Investigating the Effect of Multiple Smoking Exposures on Lung Function and Structure in Young Persons Using Hyperpolarized ^{129}Xenon MRI and CT

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Introduction

- Cannabis legalization and vaping have increased multiple smoking exposures among Canadian young adults[1]
- Long-term cigarette effects are well known, but combined effects of cigarettes, cannabis, and vaping remain under-researched
- ^{129}Xe MRI and computed tomography (CT) are more sensitive to early lung abnormalities compared to traditional pulmonary tests[2]

What are the effects of multiple smoking exposures on the lungs?

Objective

Evaluate how multiple smoking exposures may alter lung structure via ^{29}Xe MRI.

Methods

Study Participants and Design

- Participants ≥19yrs were enrolled:
  - Self-reported current or previous vaping, cigarette smoking, or cannabis joint smoking
  - Age matched and healthy, never-vaping, never-smoking controls
- Pulmonary function tests (PFT) reported using GLI race-neutral reference equations[3]
- COPD assessment test (CAT) and St. George's Respiratory Questionnaire (SGRQ) administered

MRI

- ^{129}Xe MRI performed using 3.0T Vida (Siemens Healthineers), 1-point Dixon gas exchange (**Figure 1**)[4]:
  - Ventilation defect percent (VDP)
  - Membrane to gas ratio (Mem/Gas)
  - RBC to gas ratio (RBC/Gas)
  - RBC to membrane ratio (RBC/Mem)

