

Introduction

- CAPTAIN study evaluated exacerbation rate, FEV₁ and ACQ-7 responses to FF/UMEC/VI for a variety of doses¹
- Effect of FF/UMEC/VI on small-airways dysfunction in asthma has not been evaluated
- ¹²⁹Xe MRI measures small-airways dysfunction quantified as ventilation defect percent (VDP)²
- Oscillometry also measures distal-airways resistance which is quantified as resistance at 5Hz (R₅) minus the resistance at 19Hz (R₁₉)³

Hypothesis

In asthma patients, ¹²⁹Xe MRI VDP -a marker of small-airways dysfunction, significantly improves in response to daily FF/UMEC/VI

Objectives

- Measure MRI VDP and oscillometry distal airways resistance (R₅₋₁₉) prior to and following daily FF/UMEC/VI for 6 weeks
- Determine the significant predictors of VDP response among type-2 and non-type-2 inflammation asthma measurements

Methods

- Thirty-one participants with asthma, aged 18-70 years with ACQ ≥ 1.5, provided written informed consent (NCT04651777)
- Pulmonary function tests, ¹²⁹Xe MRI and asthma questionnaires were performed at baseline and at the 6-week follow-up
- Daily inhaled FF/UMEC/VI (200/62.5/25 µg) initiated at baseline
- VDP quantified using semi-automatic software²
- Differences determined using Holm-Bonferroni corrected paired samples t-tests
- Multivariable linear regression to predict 6-week change in VDP

