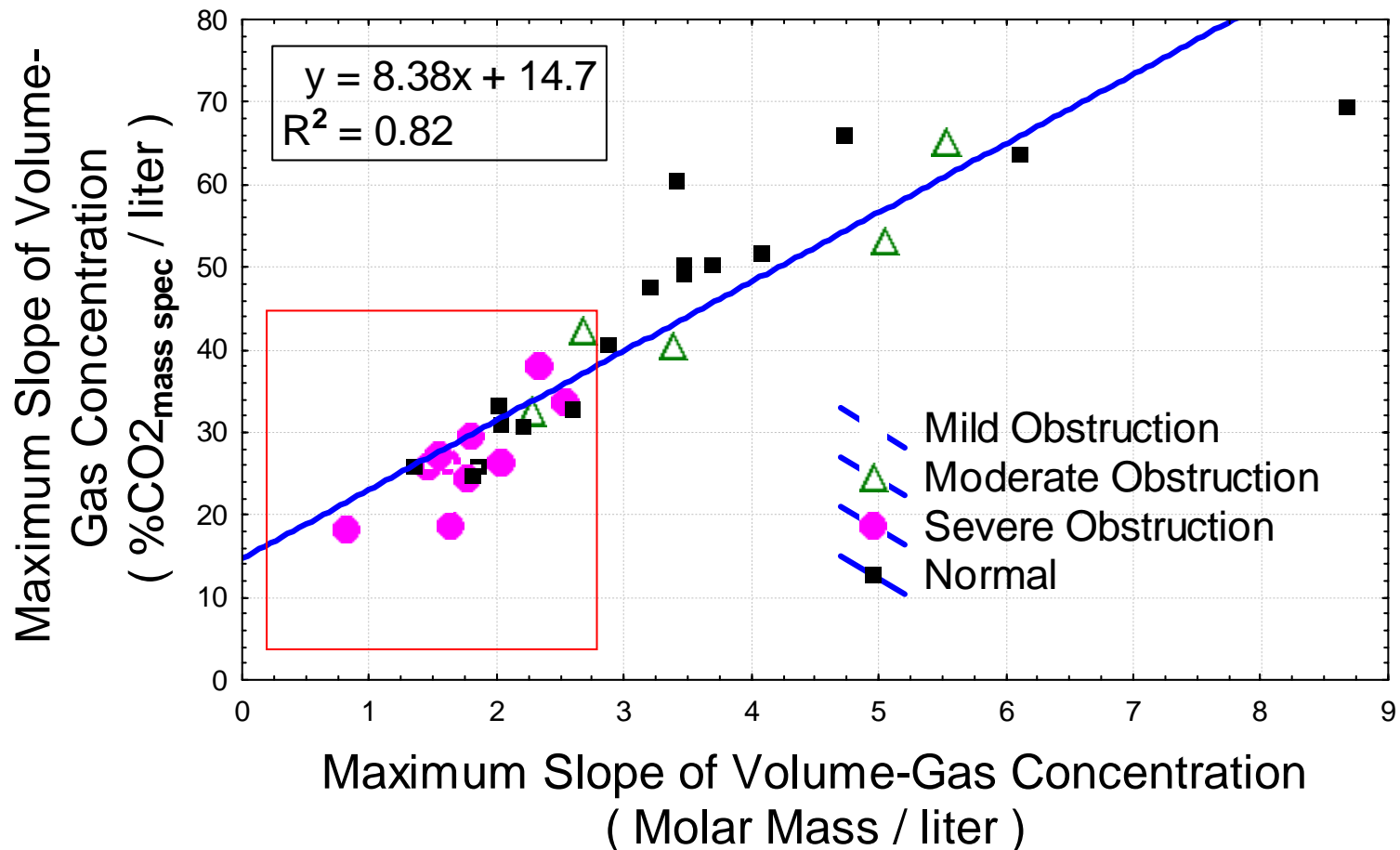
Correlation of Maximum Slope between CO₂ (mass spec) and Molar Mass (MM)