** Figure of Gas Exchange Scheme **

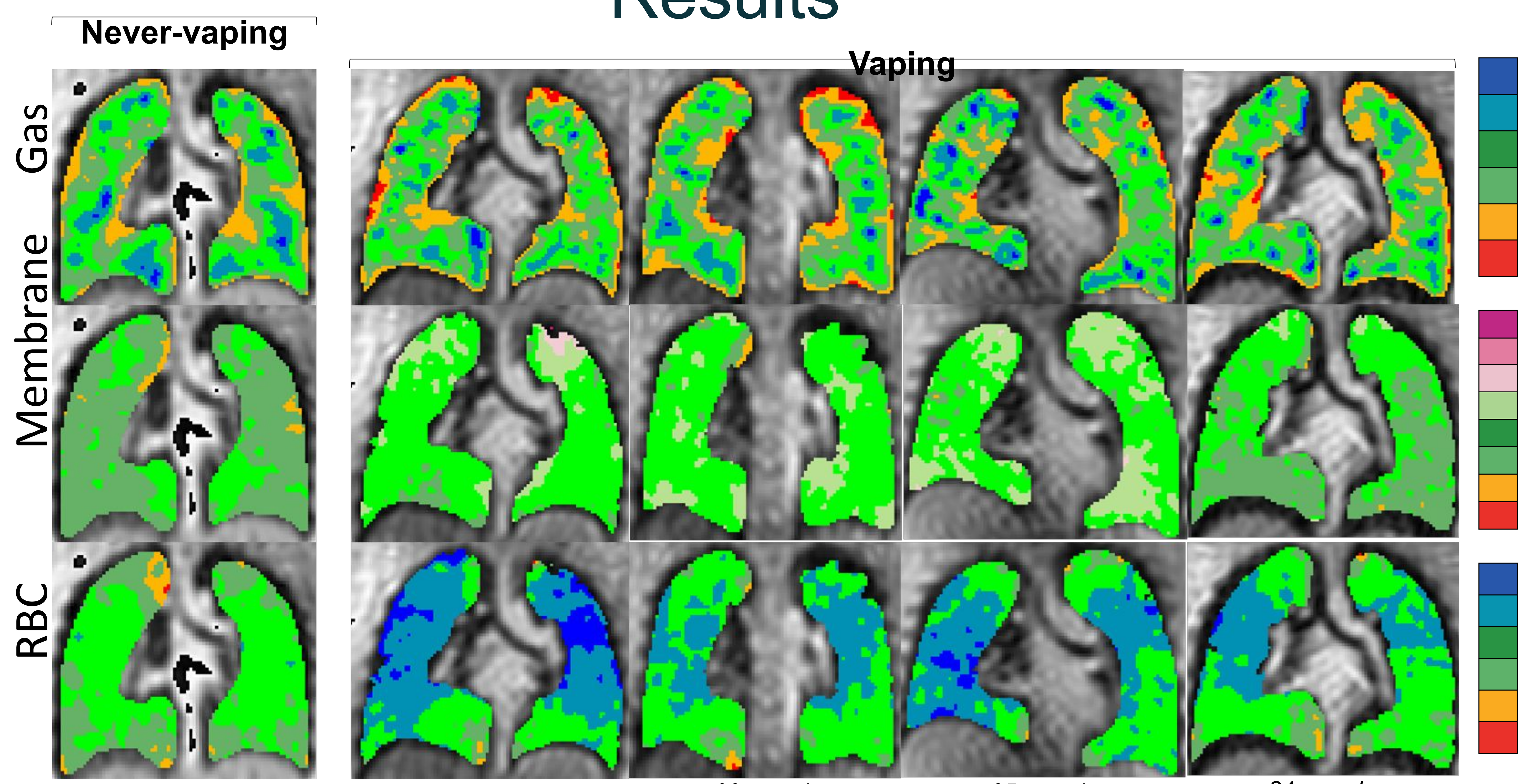
CT

- CT performed at full inspiration using Revolution HD (GE Healthcare) to measure quantitative lung density (VIDA insights)

Statistical Analysis

- Measurements compared using the Wilcoxon rank-sum test

Results



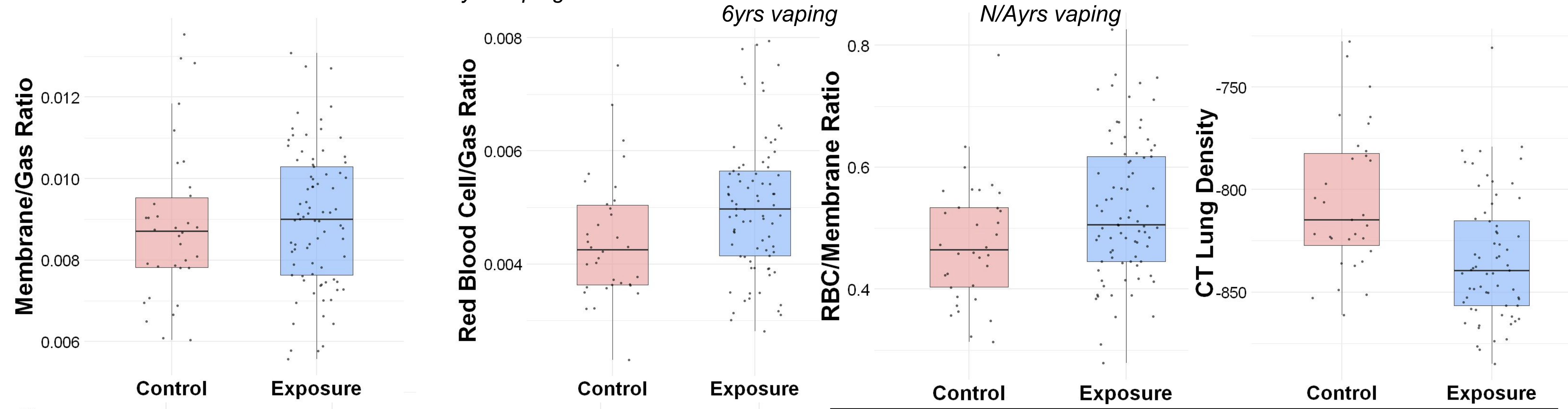
26yo female

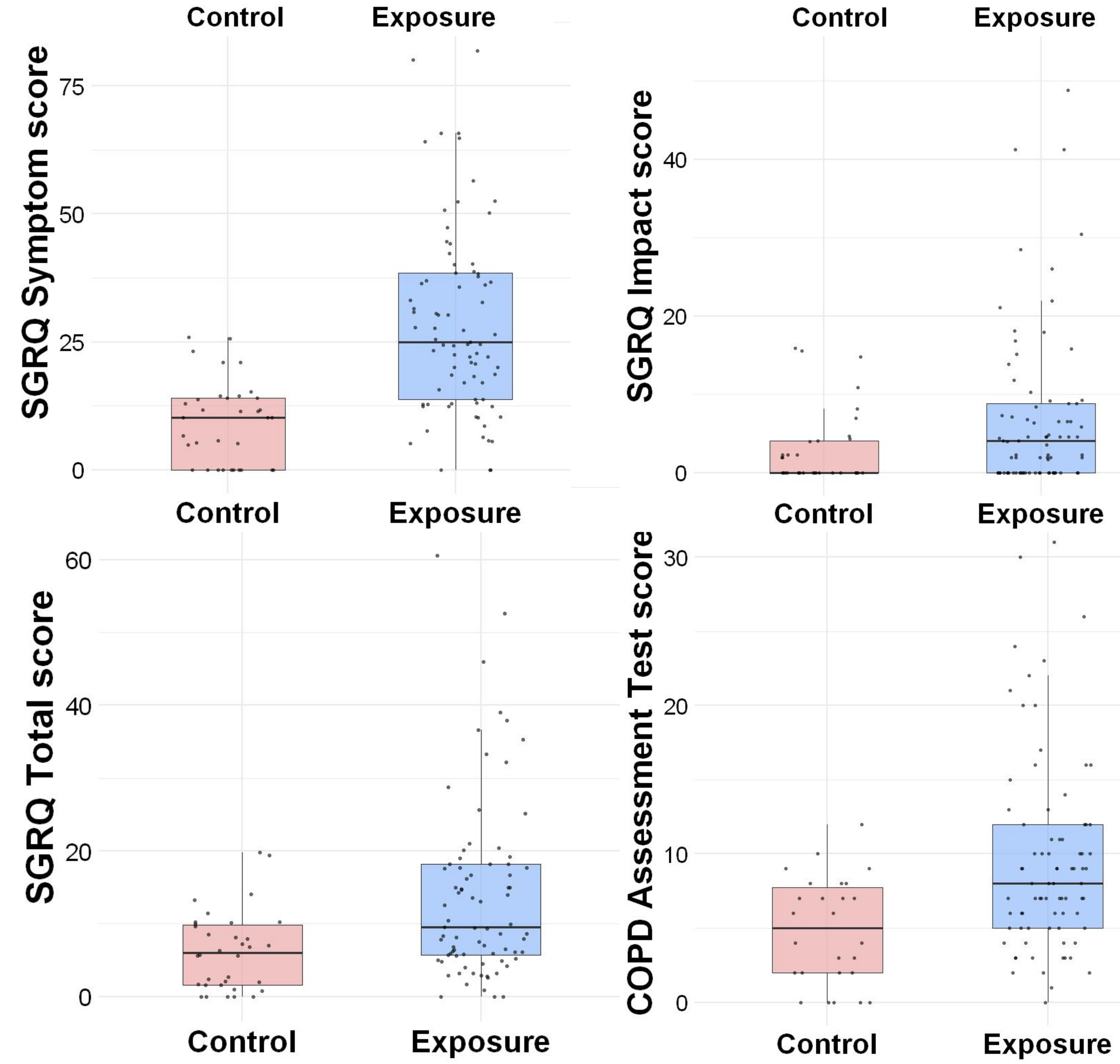
20yo male, THC/CBD/nicotine, 3yrs cannabis 5yrs vaping

23yo male, THC/CBD/nicotine, 3yrs cannabis 2yrs smoking 6yrs vaping

25yo male, THC/CBD/nicotine 12yrs cannabis 13yrs smoking N/Ayrs vaping

24yo male, THC/CBD/nicotine 5yrs cannabis 3yrs vaping





Mean ± SD *or* Median (range)	**Control (n=34)**	**Exposure (n=81)**	**p-value**
Age yrs	32 ± 9	30 ± 8	
Male n (%)	9 (26)	41(51)	
BMI kg/m^2	25 ± 4	25 ± 4	
Exposure			
Yrs vaping	-	3 (0.5 - 6)	
Vaping times/day	-	5 (1-175)	
THC/CBD only n (%)	-	12 (48)	
Nicotine only n (%)	-	8 (32)	
THC/CBD & nicotine n (%)		5 (20)	
PFTs			
Pre fev1 pp gli	104 ± 14	110 ± 14	0.03083
Pre Fev1 FVC	83 ± 7	80 ± 6	0.02944
Pre fvc pp gli	106 ± 15	117 ± 15	0.00092
Post fev1 pp gli	109 ± 13	115 ± 15	0.03174
DLCO pp gli	105 ± 13	108 ± 17	0.4528

BMI=body mass index; FEV_1=forced expiratory volume in 1s; $\%_{pred}$=GLI percent predicted; FVC=forced vital capacity; DL_{CO}=diffusing capacity of the lungs for carbon monoxide.

Discussion

Symptoms

- Exposure group has greater respiratory symptoms than controls

PFTs

- Decreased FEV1 and FVC in exposure group compared to controls

^{129}XenonMRI

- ***RBC/Gas ratio exposure > control***

CT Scan

- ***mean lung density control >> exposure***

Study Challenges

- Symptom questionnaires rely on self reported information, subjective and may be biased
- Large amount of variability in smoking exposure (current, previous, years, frequency)

Future Work

- Longer term continuous study tracking participants over years
  - Long term effects on function and structure change
  - Determines whether early structural abnormalities detected via 129Xenon can progress into chronic conditions
- RBC signal has been found to be increased increased in males
  - Future work should further investigate this by controlling for sex and by sex matching the exposure and control group

Conclusion

While both the exposure and control groups were young and relatively healthy, but symptomatic and had **similar MRI results**, it was found that there were **signs that potentially indicated early disease manifestation**, such as lower lung density and higher red blood cell to gas ratio.

References

1. Statistics Canada, 2023
2. Rao *et al. European Radiology.* 2024;34(11);, 7450–7459

Acknowledgments

Investigating the Effect of Vaping on Lungs Using ^{129}Xe MRI

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Introduction

- Vaping rates among Canadian teens and young adults have surged over the past decade[1]
- There is limited information about the short- and long-term effects of vaping
- Traditional tools such as pulmonary function tests (PFT) and computed tomography (CT) are not sensitive enough to to detect early-stage pulmonary abnormalities that may manifest in the small airways[2]

What are the effects of vaping on lungs?

Objective

Evaluate the lung structure-function effects of vaping using ^{129}Xe MRI.

Methods

Study Participants and Design

- Participants ≥19yrs were enrolled:
  - Self-reported current vaping with <1.5 pack-year cigarette smoking and joint-year cannabis smoking
  - Age and sex-matched healthy, never-vaping, never-smoking controls
- Pulmonary function tests (PFT) reported using GLI race-neutral reference equations[3]
- COPD assessment test (CAT) and St. George's Respiratory Questionnaire (SGRQ) administered

MRI

- ^{129}Xe MRI performed using 3.0T Vida (Siemens Healthineers), 1-point Dixon gas exchange (**Figure 1**)[4]:
  - Ventilation defect percent (VDP)
  - Red blood cell (RBC) defect percent
  - Membrane to gas ratio (Mem/Gas)
  - RBC to gas ratio (RBC/Gas)
  - RBC to membrane ratio (RBC/Mem)
  - High and low signal % of membrane and RBC

