

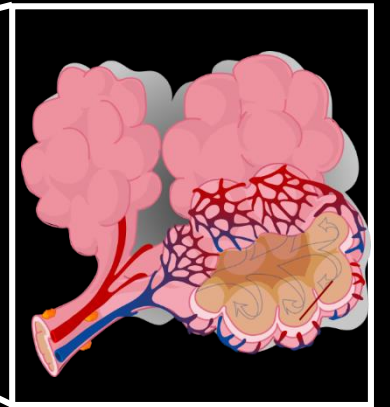
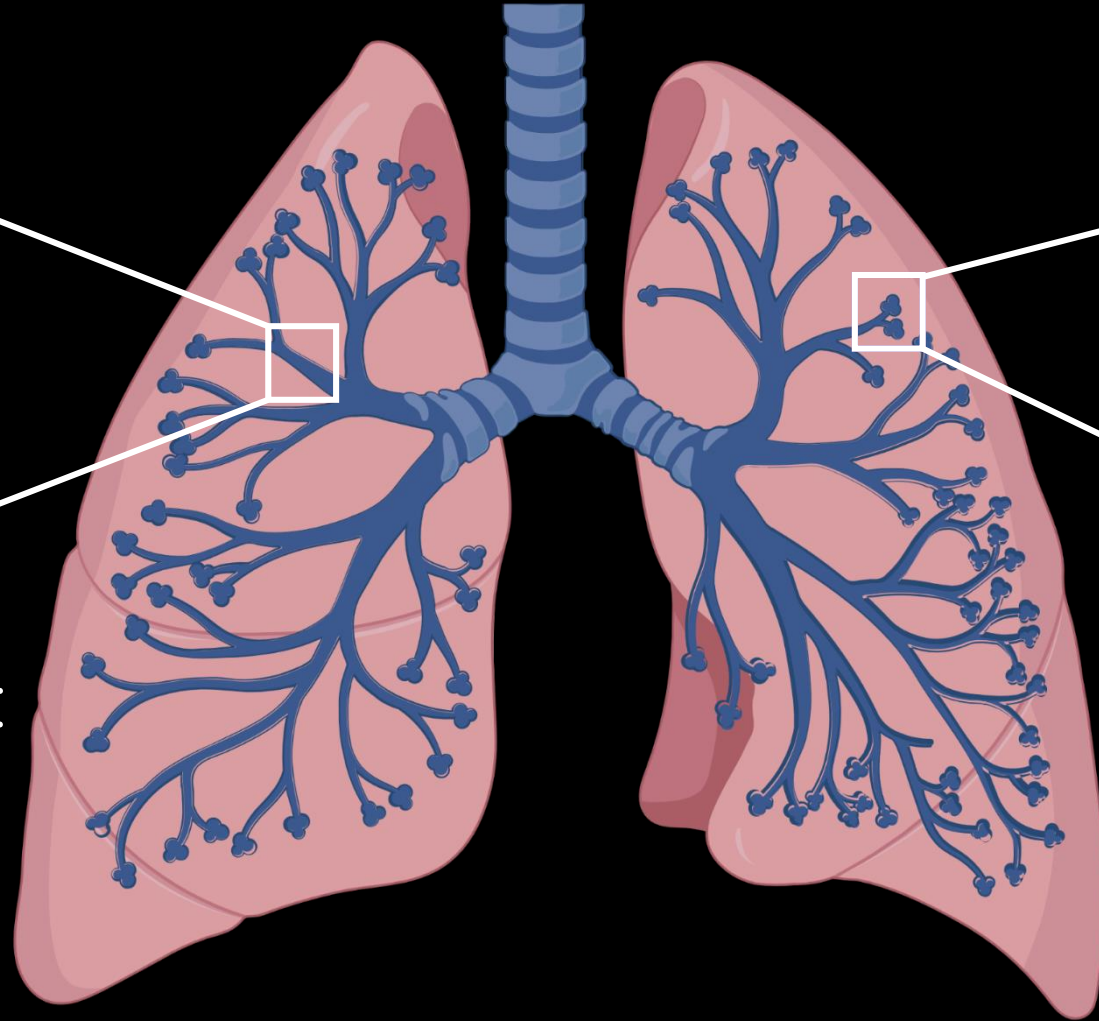
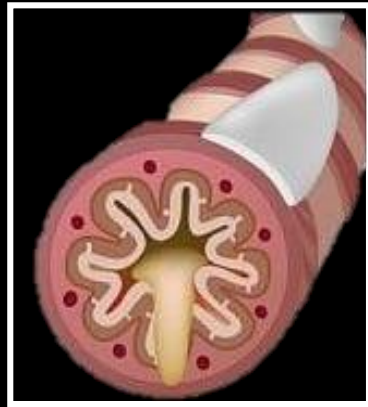
^{129}Xe MRS Biomarkers Predict 6-Week Response to ICS/LAMA/LABA in Moderate Asthma

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Asthma: Beyond Airways Disease



Pathology of asthma:

- Wall thickening^{1,2}
- Mucus plugging³
- Airway loss⁴

Gas-exchange in asthma:

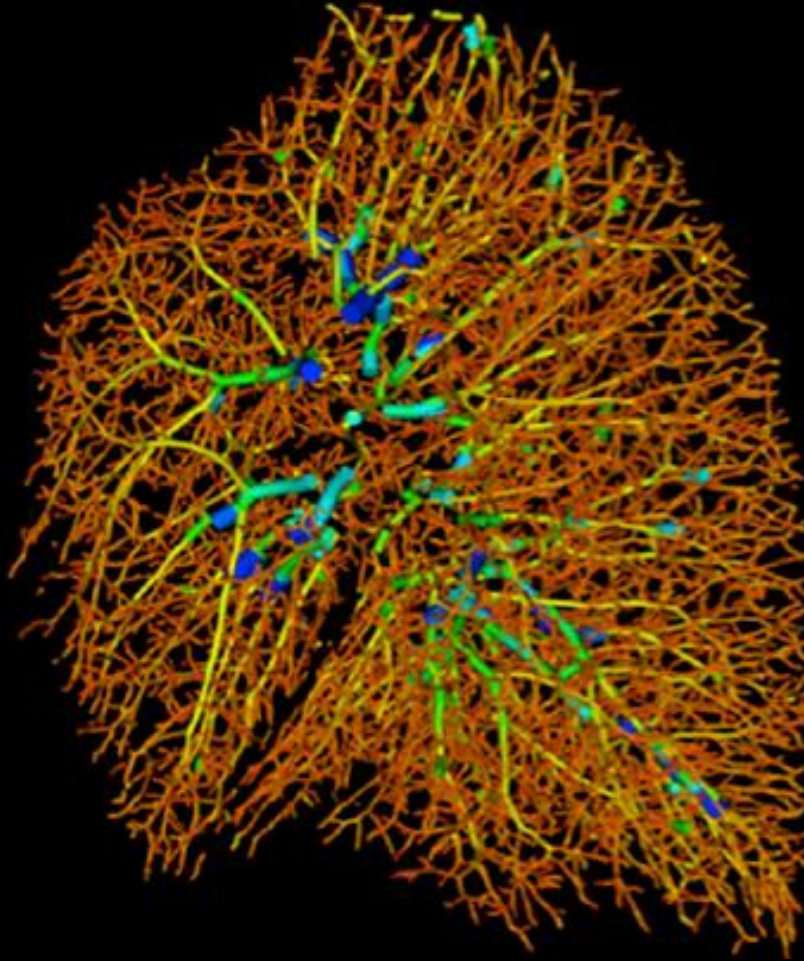
- Elevated DL_{CO} ⁵
- Vascular pruning⁶

¹Niimi et al. *Am J Med* (2004) ²Park et al. *J Investig Allergol Clin Immunol* (1997)

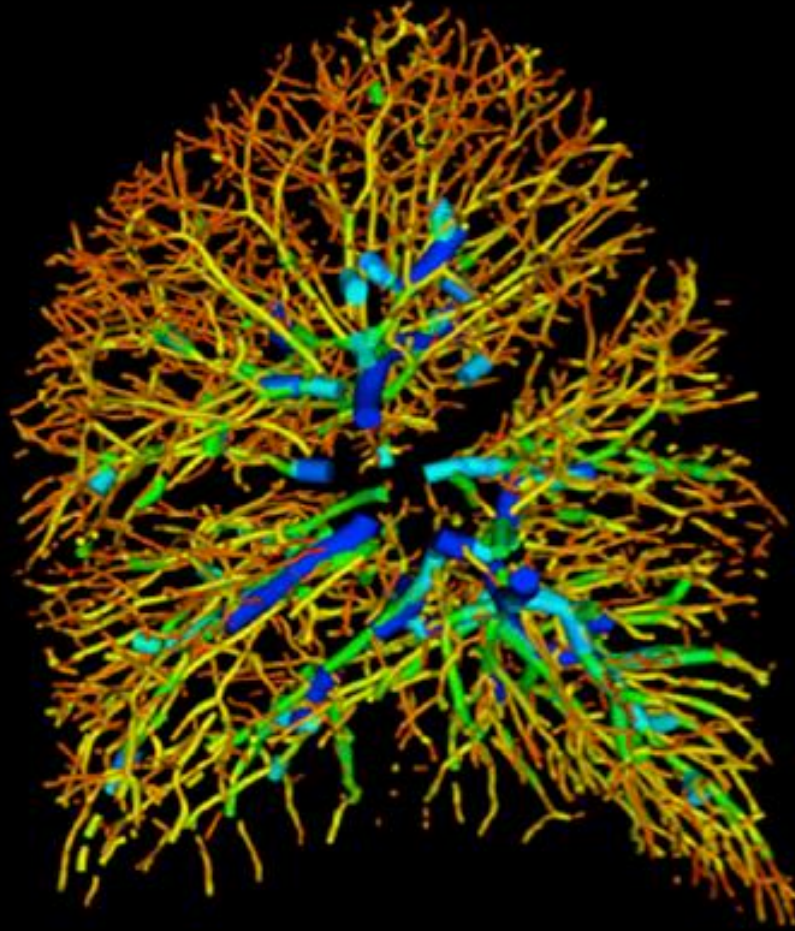
³Dunican et al. *J Clin Invest* (2018) ⁴Eddy et al. *AJRCCM* (2020) ⁵Saydain et al. *Chest* (2004) ⁶Ash et al. *AJRCCM* (2018)

CT Pulmonary Vessels in Asthma

Healthy



Asthma

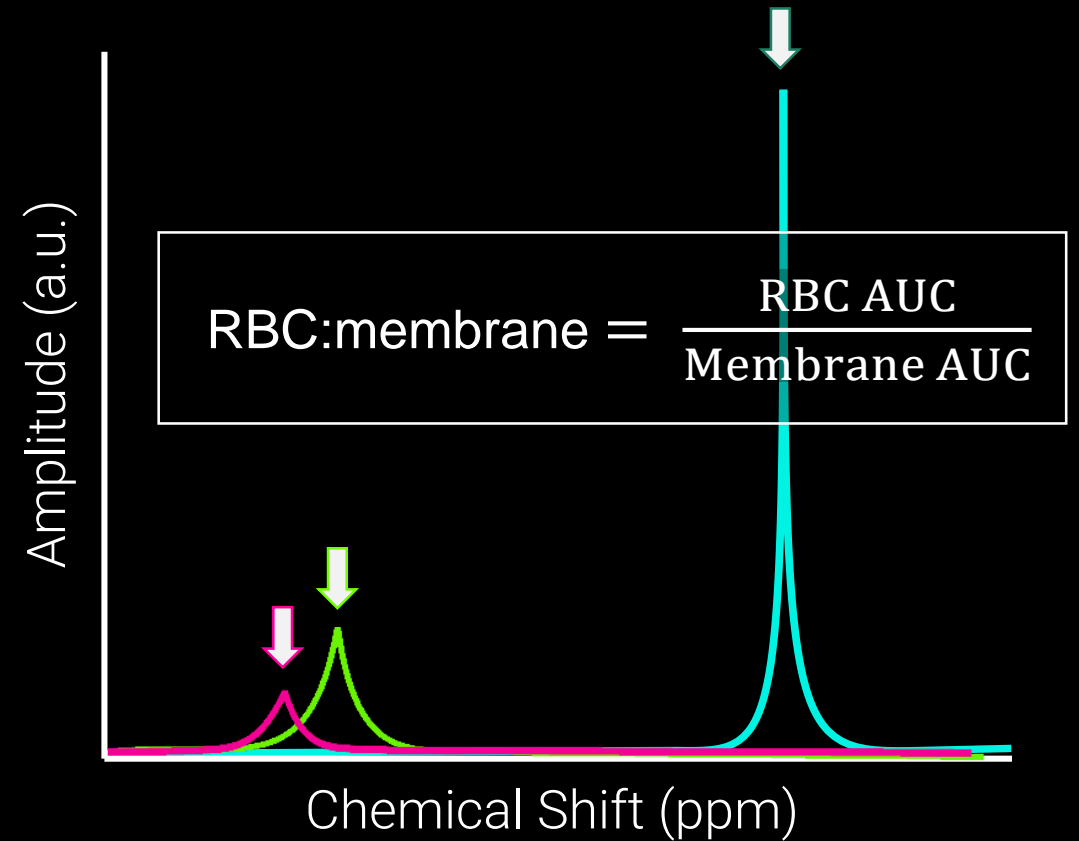
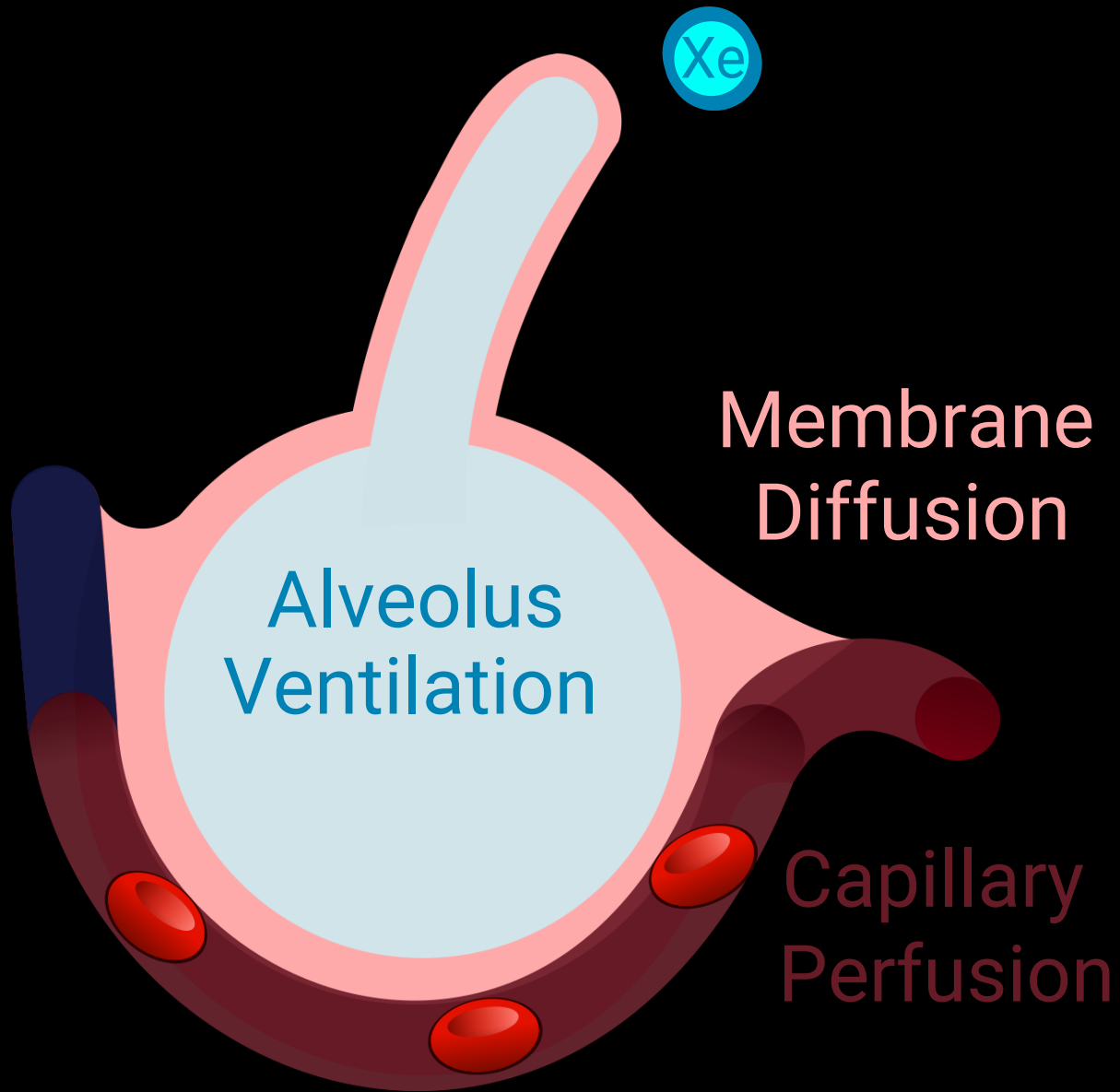


- Associated with exacerbations, severity, control and eosinophilia in asthma¹
- Small vessel volume increased with smoking cessation in COPD²

Treatment Response

- Normalization of BV₁₀, BV₅ in severe asthma after 2.5 years of anti-IL-5R α therapy³

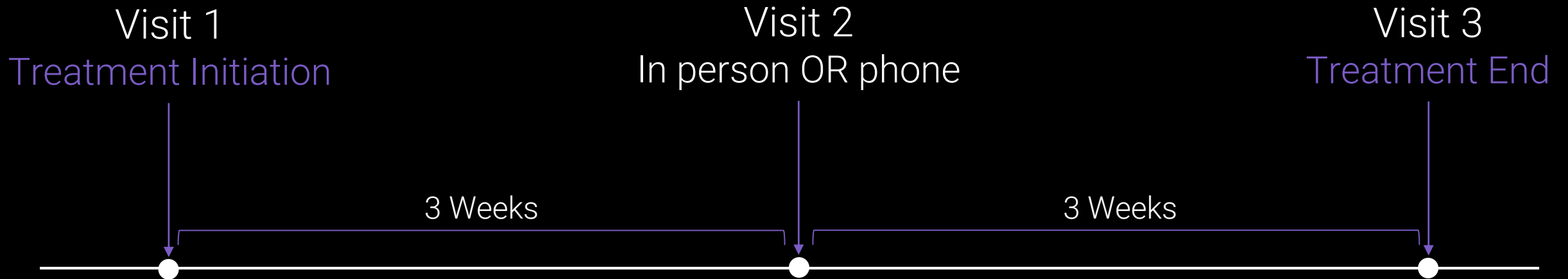
^{129}Xe MR Spectroscopy



- Inhale into terminal airways
- Diffuses across membrane
- Binds to lung capillary RBC

Asthma Triple Therapy Study Visit Timeline

Study Drug: fluticasone furoate (ICS), umeclidinium (LAMA), vilanterol (LABA)



Study visits included:

- Baseline CT
- ^{129}Xe MRI and MRS
- Pulmonary function tests
- Quality-of-life questionnaires

Asthma Triple Therapy Study Visit Timeline

Study Drug: fluticasone furoate (ICS), umeclidinium (LAMA), vilanterol (LABA)

Visit 1
Treatment Initiation

Visit 2
In person OR phone

Visit 3
Treatment End

Do ^{129}Xe MRS gas-exchange measurements influence response to ICS/LAMA/LABA in moderate-severe asthma?

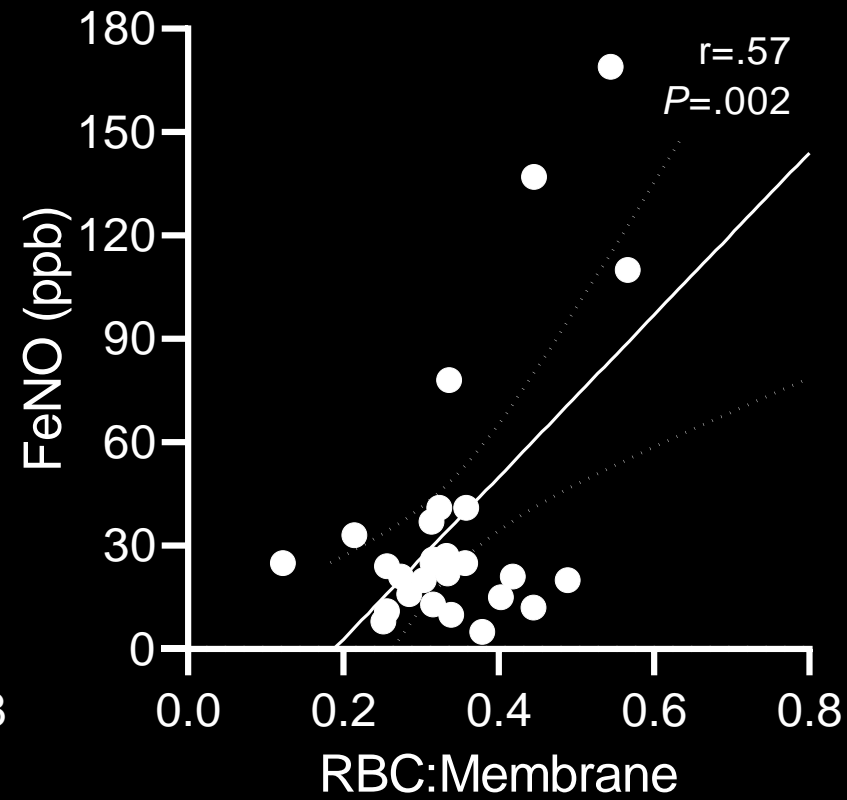
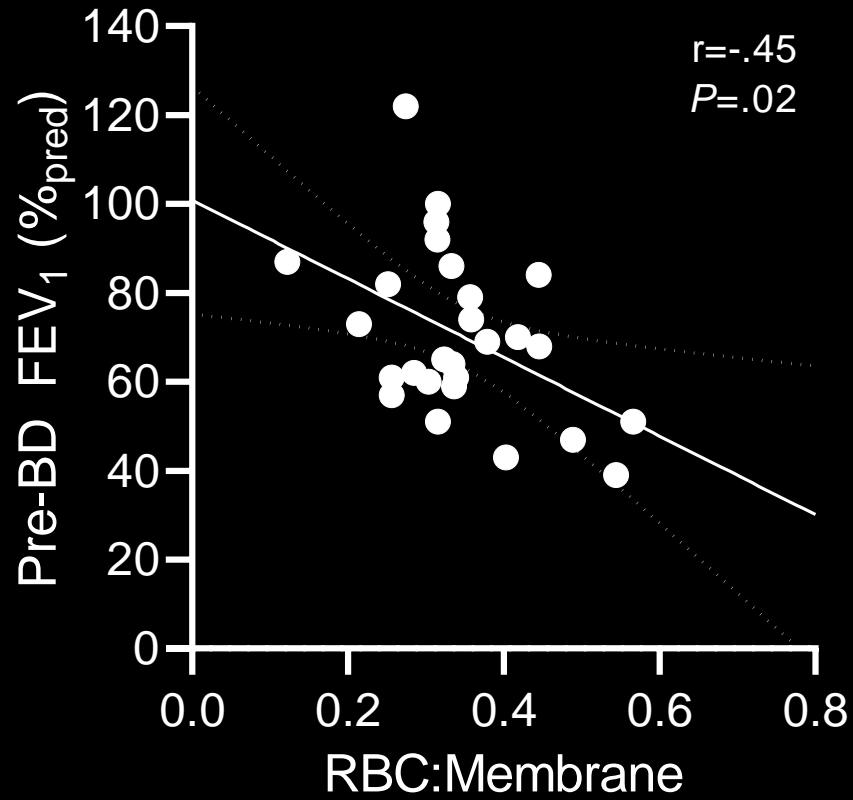
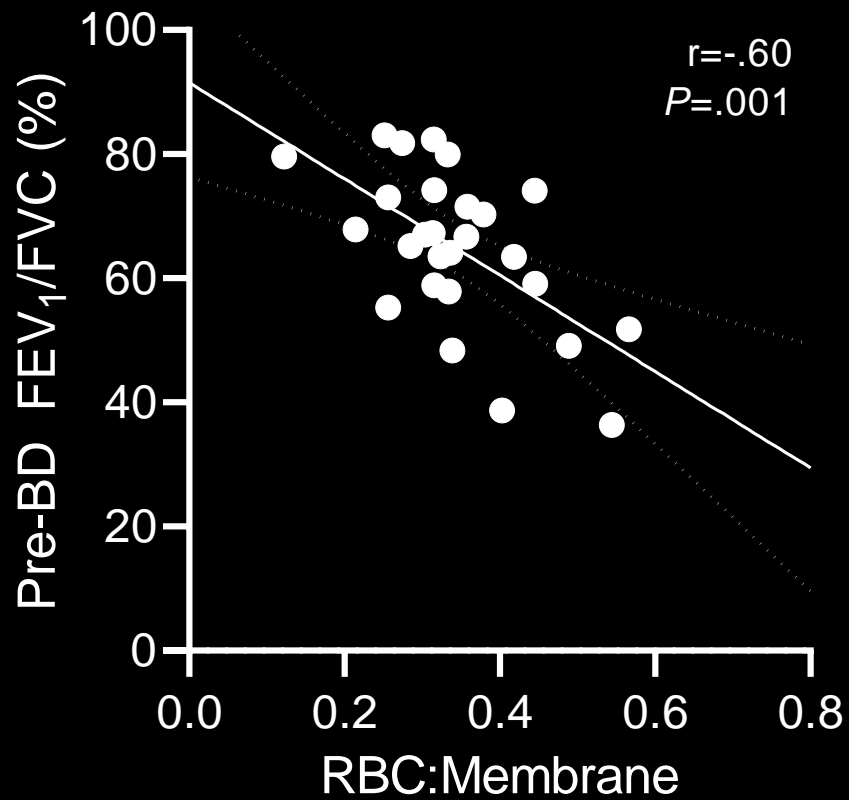
Study visits included:

- Baseline CT
- ^{129}Xe MRI and MRS
- Pulmonary function tests
- Quality-of-life questionnaires

Participant Demographics

Parameter mean \pm SD	Week 0 (n=27)	Week 6 (n=27)	Sig. <i>P</i>
Age years	54 \pm 15	54 \pm 15	-
Female n (%)	20 (74%)	20 (74%)	-
BMI kg/m ²	30 \pm 7	30 \pm 7	-
FeNO ppb	37 \pm 40	27 \pm 17	.1
Pre-BD FEV ₁ % _{predicted}	70 \pm 19	78 \pm 19	.003
Pre-BD FVC % _{predicted}	86 \pm 12	89 \pm 15	.4
Pre-BD FEV ₁ /FVC %	65 \pm 13	70 \pm 11	<.001
Pre-BD R ₅ cmH ₂ O•s/L	5.5 \pm 1.7	4.4 \pm 1.4	<.001
Pre-BD R ₁₉ cmH ₂ O•s/L	3.6 \pm 1.2	3.3 \pm 1.1	.01
Pre-BD R ₅₋₁₉ cmH ₂ O•s/L	1.9 \pm 1.0	1.1 \pm 0.7	<.001
Pre-BD X ₅ cmH ₂ O•s/L	-3.1 \pm 1.5	-2.2 \pm 1.4	<.001
Pre-BD MRI VDP %	14 \pm 12	9 \pm 8	.004

Baseline Relationships



Multivariable Linear Regression Model

Parameter	R ²	ANOVA P	Unstandardized B	Standardized β	Coefficients P
Δ FEV ₁ /FVC					
<i>Model</i>	0.365	.007			
Constant			-10.056 ± 4.508		.03
MRS RBC:membrane			30.256 ± 10.127	.517	.007
Pre-BD X ₅			-1.564 ± 0.638	-.425	.02

- FEV₁/FVC gold standard measurement of airflow obstruction
- RBC:membrane measures gas-exchange, pulmonary vascular red blood cell density, and alveolar-capillary membrane thickness
- Improved obstruction post-therapy influenced by baseline MRI gas-exchange and respiratory elastance (X₅) measurements

Conclusions

- RBC:membrane correlated with markers of airway inflammation and obstruction
- ^{129}Xe MRS RBC:membrane predicted significantly improved obstruction in response to ICS/LAMA/LABA

^{129}Xe MRS gas-exchange measurements significantly predict clinically relevant response to ICS/LAMA/LABA in moderate-severe asthma, suggestive of a pulmonary vascular component in severe, advanced asthma