MM and CO₂ Phase II slope comparison
MM and CO₂ slope are quite similar

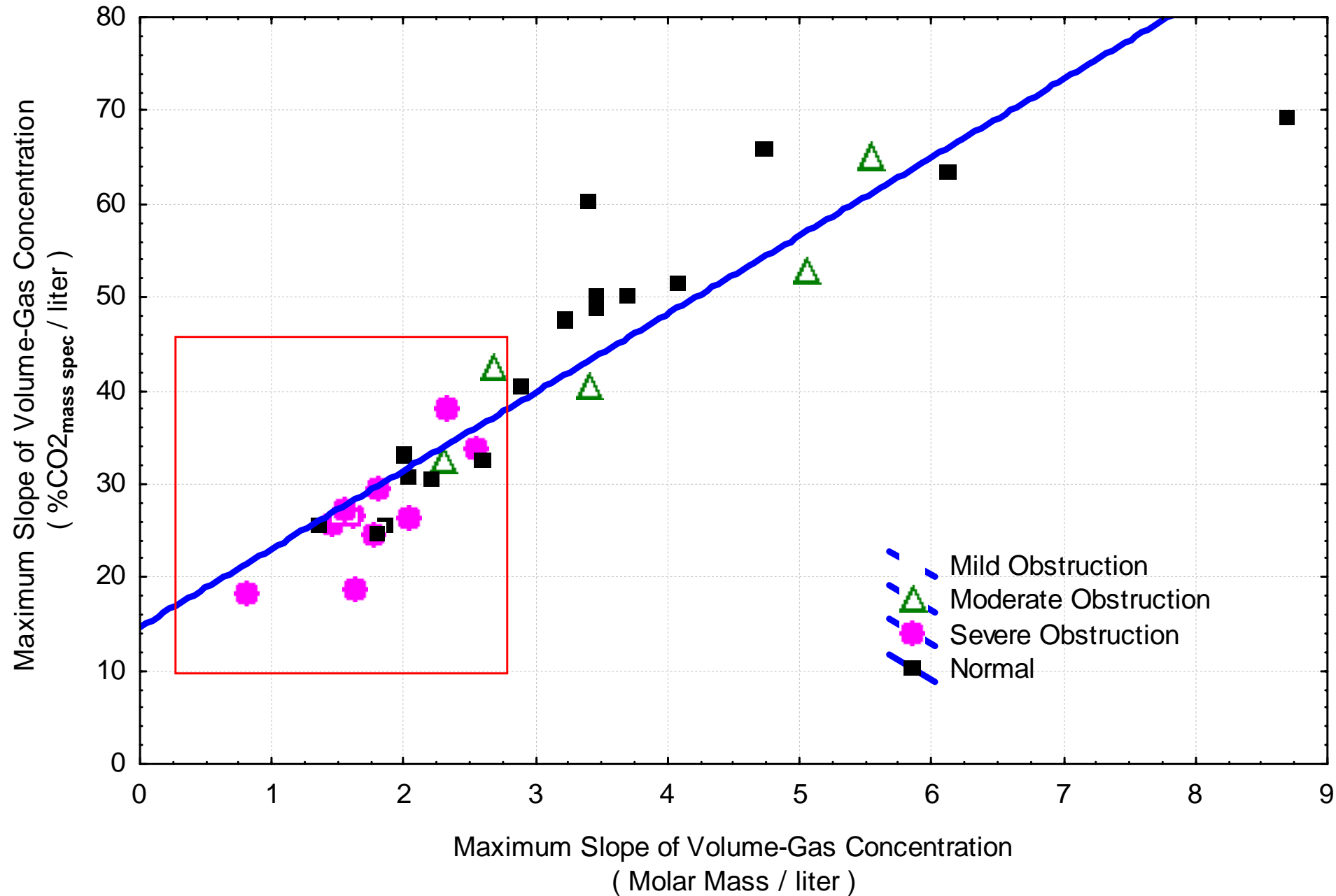


Correlation of maximum slope between CO₂ (mass spec) and molar mass

Graph of Maximum Volume-Gas Change Using Molar Mass and Mass Spectrometer [CO₂]