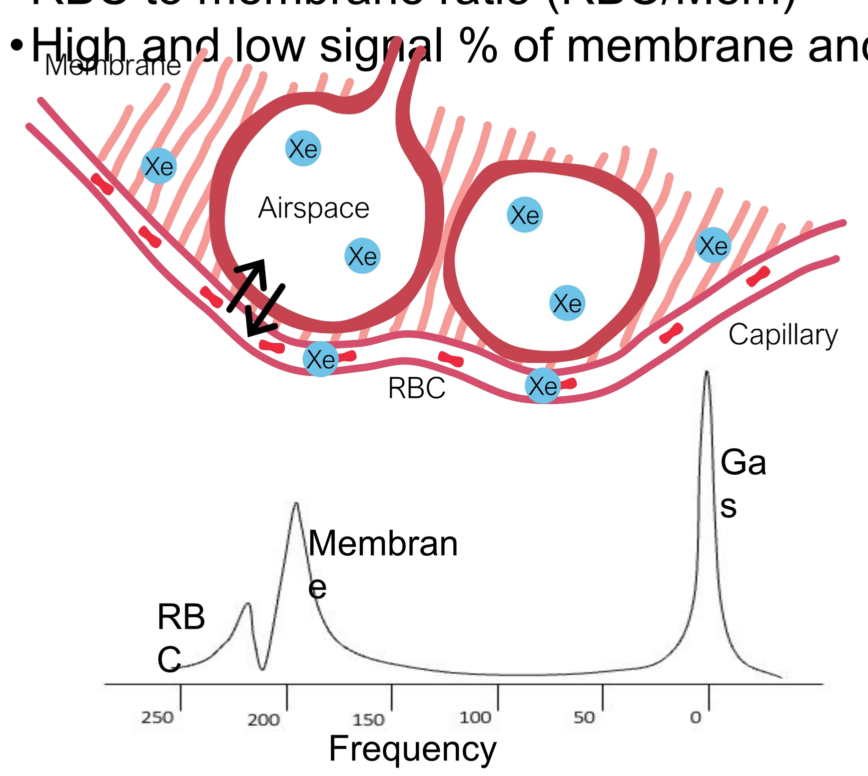

Figure 1. Schematic of ^{129}Xe MRI gas exchange and chemical shift.

Statistical Analysis

- Measurements compared using the Wilcoxon rank-sum test

Results

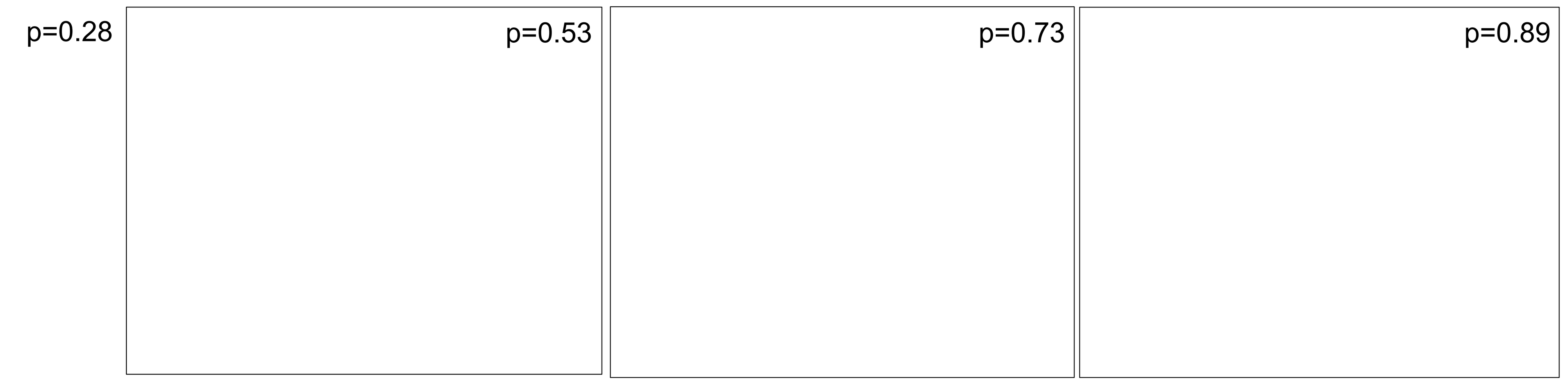

Figure 2. Comparison between vaping and never-vaping groups show no difference in ^{129}Xe MRI measurements.