Results

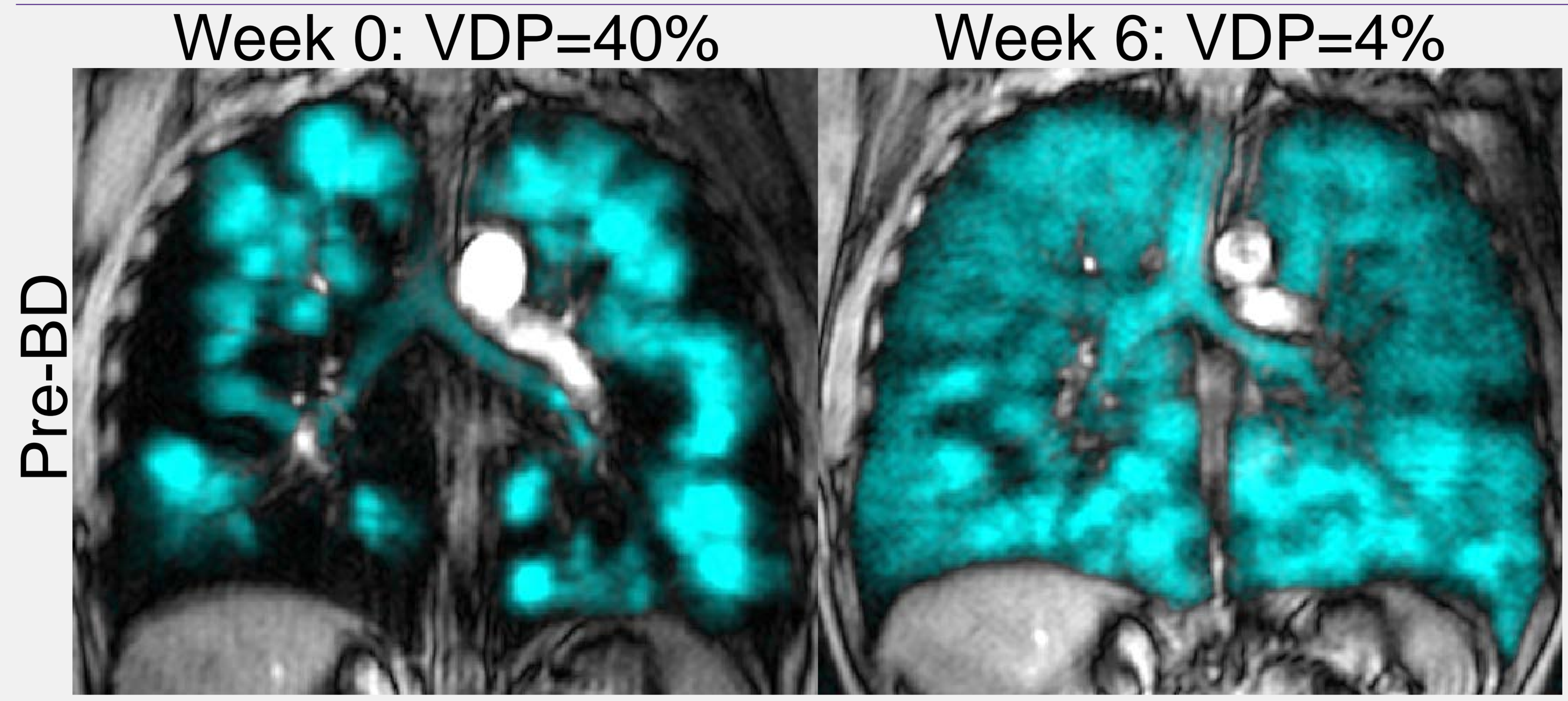


Figure 1. Pre-BD MRI VDP at 0-week and 6-week follow-up. V1 pre-BD FEV₁ %_{pred}=39%; ACQ-6=1.8; AQLQ=4.9; pre-BD VDP=40%; mucus-score=10. V2 pre-BD FEV₁ %_{pred}=68%; ACQ-6=0.0; AQLQ=6.6; pre-BD VDP=4%.

Table 1. Demographics, Pulmonary Function, Questionnaire and Imaging

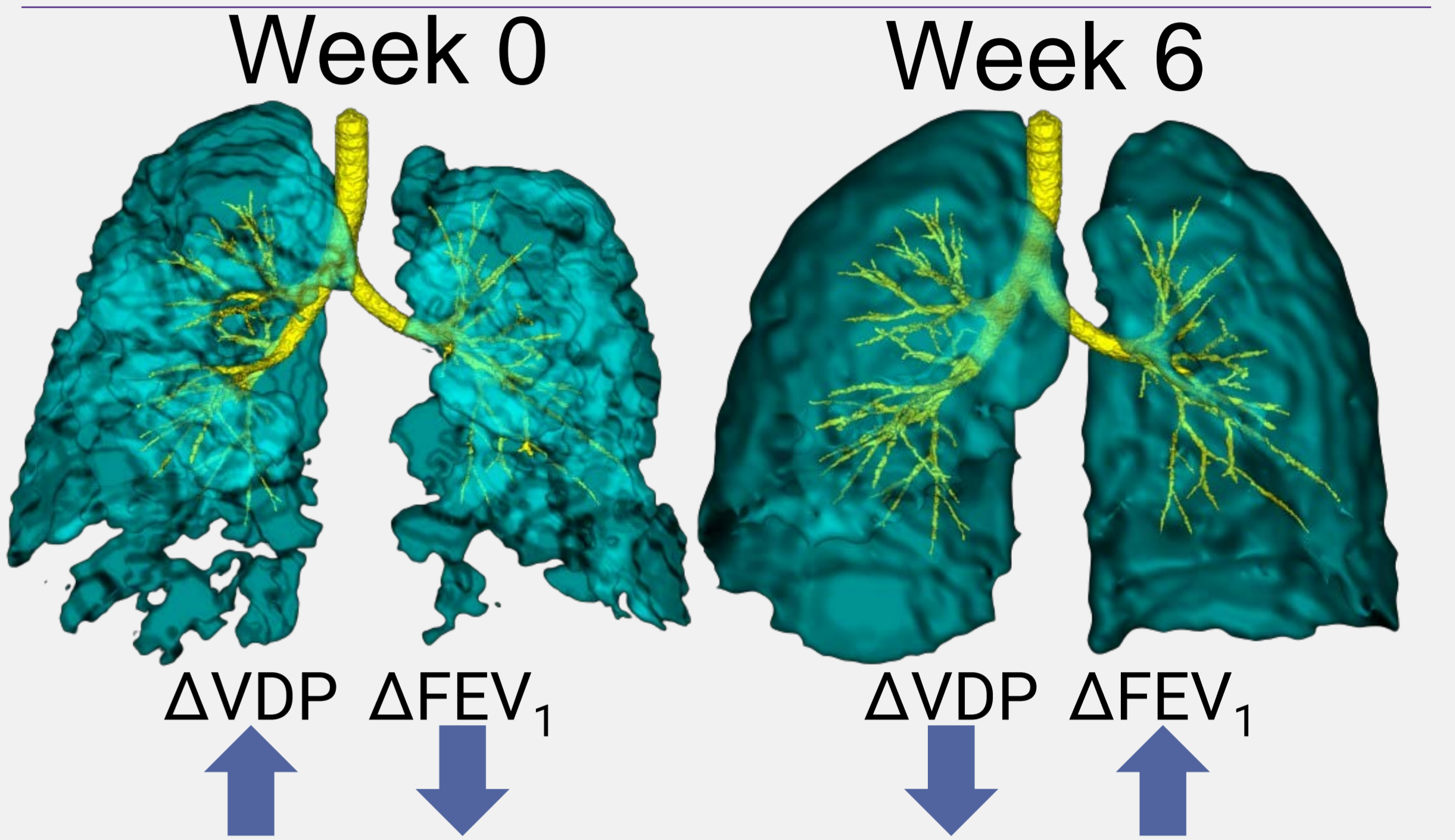
Parameter	Mean (SD)	Week 0 (n=28)	Week 6 (n=28)	p
Age years	55 (15)	-	-	-
BMI kg/m ²	30 (7)	-	-	-
Female n(%)	21 (75)	-	-	-
Eos cells/µL	360 (250)	-	-	-
Pre-BD VDP %	15 (12)	9 (9)		.02
Pre-BD FEV ₁ L	2.1 (0.7)	2.3 (0.8)		.04
Pre-BD FVC L	3.3 (1.0)	3.4 (1.2)		>.99
Pre-BD FEV ₁ /FVC %	65 (13)	70 (11)		.01
Pre-BD RV/TLC %	43 (8)	42 (12)		>.99
Pre-BD R ₅₋₁₉ cm H ₂ O sec/L	1.9 (1.0)	1.1 (0.8)		.002
FeNO ppb	36 (40)	29 (17)		.4
ACQ-6	2.0 (1.0)	1.4 (1.3)		.04
AQLQ	4.5 (1.2)	5.4 (1.2)		.02
SGRQ	47 (17)	35 (21)		.006