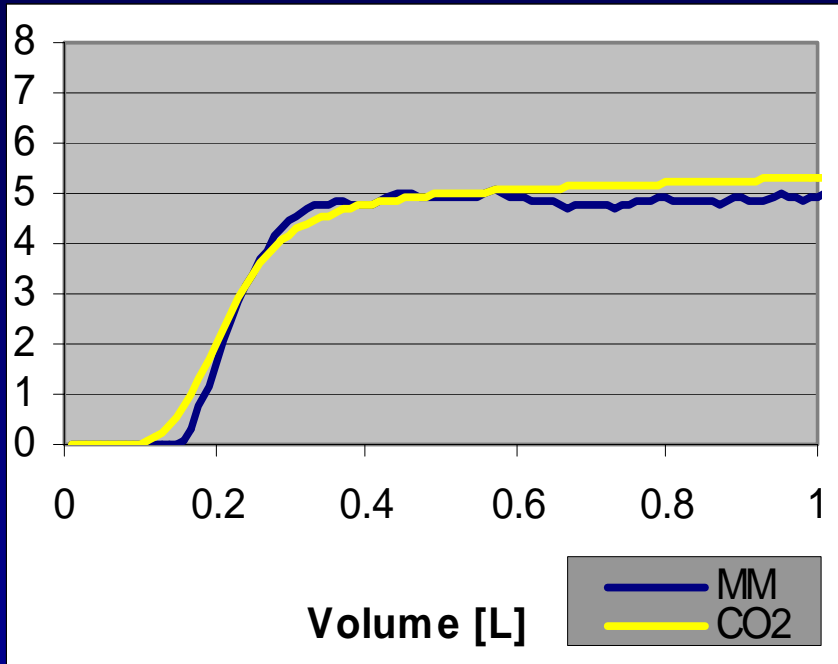


Graph of Maximum Volume-Gas Change
Using Molar Mass and Mass Spectrometer [CO₂]

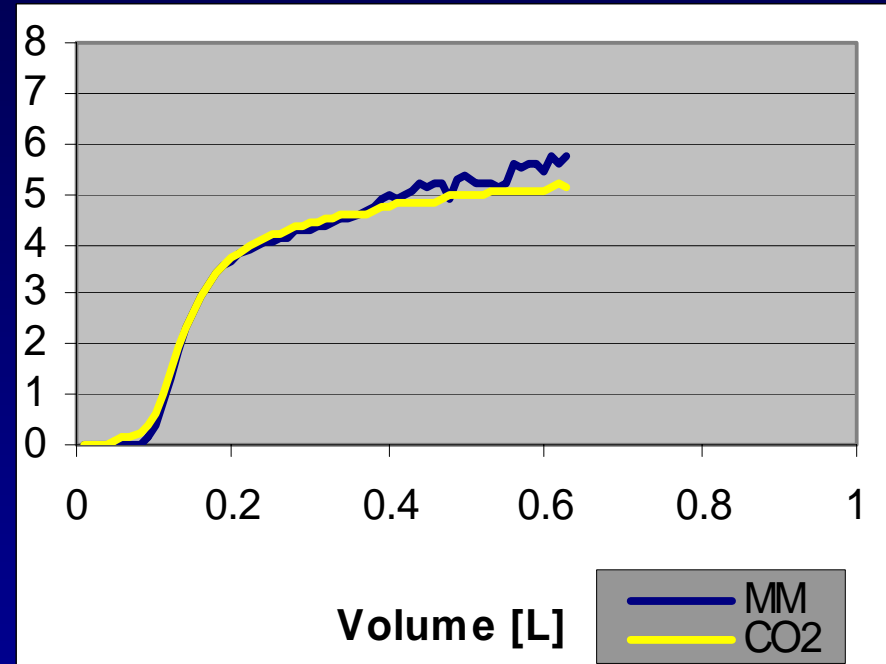


Category Comparisons

Normal



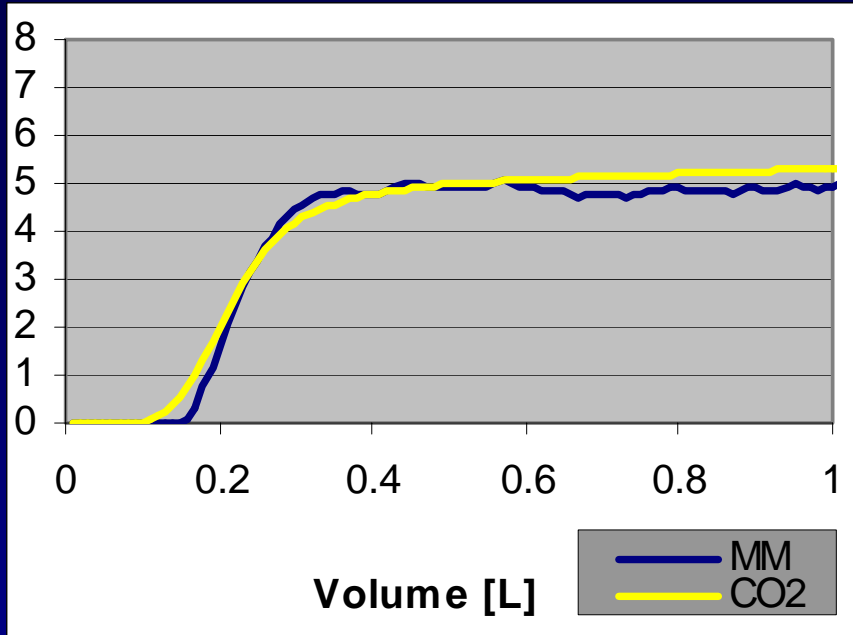
Mild Obstruction



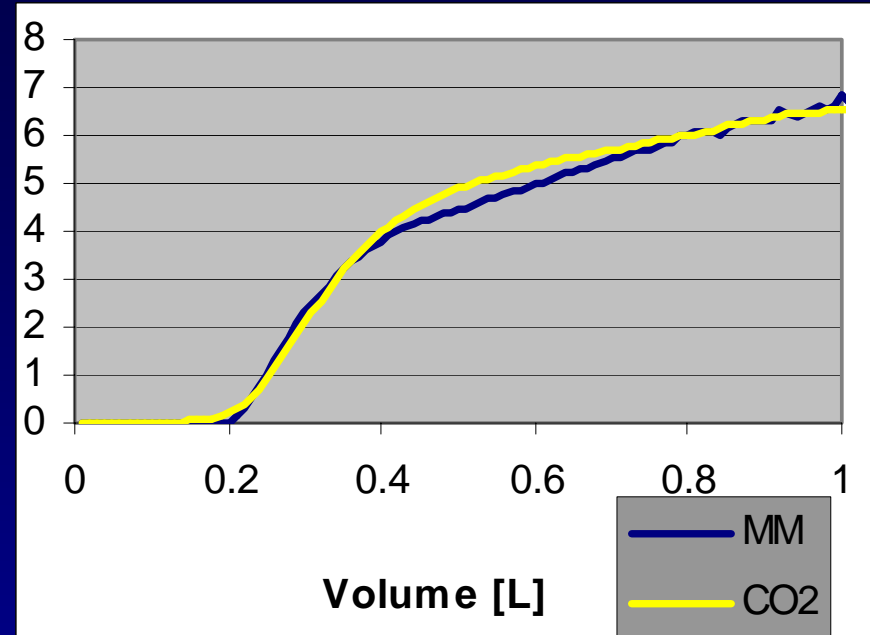
	Average For Normal Group
FVC/FEV1	77.9 %
Max $\Delta\%CO_2/L$	3.54
Volume Max Slope (L)	0.120

	Average For Mild Group
FVC/FEV1	66.3 %
Max $\Delta\%CO_2/L$	2.82
Volume Max Slope (L)	0.172