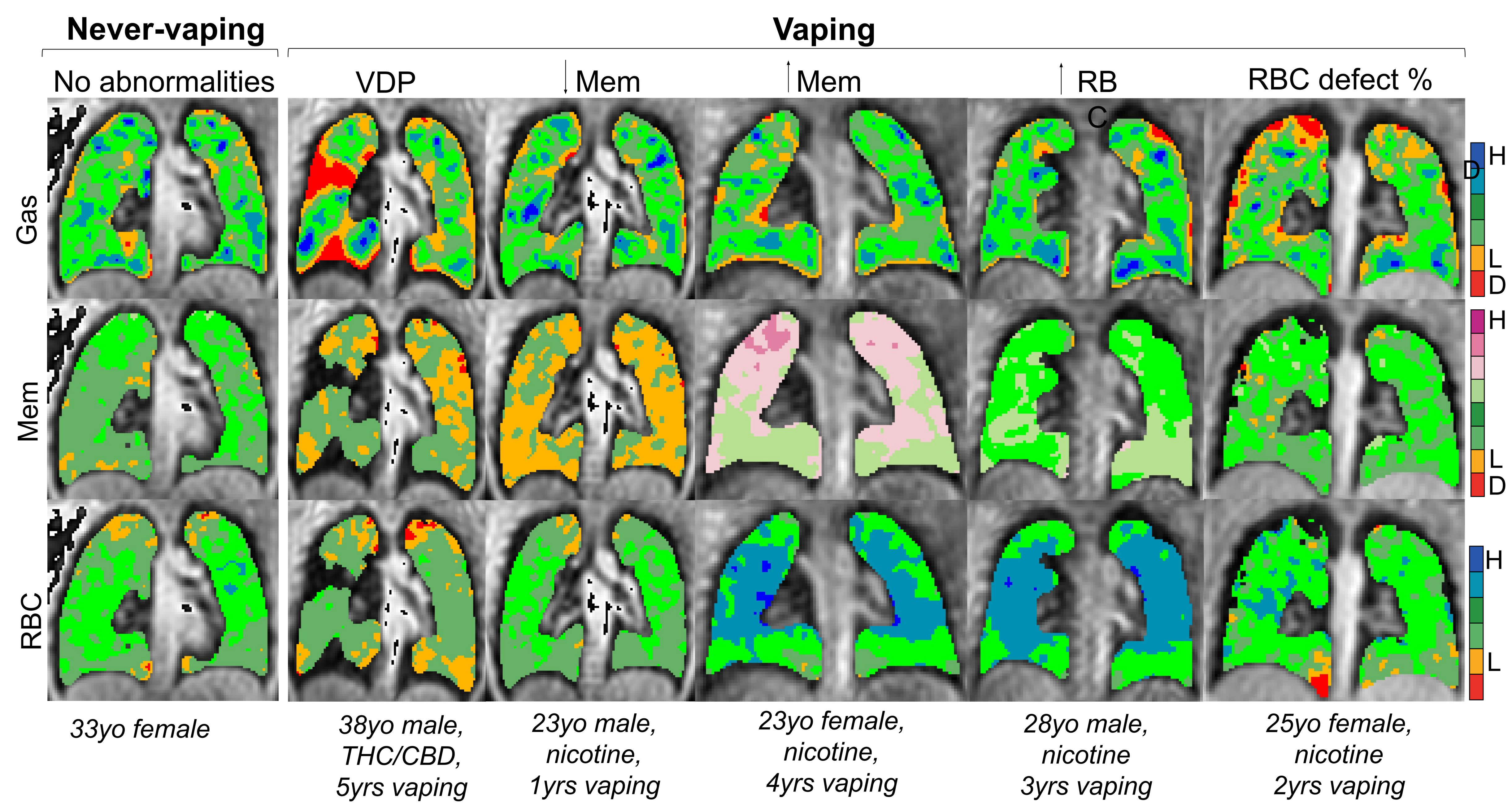

Figure 3. Further by participant inspection revealed ^{129}Xe MRI gas exchange abnormalities in vaping participants. D=defect (no signal); L=low signal; H=high signal.

