

Role of spontaneous breathing during mechanical ventilation in ARDS – Pro

Korea University Guro Hospital

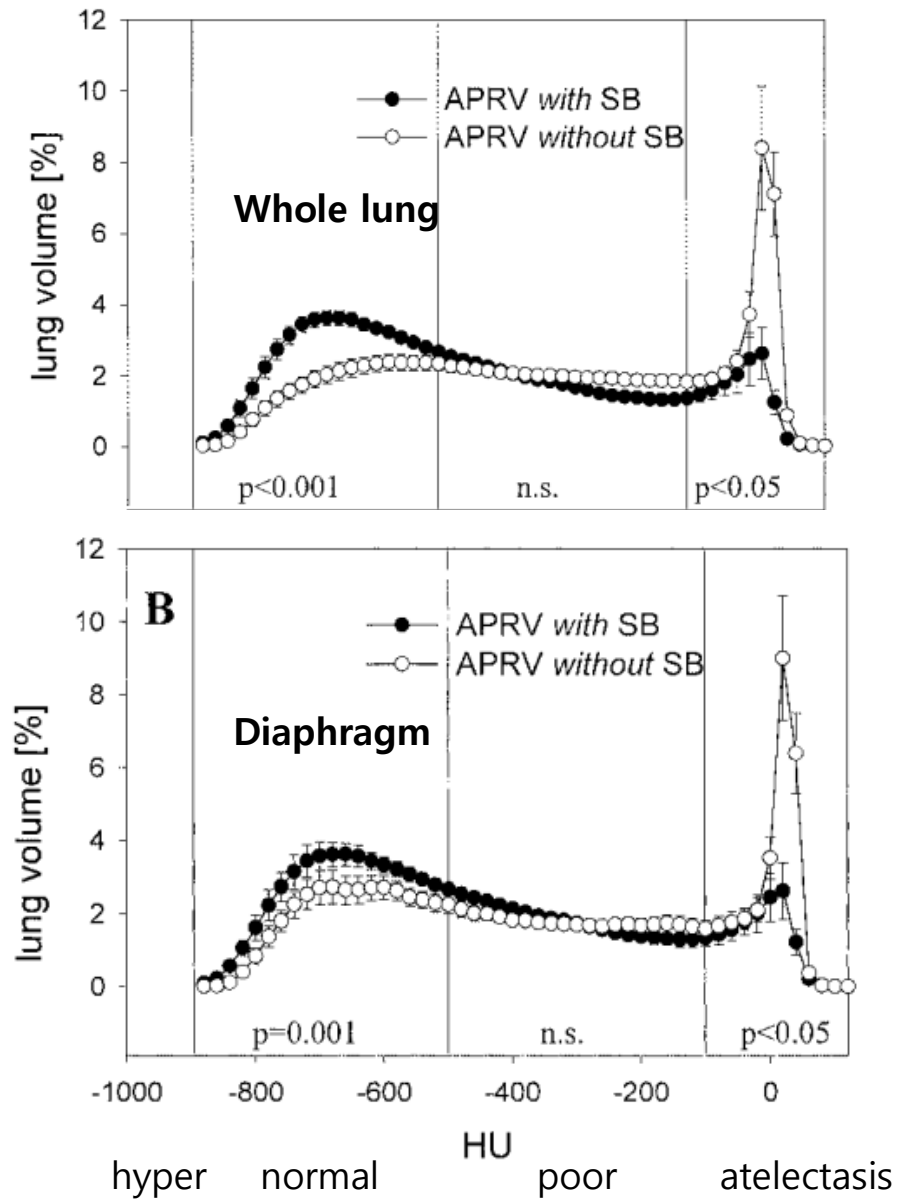
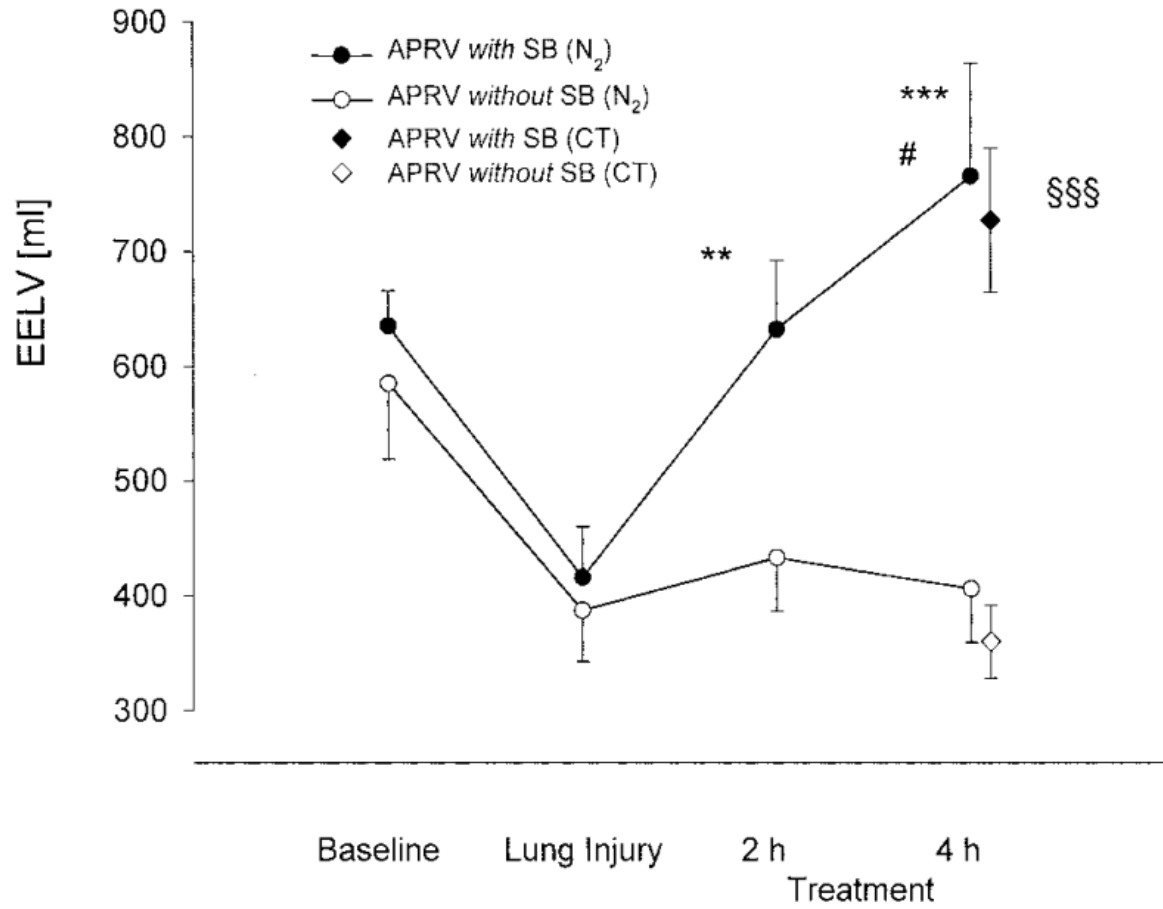
Jae Kyeom Sim

Physiological evidence

Spontaneous Breathing Improves Lung Aeration in Oleic Acid-induced Lung Injury

Hermann Wrigge, M.D.,* Jörg Zinserling, M.Sc.† Peter Neumann, M.D., Ph.D.,‡ Jerome Defosse,§
Anders Magnusson, M.D., Ph.D.,|| Christian Putensen, M.D., Ph.D.,# Göran Hedenstierna, M.D., Ph.D.**

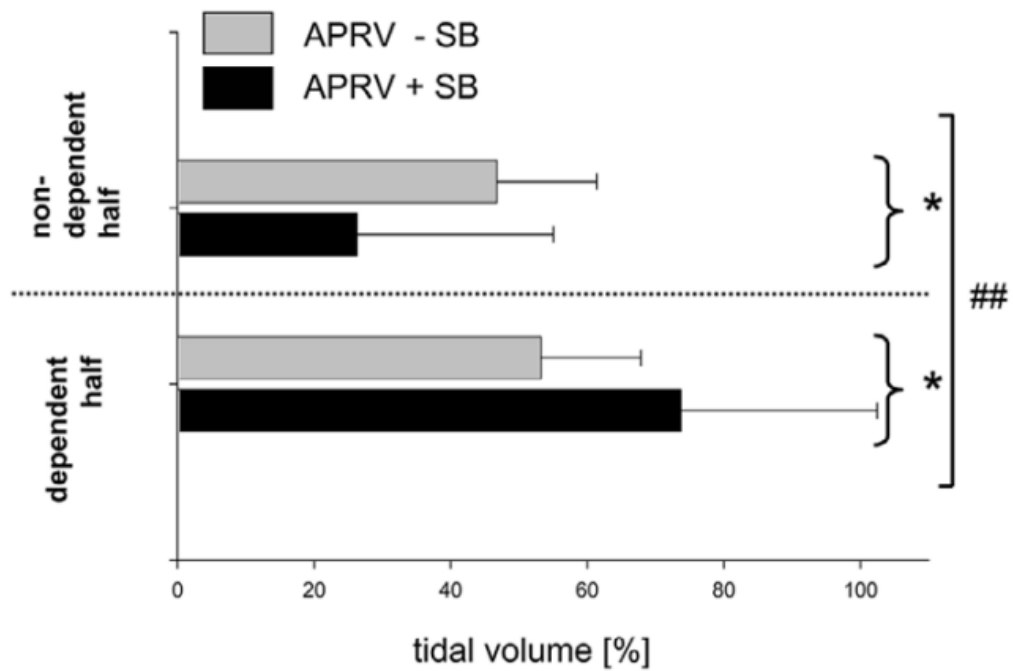
- Subject: Pig
- Model: Oleic-acid induced lung injury
- Spontaneous breathing (SB): Airway pressure released ventilation (APRV) without NMB
- Passive ventilation: APRV with NMB (= PCV)
- APRV setting: PEEP 5 cmH₂O, I:E ratio 1:1, TV 10 mL/kg, FiO₂ 0.5
- End-expiratory lung volume (EELV) measurement by nitrogen washout and CT
- Aeration assess by CT (HU): hyperinflation – normal aeration – poor aeration - atelectasis
- P/F ratio after lung injury ≈ 200



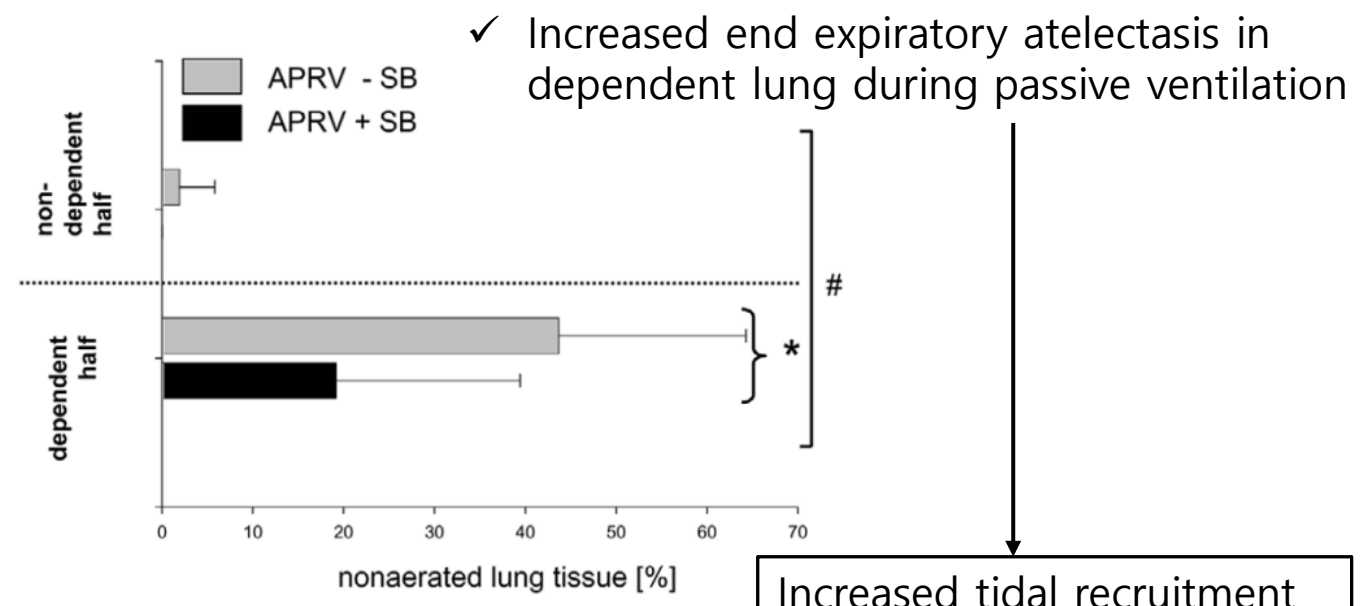
Spontaneous breathing with airway pressure release ventilation favors ventilation in dependent lung regions and counters cyclic alveolar collapse in oleic-acid-induced lung injury: a randomized controlled computed tomography trial

Hermann Wrigge¹, Jörg Zinserling², Peter Neumann³, Thomas Muders⁴, Anders Magnusson⁵, Christian Putensen⁶ and Göran Hedenstierna⁷

- Subject: Pig
- Model: Oleic-acid induced lung injury
- Spontaneous breathing (SB): Airway pressure released ventilation (APRV) without NMB
- Passive ventilation: APRV with NMB
- APRV setting: PEEP 5 cmH₂O, I:E ratio 1:1, TV 10 mL/kg, FiO₂ 0.5
- Dynamic CT scan: regional distribution, atelectasis, reaeration at diaphragm level
- P/F ratio after lung injury ≈ 200

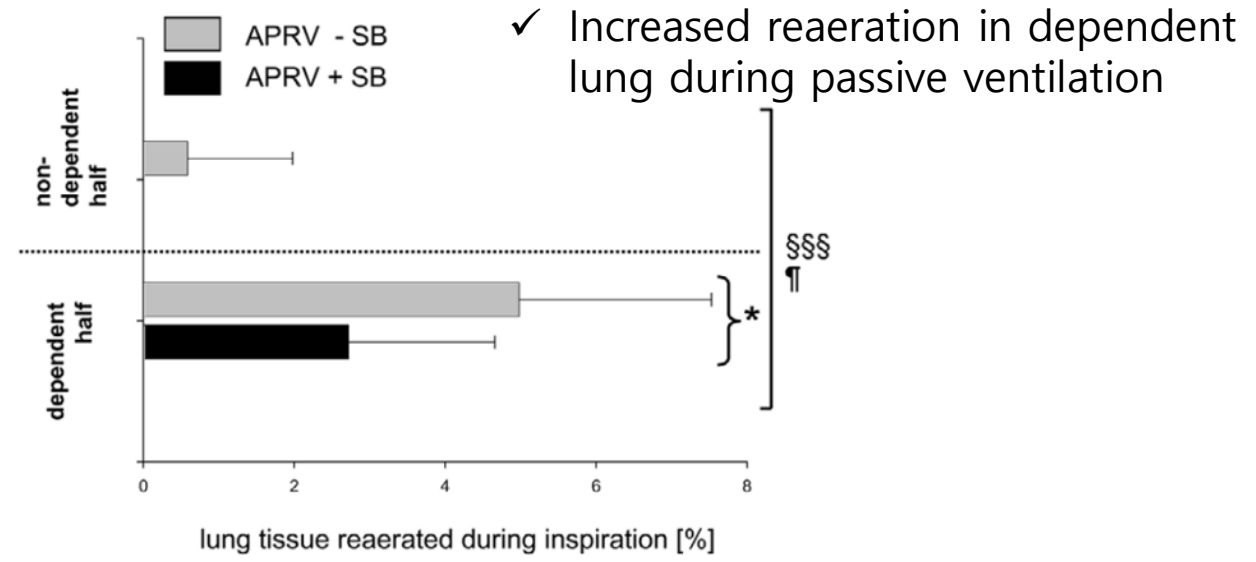


✓ Increased regional distribution in dependent lung during SB



✓ Increased end expiratory atelectasis in dependent lung during passive ventilation

Increased tidal recruitment during passive ventilation



✓ Increased re-aeration in dependent lung during passive ventilation

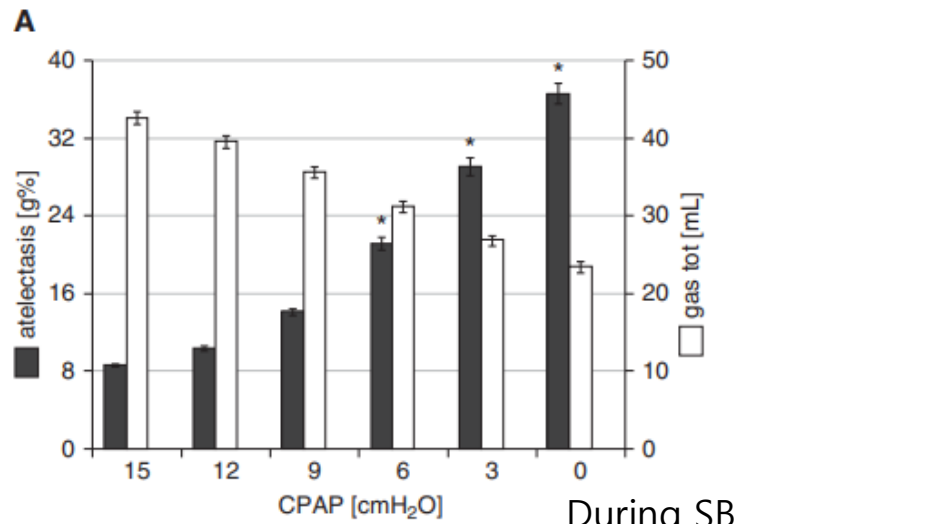
The Diaphragm Acts as a Brake during Expiration to Prevent Lung Collapse

Mariangela Pellegrini^{1,2}, Göran Hedenstierna³, Agneta Roneus¹, Monica Segelsjö⁴, Anders Larsson¹, and Gaetano Perchiazzi^{1,2}

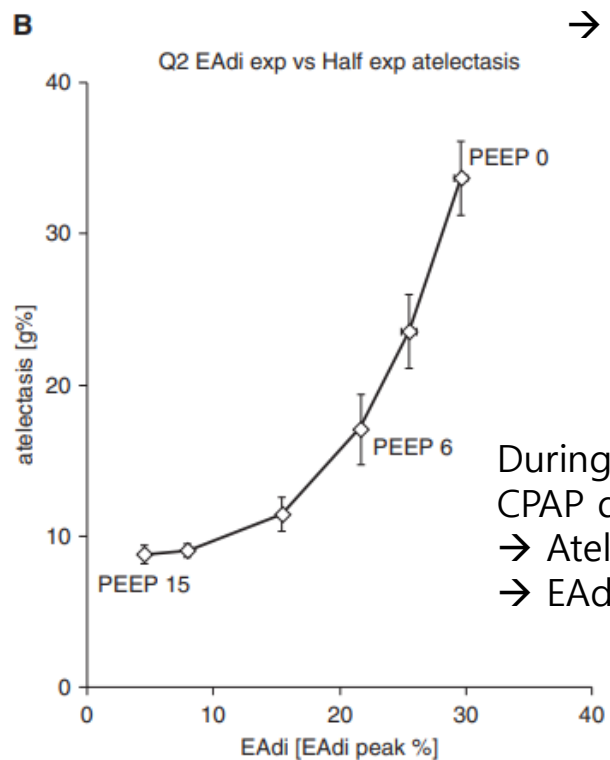
- Subject: Pig
- Model: Lung lavage induced lung injury
- Spontaneous breathing (SB): CPAP 0~15 cmH₂O
- Passive ventilation: Controlled mechanical ventilation with NMB (PEEP 0~15 cmH₂O)

- Atelectasis assess by CT
- Diaphragmatic electric activity (EAdi) & Transdiaphragmatic pressure (Pdi)

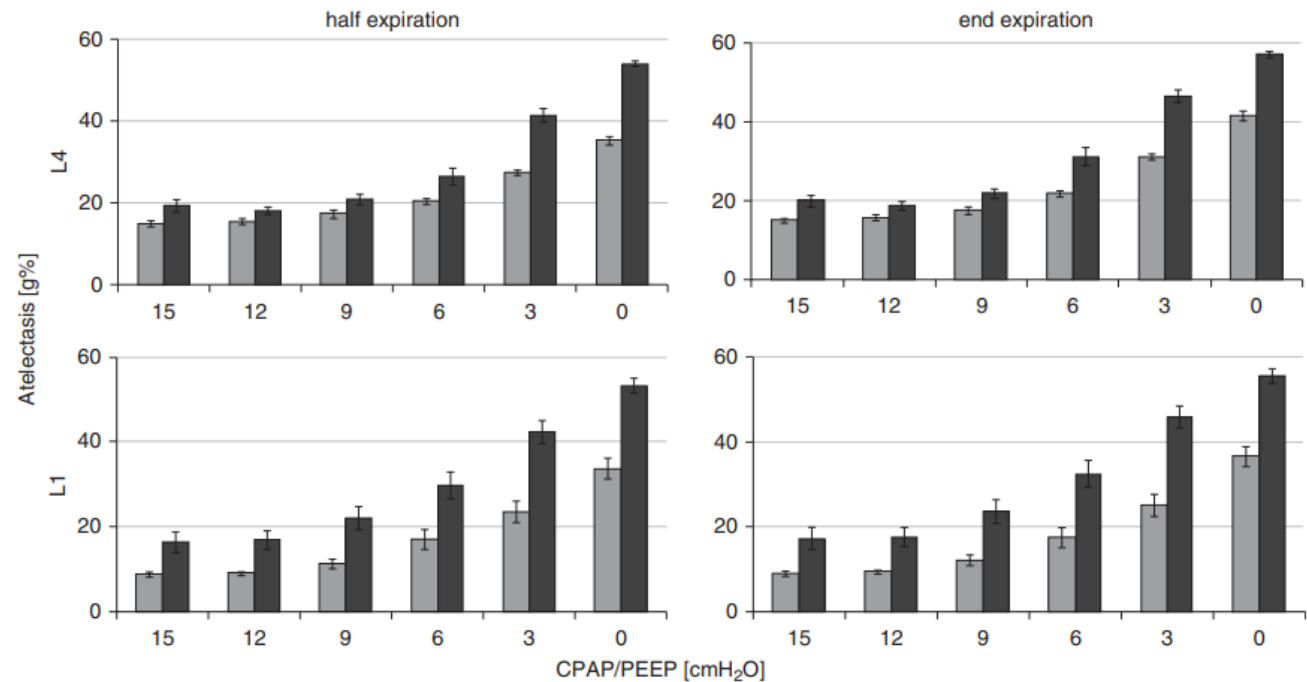
- P/F ratio after lung injury = 223



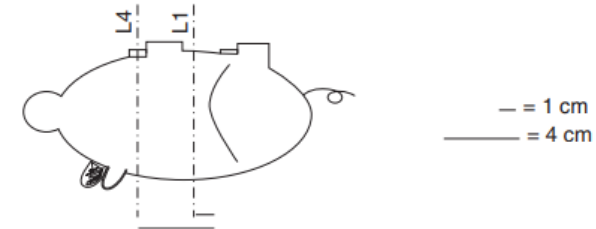
During SB
CPAP decrease
→ Atelectasis increase



During SB
CPAP decrease
→ Atelectasis increase
→ EAdi increase



SB
MV



- ✓ During MV, atelectasis is not different between half- and end-expiration, and is not different between L4 and L1 (diaphragm)
- ✓ During SB, atelectasis is lower in L1 (diaphragm)
- ✓ Diaphragm prevents early and dependent lung atelectasis

Higher Levels of Spontaneous Breathing Induce Lung Recruitment and Reduce Global Stress/Strain in Experimental Lung Injury

Andreas Güldner, M.D., Anja Braune, M.Sc., Nadja Carvalho, Ph.D., Alessandro Beda, Ph.D., Stefan Zeidler, M.S., Bärbel Wiedemann, Ph.D., Gerd Wunderlich, Ph.D., Michael Andreeff, Ph.D., Christopher Uhlig, M.D., Peter M. Spieth, M.D., Thea Koch, M.D., Ph.D., Paolo Pelosi, M.D., Jörg Kotzerke, M.D., Ph.D., Marcelo Gama de Abreu, M.D., M.Sc., Ph.D., D.E.S.A.

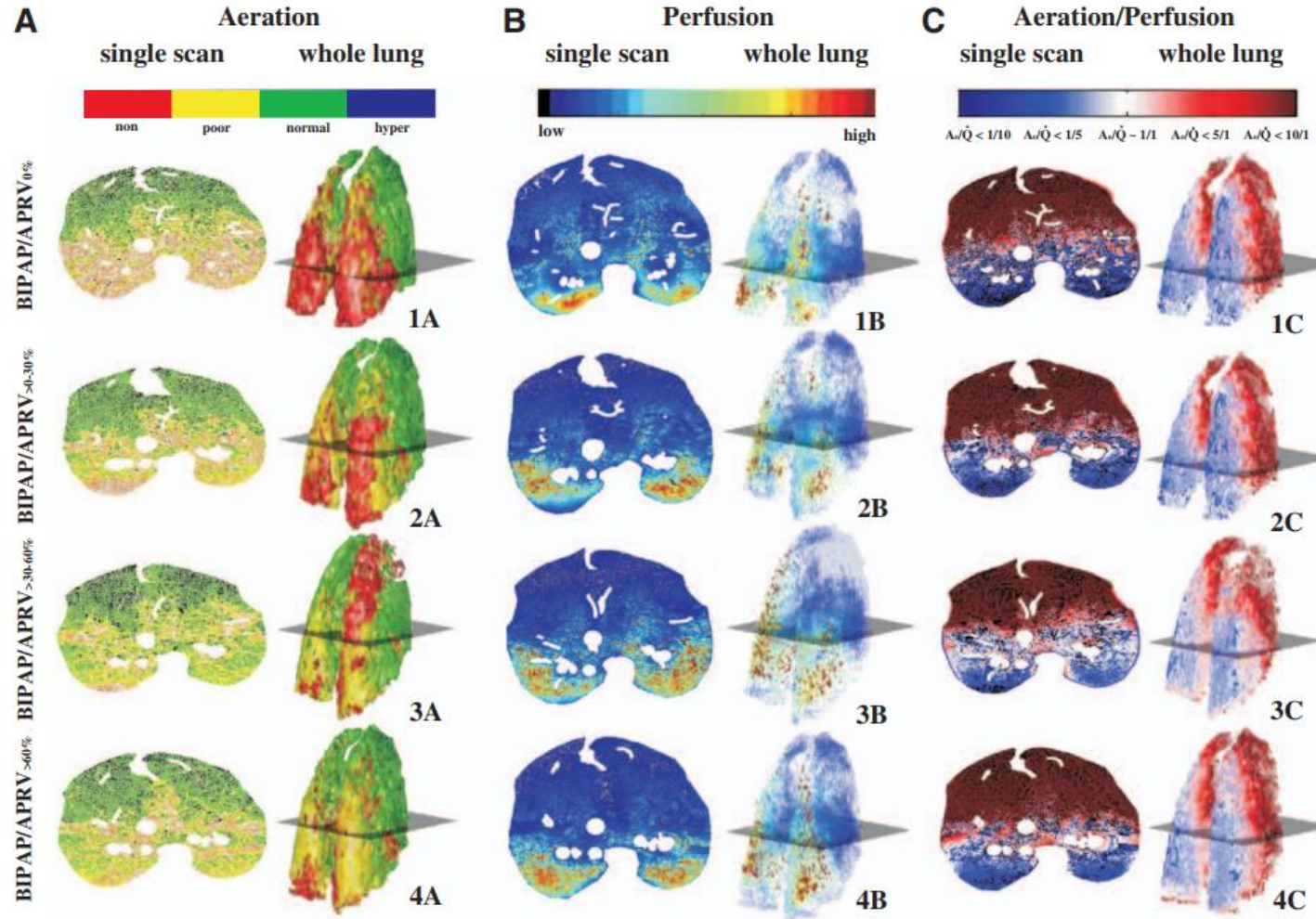
- Subject: Pig
- Model: Lung lavage induced lung injury
- APRV mode with different levels of contribution of SB to minute ventilation
- - PEEP 10 cmH₂O, I:E ratio 1:1, TV 6 mL/kg, FiO₂ 0.5
- - SB 0% vs SB 0~30% vs SB 30~60% vs SB > 60%

- Ventilation assess by CT
- Perfusion assess by ⁶⁸Ga-labeled tracer and PET scanning

- P/F ratio after lung injury = 72 ~ 155

Table 2. Gas Exchange and Hemodynamic Variables

	BL	IN	BL2	BIPAP/ APRV _{0%}	BIPAP/ APRV _{>0-30%}	BIPAP/ APRV _{>30-60%}	BIPAP/ APRV _{>60%}
Pao ₂ /Fio ₂	523.4 ± 41.8	72.5 ± 20.2	155.2 ± 26.5	278.9 ± 89.9	358.8 ± 94.7	381.7 ± 96.6	388.1 ± 57.7*
MPAP (mmHg)	22.1 ± 3.4	31.1 ± 5.9	34.1 ± 5.8	29.4 ± 5.1	25.3 ± 5.4*	25.2 ± 5.1*	25.7 ± 4.5*



- ✓ Increased dorsal aeration with increased SB
- ✓ Higher dorsal perfusion regardless of SB
- ✓ Increased dorsal V/Q matching with increased SB

Spontaneous Breathing During Ventilatory Support Improves Ventilation–Perfusion Distributions in Patients with Acute Respiratory Distress Syndrome

CHRISTIAN PUTENSEN, NORBERT J. MUTZ, GABRIELE PUTENSEN-HIMMER, and JÖRG ZINSERLING

- Subject: Twenty-four mechanically ventilated patients with ARDS (AECC criteria)
- Diagnosis: Trauma or post-surgery in 22 patients
- PSV vs APRV without SB vs APRV with SB under equal airway pressure (or minute ventilation)
- Oxygenation: FiO_2 0.58(0.59), PaO_2 83(82)mmHg \therefore PF ratio \approx 143(139)

Cardiac index and RV ejection fraction were higher in PSV than in APRV w/o SB (PCV)

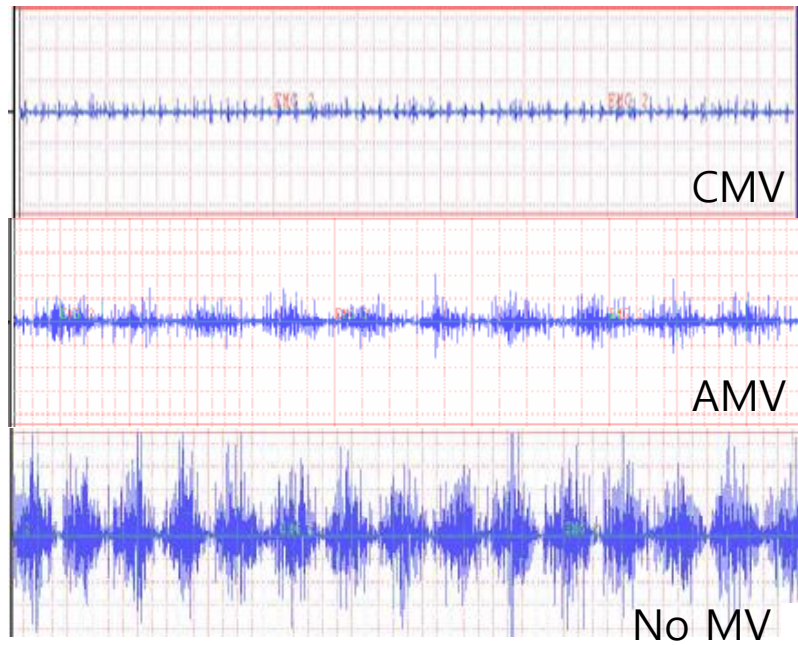
	Baseline [†]	PSV [†]	APRV [†] without Spontaneous Breathing	APRV [†] with Spontaneous Breathing
CI, L · min ⁻¹ · m ⁻²	5.1 ± 0.2	5.3 ± 0.2	5.0 ± 0.2 [§]	5.6 ± 0.2 [§]
SVR, dyn · s · cm ⁻⁵	550 ± 25	550 ± 25	565 ± 31	521 ± 24
PVR, dyn · s · cm ⁻⁵	126 ± 12	115 ± 15	130 ± 19	95 ± 17 [§]
RVEF, %	33 ± 2	36 ± 1	32 ± 2 [§]	41 ± 2 [§]
RVEDVI, ml · m ⁻²	122 ± 3	128 ± 4	123 ± 5 [§]	136 ± 4 [§]
RVESVI, ml · m ⁻²	86 ± 7	82 ± 2	87 ± 3	82 ± 2

Assist–Control Mechanical Ventilation Attenuates Ventilator-induced Diaphragmatic Dysfunction

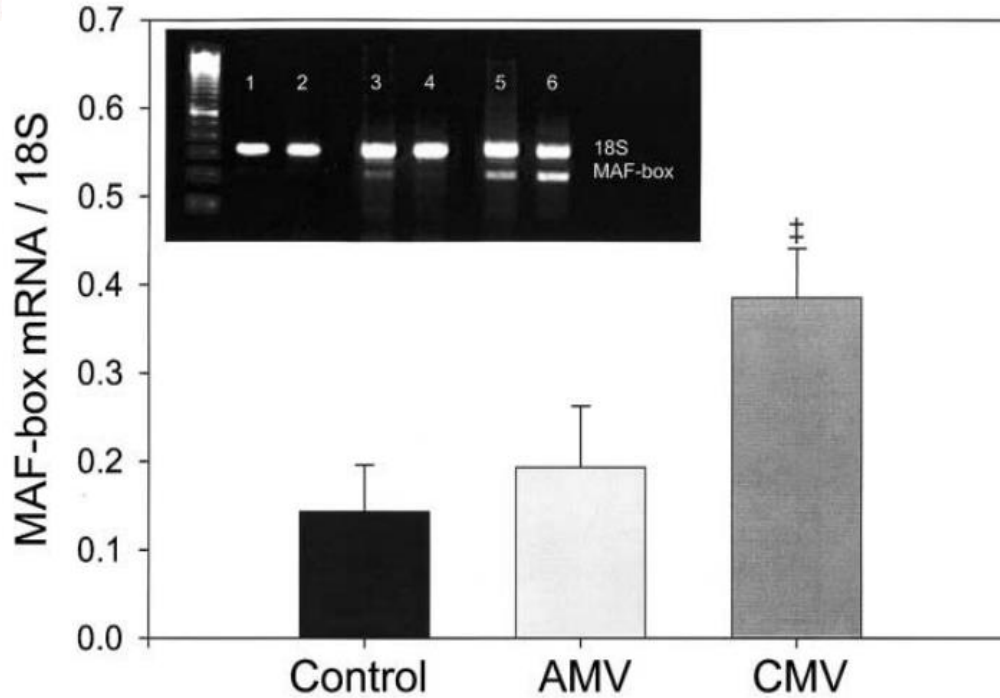
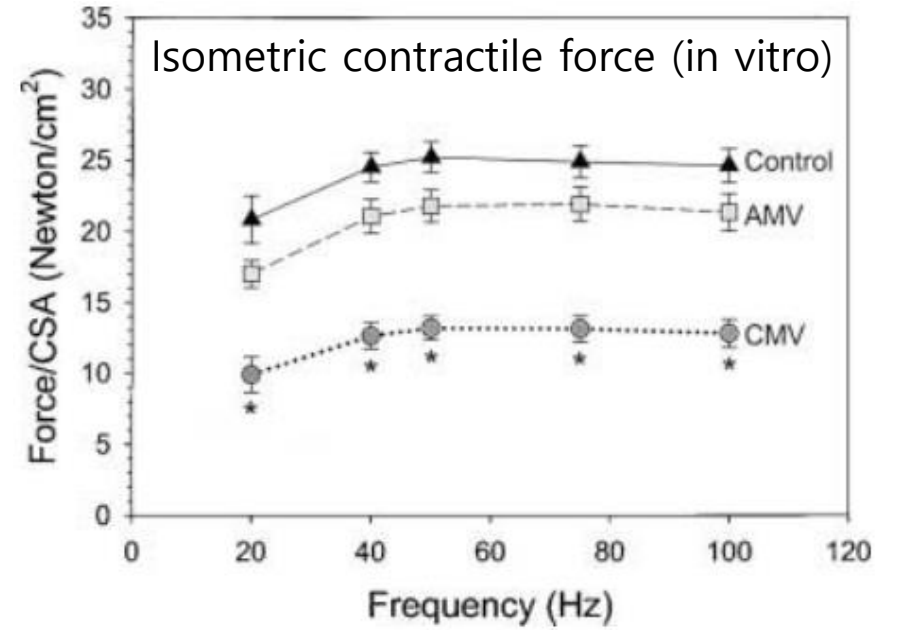
Catherine S. H. Sassoon, Ercheng Zhu, and Vincent J. Caiozzo

- