Cardiovascular Consequences of Positive Pressure Ventilation during Severe Hemorrhage

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Project Motivation: PCLC Ventilation

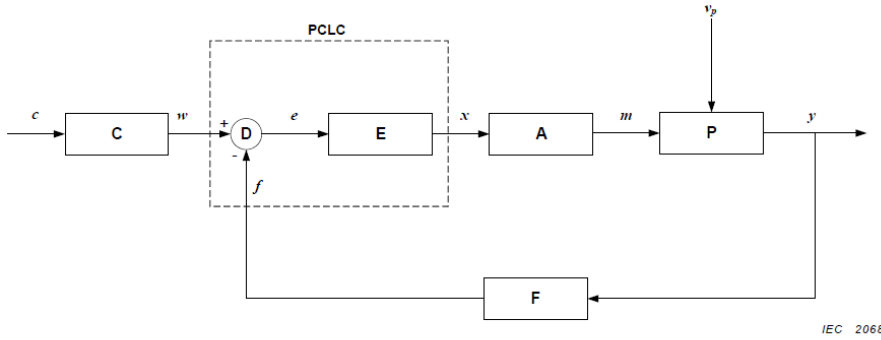
Noninferiority Study: FIO_2 PCLC vs. Manual Control
- Prospective, parallel trial design
- N = 210 randomized; N = 195 completed the study
- Study duration: 12 hours

Endpoints:

- *Effectiveness:* PCLC is *not inferior* compared to manual control
  - Relative duration 92% ≤ SpO_2 ≤ 96% or SpO_2 ≥ 92% when FIO_2 = 21%
    - 0.63 (0.11) (PCLC) vs. 0.54 (0.12) (Manual)

- *Safety:* Proportion of Patient with SpO_2 ≤ 88% for any duration
  - 30% (PCLC) vs. 48% (Manual)
  - Risk Difference: -18% (-31%,-5%) (95% CI)

- The study identified no additional risks for FIO_2 PCLC
  - No Serious Adverse Events in PCLC group



Elements		Variables	
PCLC	PHYSIOLOGIC CLOSED-LOOP CONTROLLER		
A	ACTUATOR	m	MANIPULATED VARIABLE
C	COMMAND TRANSFER ELEMENT	w	REFERENCE VARIABLE
D	COMPARING ELEMENT	e	ERROR VARIABLE
E	CONTROL TRANSFER ELEMENT	x	CONTROLLER OUTPUT VARIABLE
F	MEASURING TRANSFER ELEMENT	f	FEEDBACK VARIABLE
P	PATIENT TRANSFER ELEMENT	y	CONTROLLED PHYSIOLOGIC VARIABLE
		v_p	PATIENT DISTURBANCE VARIABLE
		c	COMMAND VARIABLE

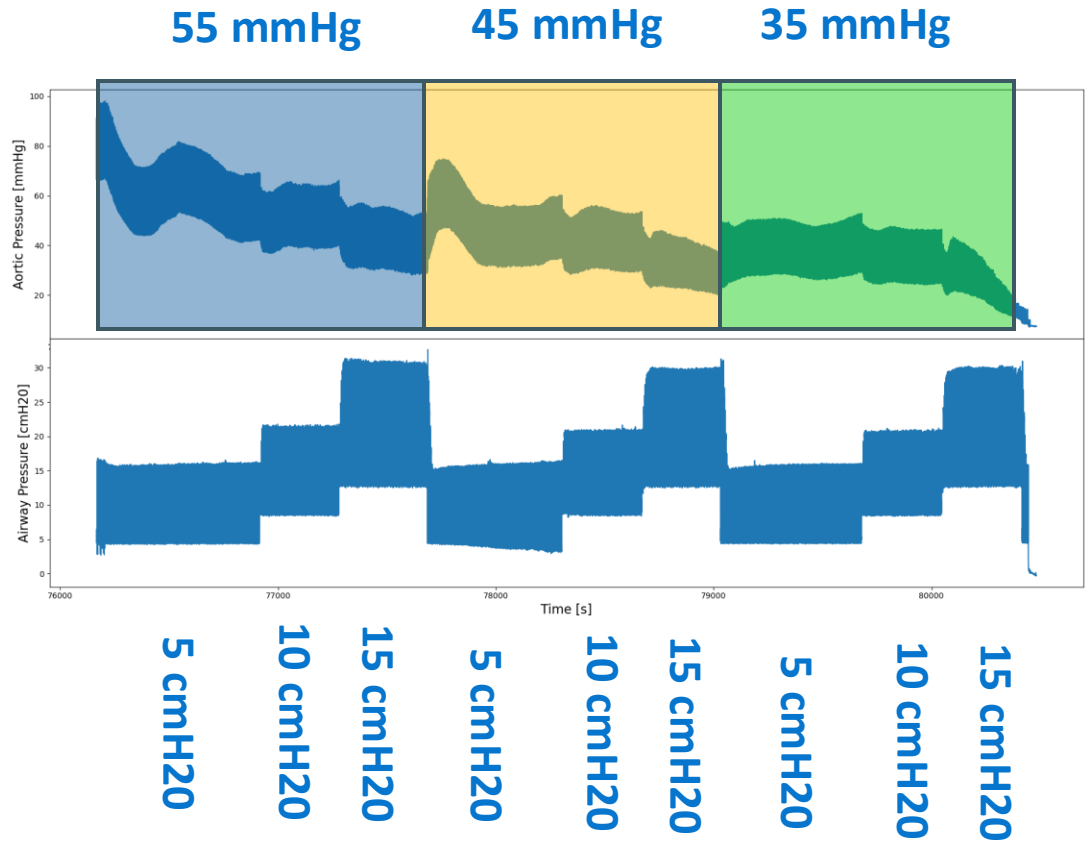
From IEC 60601-1-10 2020

Animal Protocol

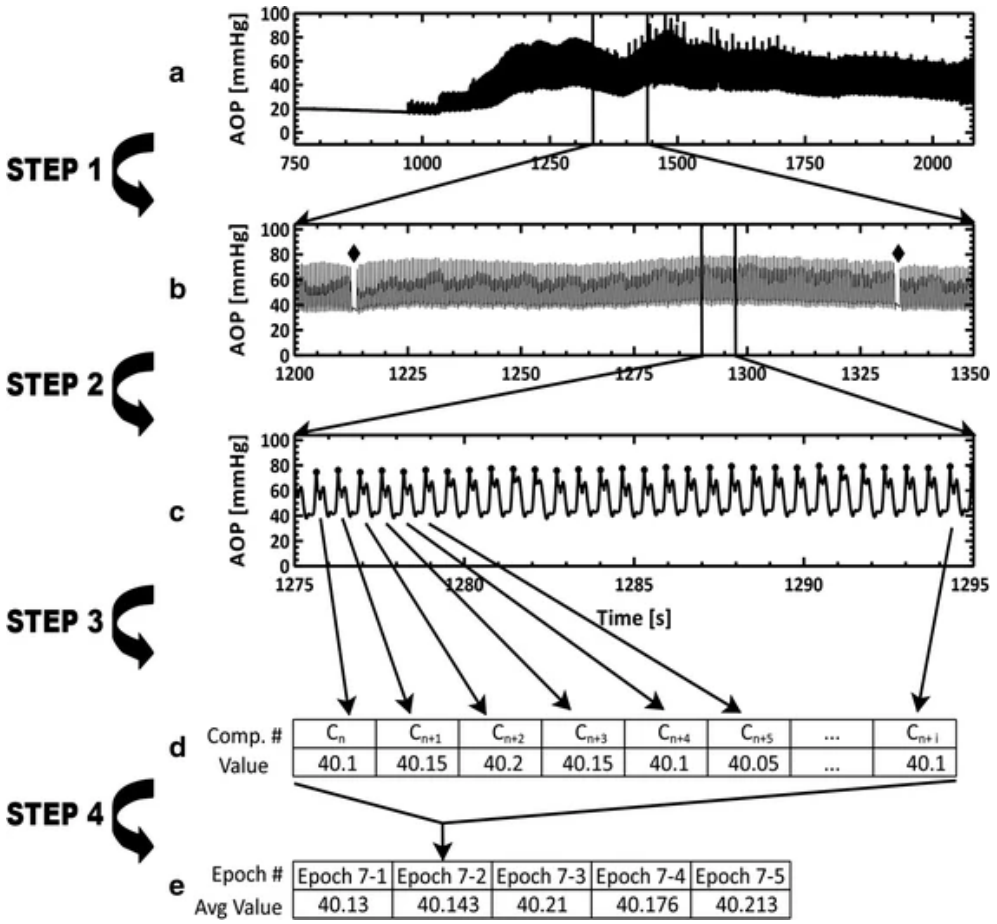
4 female swine (~30 kg)

Surgical Prep

- CRI Ketamine/Midazolam
- Invasive Blood Pressures
- Invasive Blood Flows
- Hans Rudolph
- Bleed managed manually

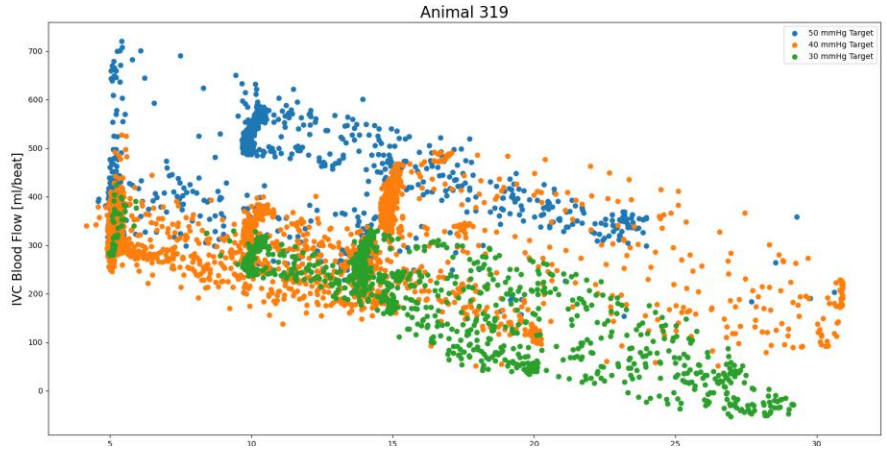


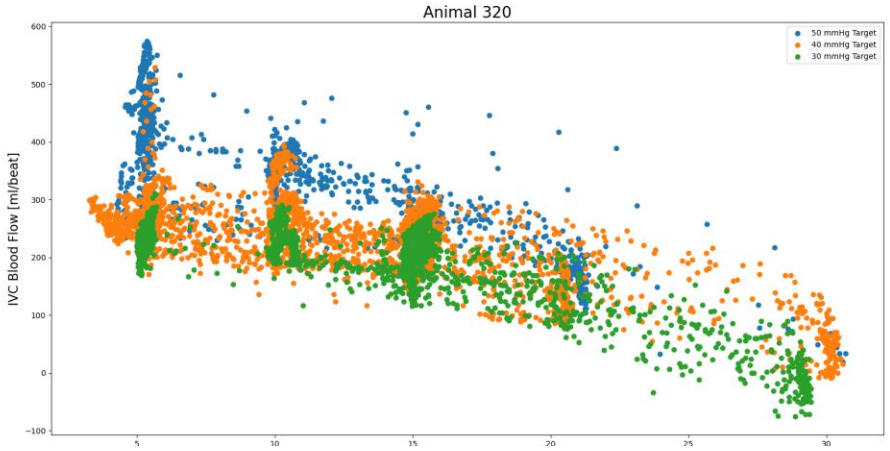
Data Analysis

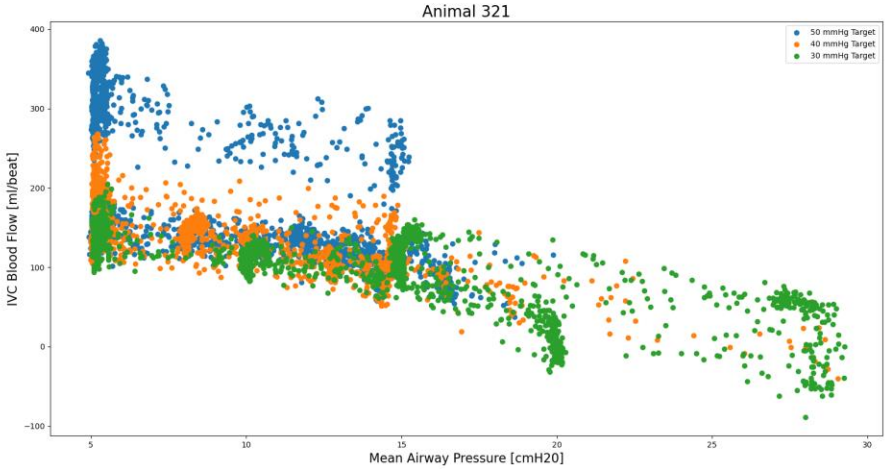


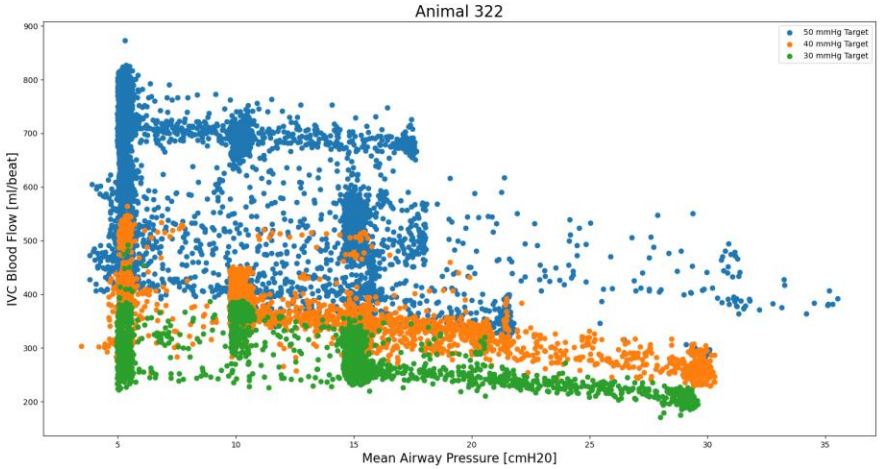
- Physiological parameters were calculated on a per compression basis using python scripts
- Statistics were calculated using Stata IC 15

IVC Blood Flows







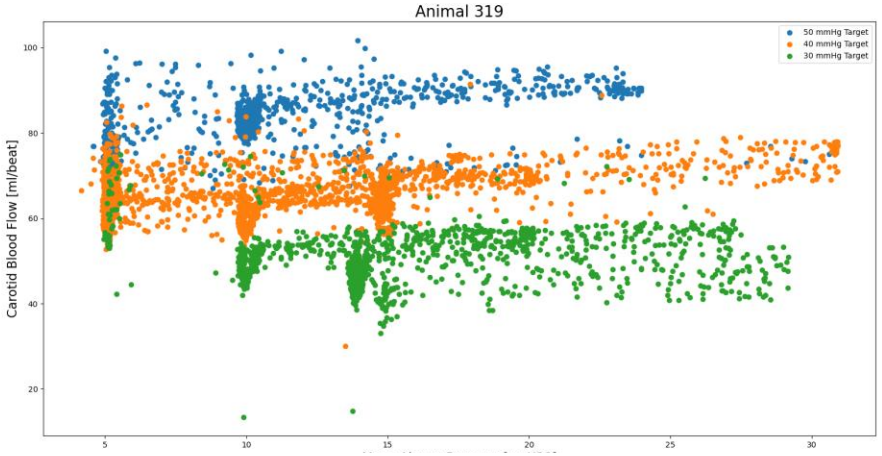


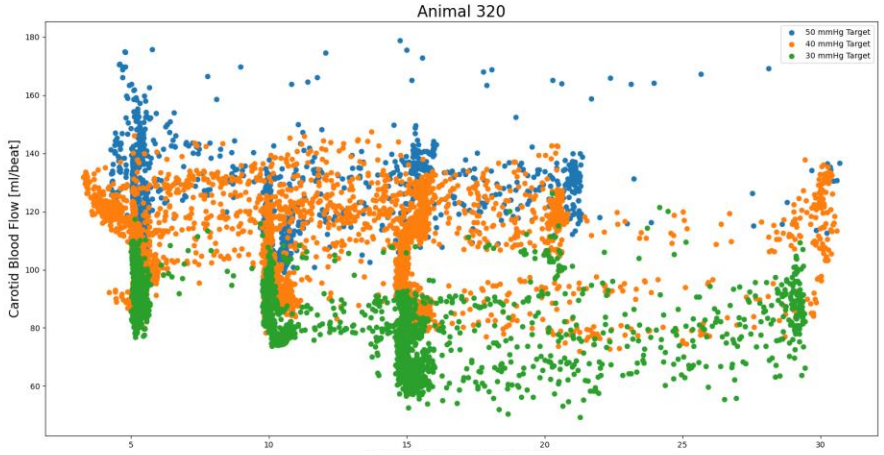
55 mmHg target

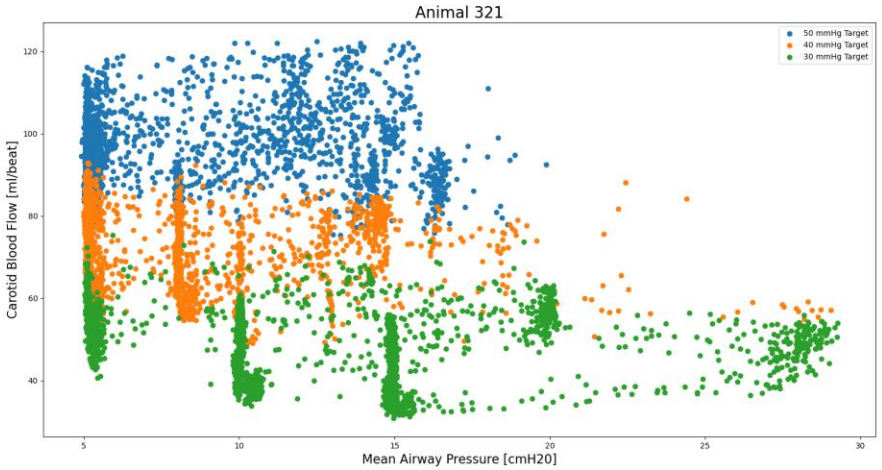
45 mmHg target

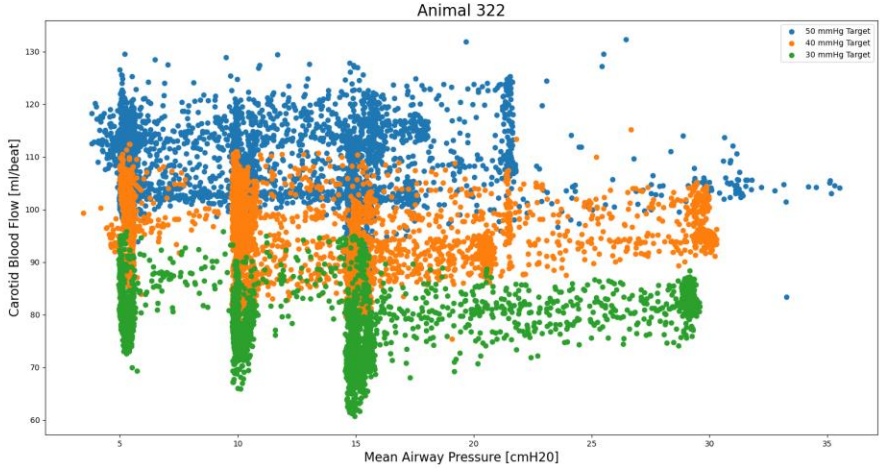
35 mmHg target

Carotid Blood Flows









55 mmHg target

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Linear Regression

$$Flow_x = P_{Airway} + P_{Aorta} + Animal$$

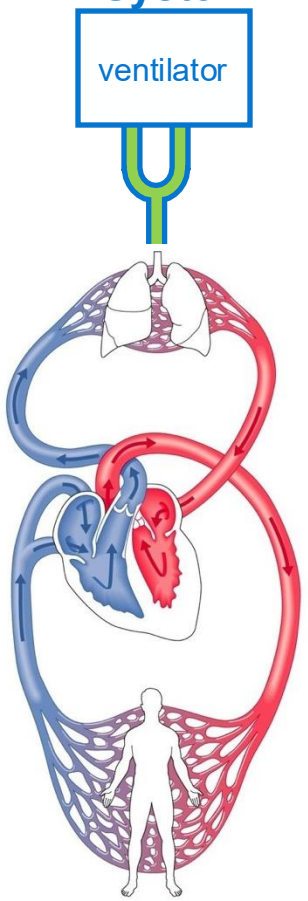
Carotid Flow	Coef	Std Err	95% CI	P
Mean Airway Pressure	0.068	.01	(0.040 , 0.09)	<0.05
Mean Aortic Pressure	1.78	.006	(1.77, 1.79)	<0.05
Animal	1.99	.07	(1.8, 2.1)	<0.05
const	8.4	.4	(7.6, 9.2)	<0.05

IVC Flow	Coef	Std Err	95% CI	P
Mean Airway Pressure	-5.1	0.1	(-5.27, -4.8)	<0.05
Mean Aortic Pressure	13.2	0.05	(13.1, 13.3)	<0.05
Animal	39.9	0.6	(38, 41)	<0.05
const	-270	3.2	(7.6, 9.2)	<0.05

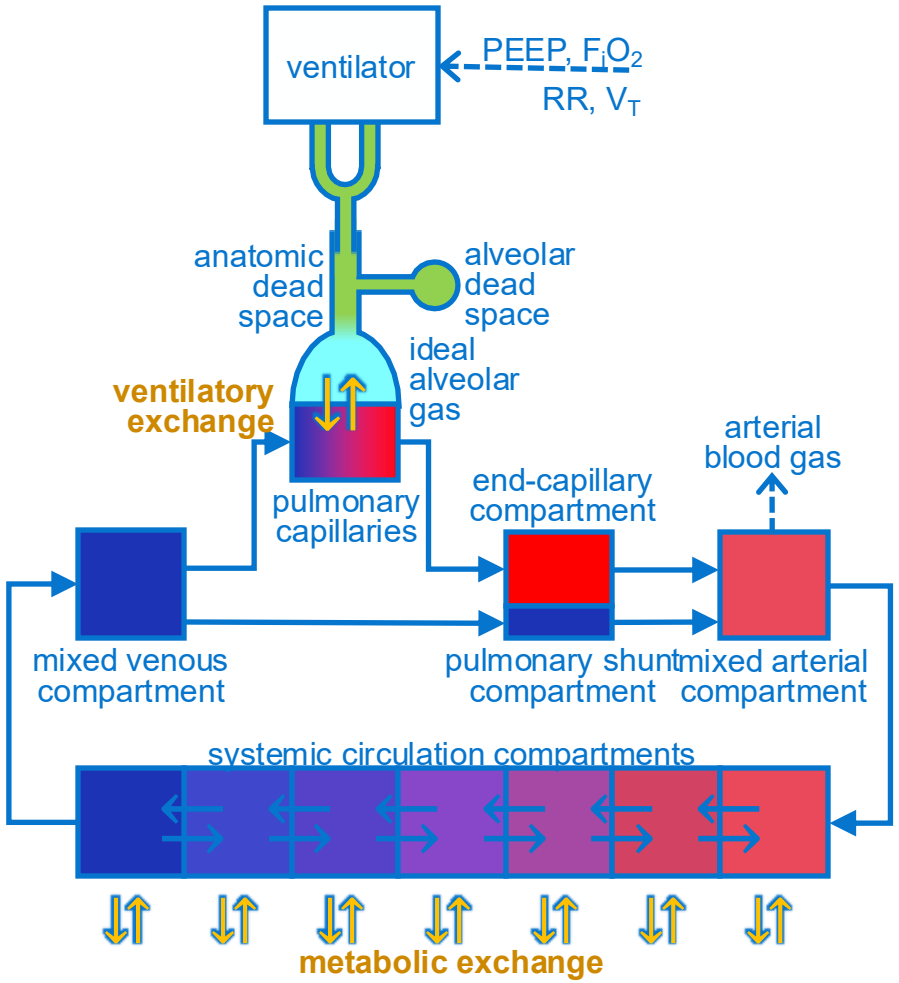
Changes in Airway Pressure impact venous return but not blood supply to the brain

Cardiopulmonary Model

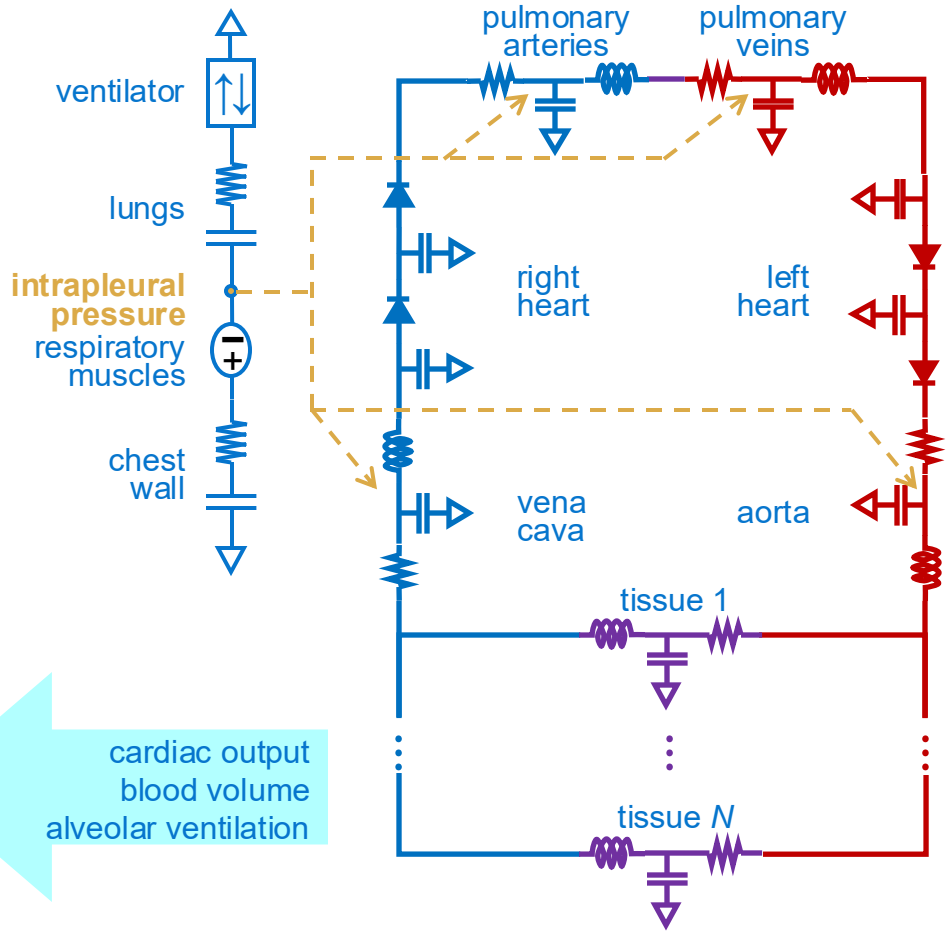
A. Patient-Ventilator System



B. Gas Exchange Model



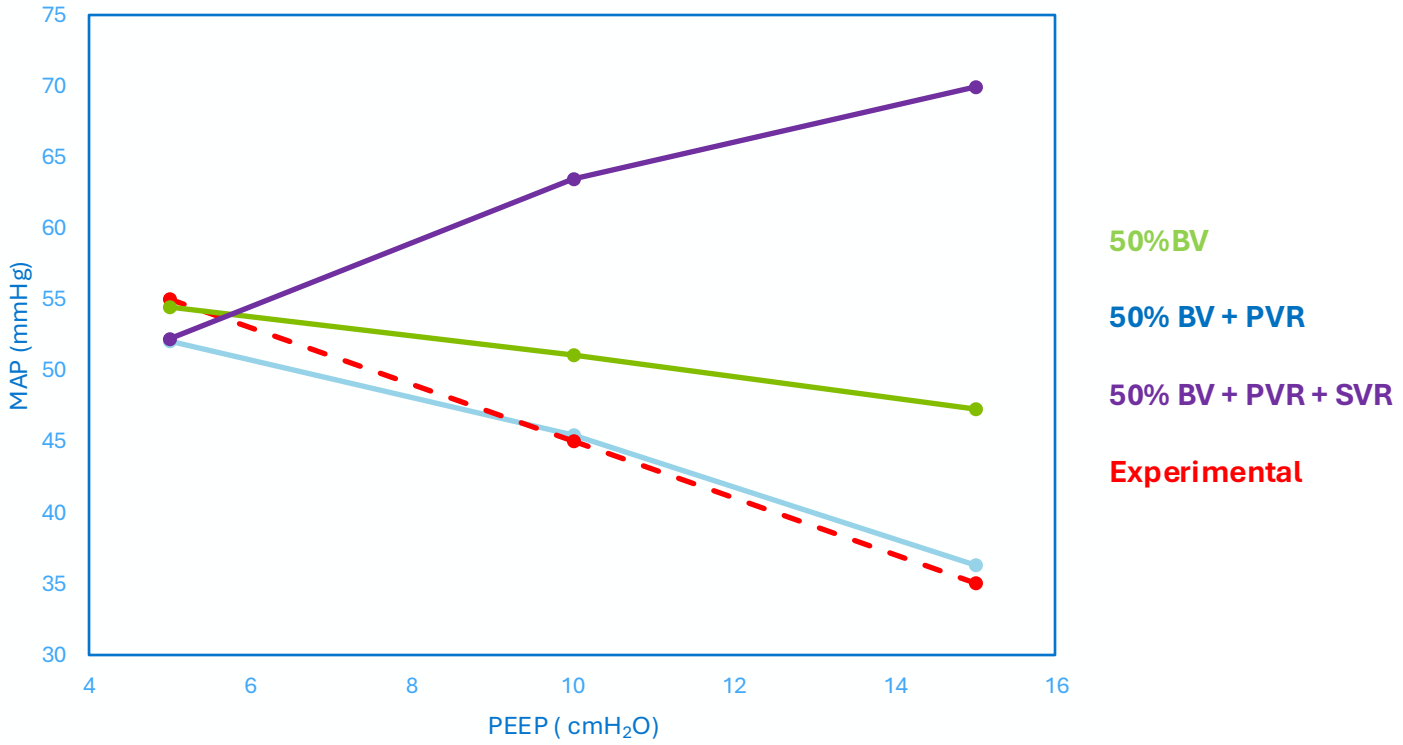
C. Pneumatic & Hydraulic Circuit Models (electrical analogy)



Mihiret Redhi, Jacob Herrmann, David Kaczka Ulowa

Exploring Ventilation during Hemorrhage using modeling

- Animals were bled to a MAP of 55 mmHg and provided mechanical ventilation at PEEP values of 5, 10, or 15 cmH_2O
- Simulations included
  - 50% blood loss
  - 50% blood loss and increased pulmonary vascular resistance
  - 50% blood loss and increased pulmonary and systemic vascular resistance



Remaining Questions

- Validating the observation from the computational model that PEEP changes required changes in pulmonary vascular resistance to replicate our experimental results
- Understanding how to detect and navigate the differential hemodynamic changes caused by PPV
- How do these observations relate to patient outcomes

Thank you

QUESTIONS?