Table 1. Participant Demographics and PFT Measurements.

Mean ± SD *or* Median (range)	Never-Vaping (n=15)	Vaping (n=25)
Age yrs	28 ± 5	26 ± 5
Female n (%)	9 (60)	11 (44)
BMI kg/m^2	25 ± 4	25 ± 6
Vaping Frequency		
Yrs vaping	-	3 (0.5 - 6)
Vaping times/day	-	5 (1-175)
THC/CBD only n (%)	-	12 (48)
Nicotine only n (%)	-	8 (32)
THC/CBD & nicotine n (%)		5 (20)
PFTs		
FEV_1 $\%_{pred}$	106 ± 14	109 ± 17
FVC $\%_{pred}$	108 ± 14	115 ± 17
FEV_1/FVC %	84 ± 8	82 ± 8
RV/TLC $\%_{pred}$	117 ± 12	104 ± 16
DL_{CO} $\%_{pred}$	108 ± 13	105 ± 23

BMI=body mass index; FEV_1=forced expiratory volume in 1s; $\%_{pred}$=GLI percent predicted; FVC=forced vital capacity; RV=residual volume; TLC=total lung capacity; DL_{CO}=diffusing capacity of the lungs for carbon monoxide.

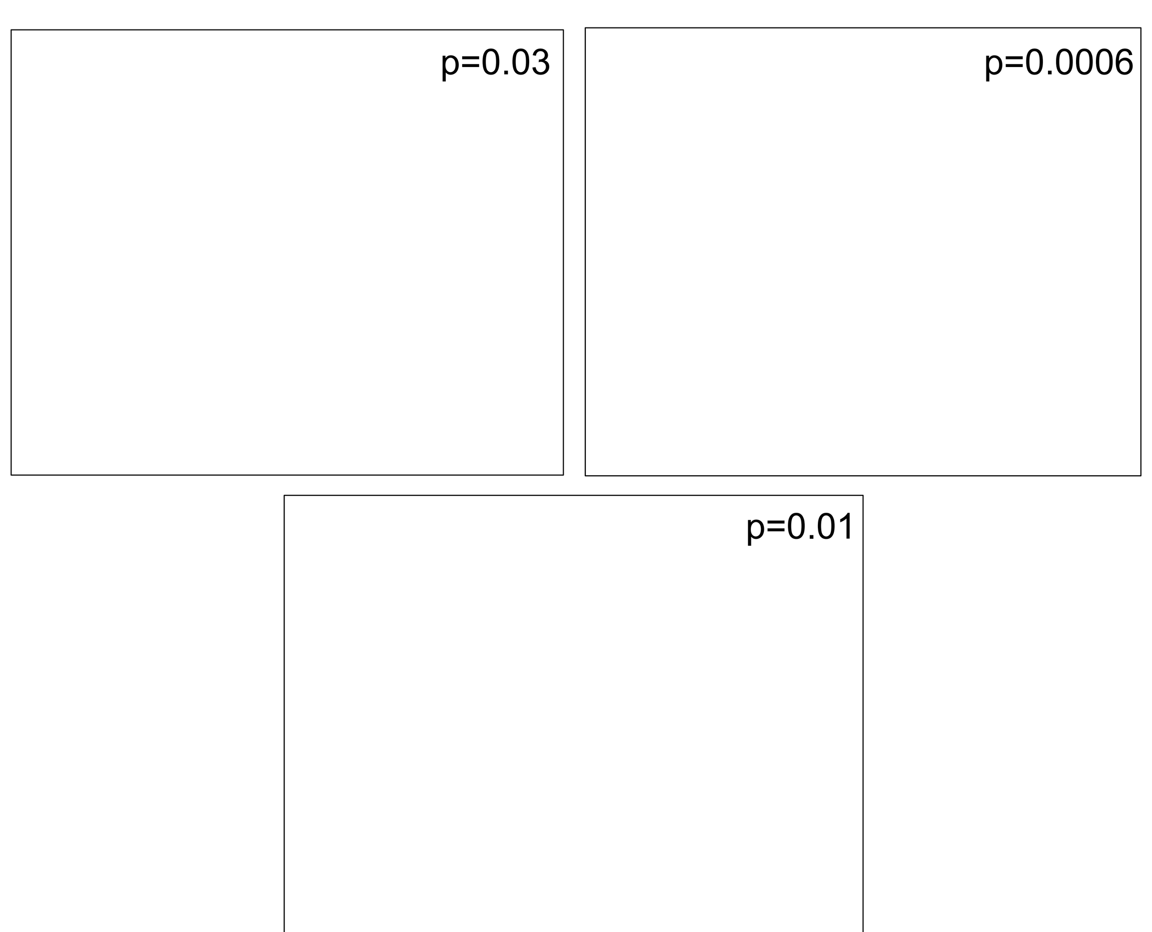

Figure 4. Vaping participants reported a greater burden of respiratory symptoms

Discussion

- Heterogenous gas exchange patterns in participants who vape, despite normal PFTs
  - n=1 VDP
  - n=3 reduced membrane xenon uptake
  - n=5 increased membrane xenon uptake
  - n=3 RBC defect percent
  - n=2 reduced RBC xenon uptake
  - n=4 increased RBC xenon uptake
- ^{129}Xe MRI may be more sensitive to early lung changes due to vaping
- ^{129}Xe MRI can be used for longitudinal monitoring and disease phenotyping

Study Challenges

- Vape use is difficult to quantify
- Sole vape users are rare
  - Compound effects of vaping in addition to smoking cigarettes and cannabis joints is poorly understood

Future Work

- Further comparison between participants who vape nicotine vs THC/CBD
- Subset of participants underwent bronchoscopy to explore cellular and molecular airway profiles of vaping participants (**Figure 5**)
- Longitudinal follow-up visits to monitor changes in lung s

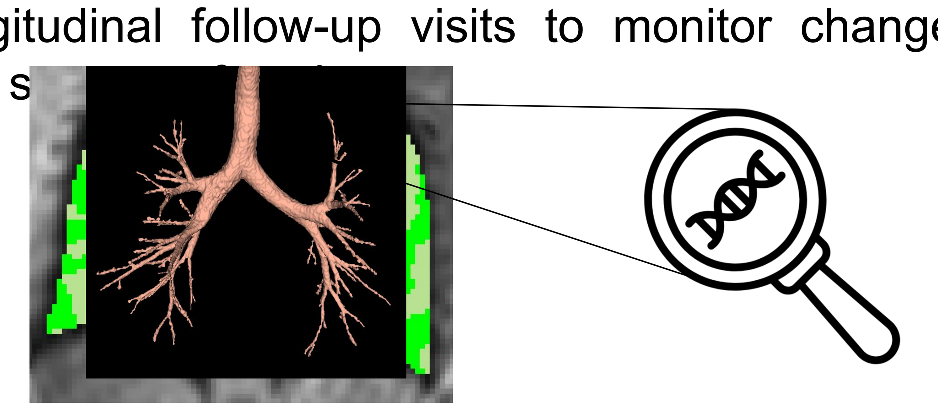

Figure 5. Image-guided bronchoscopy to characterize cellular and molecular pulmonary changes due to vaping.

Conclusions

Despite normal lung function tests, ***^{129}Xe MRI gas exchange patterns were abnormal and heterogenous*** in some participants who reported vaping. These results highlight the potential impacts of vaping, ***even before decades-long exposures***.

References

1. Government of Canada, 2023.
2. He et al. IJCOPD. 2021;16:3183-3187.
3. Bowerman *et al. AJRCCM*. 2023;207:768-74.
4. Wang *et al. Med Phys*. 2017;44(6):2415-28.

Acknowledgments

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Membrane
Xe
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Airspace
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Capillary
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RBC
Xe