Normal



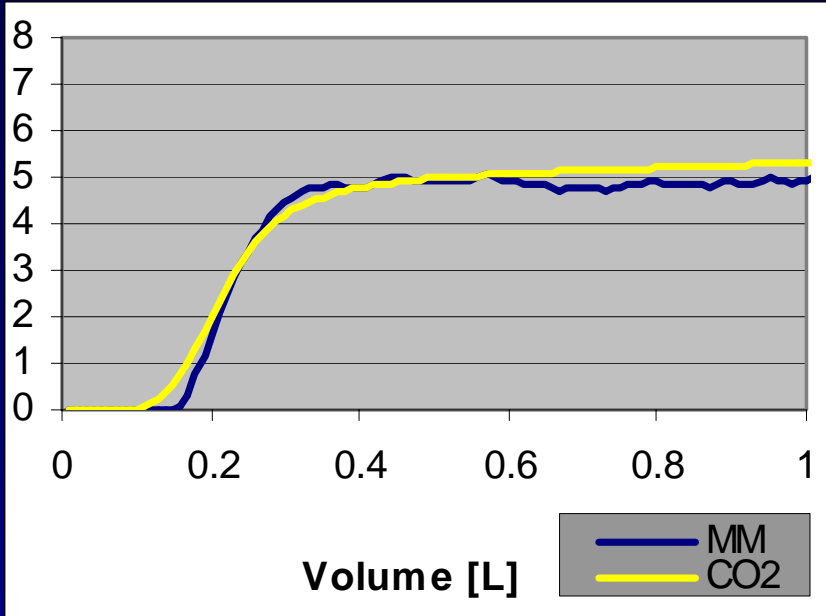
Moderate



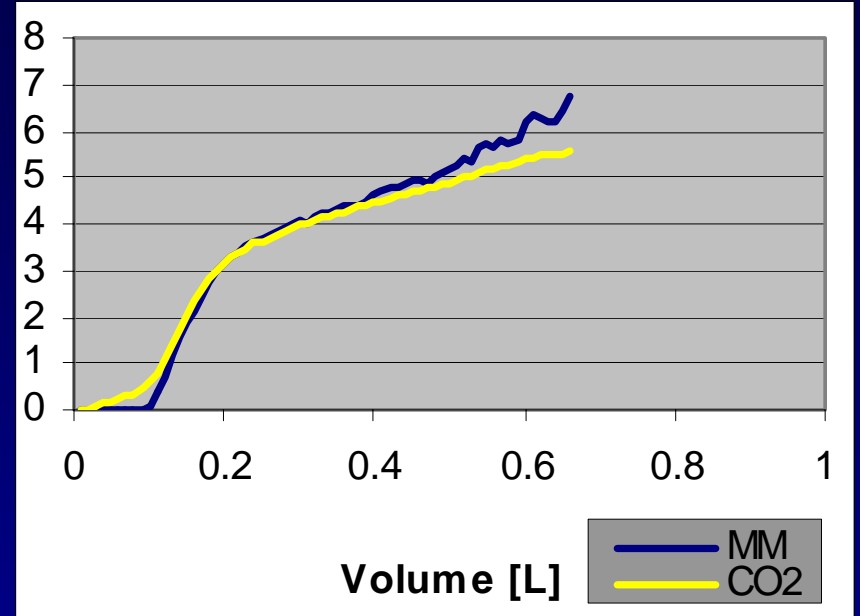
	Average for Normal Group
FVC/FEV1	77.9 %
Max $\Delta\%CO_2/L$	3.54
Volume Max Slope (L)	0.120

	Average for Moderate Group
FVC/FEV1	59.3 %
Max $\Delta\%CO_2/L$	3.37
Volume Max Slope (L)	0.123

Normal



Severe Obstruction



	Average for Normal Group
FVC/FEV1	77.9 %
Max $\Delta\%CO_2/L$	3.54
Volume Max Slope (L)	0.120

	Average for Severe Group
FVC/FEV1	46.4 %
Max $\Delta\%CO_2/L$	1.75
Volume Max Slope (L)	0.141

Discriminant Analysis Findings

- Using four parameters
 - %CO₂ correctly categorized 72% of the subjects into their spirometric “Normal” or “Obstruction” category
 - Molar Mass correctly categorized 67%
- Using only Molar Mass parameters
 - Adding Age and Gender, Molar Mass correctly categorized 78%
 - Molar Mass correctly classified 83% into either “Normal” or “Any Obstruction”

Conclusions

- Molar mass measurements may provide an effort-independent test that will diagnose airway obstruction.
- Molar mass measurements are simple.
 - No external sensors or analyzers needed
 - No calibration necessary
- May add additional information to traditional spirometry

Next Steps

- Additional data required
(larger patient databases)
- Studies in asthmatic patients
 - Pre and post bronchodilator studies
 - Changes during methacholine challenges
- Pediatric studies