p=Holm-Bonferroni corrected paired t-test; BMI=body mass index; Eos=eosinophil count; FEV₁=forced expiratory volume in one-second; FVC=forced vital capacity; RV=residual volume; TLC=total lung capacity; R₅₋₁₉=peripheral airways resistance; FeNO=fraction of exhaled nitric oxide; ACQ-6=Asthma Control Questionnaire; AQLQ=Asthma Quality-of-Life Questionnaire; SGRQ=St. George's Respiratory Questionnaire; VDP=ventilation defect percent.

Table 2. Multivariable Linear Regression Model for ΔVDP at 6-week follow-up

Parameter	R ² Value	p (ANOVA)	Unstandardized Regression Coefficient ± SE	Stand β Coefficient	p
ΔVDP at 6 weeks Model	0.695	<.001			
Eos (V2)			-19.418 ± 5.270	-0.995	.002
FeNO (V2)			-0.069 ± 0.036	-0.390	.08
Pre-BD RV/TLC (V2)			0.130 ± 0.050	0.662	.02

Discussion



- VDP response driven by measurements of type-2 inflammation
- FF/UMEC/VI effect on airway dysfunction mechanistically linked to direct effects of type-2 inflammation
- VDP and FEV₁ improvements accompanied by improved oscillometry measurements of distal-airways

Conclusion

Small-airways dysfunction measured using ¹²⁹Xe MRI VDP and oscillometry significantly improved following a 6-week course of FF/UMEC/VI; multivariable model explaining VDP response included markers of type-2 inflammation

References

1. Lee et al. Lancet Respir Med (2021).
2. Kirby et al. AcadRadiol (2012).
3. DuBois et al. J Apply Physiol (1956).
4. Svenningsen et al. Thorax (2014).
5. McIntosh & Kooner et al. Chest (2022).

Acknowledgments

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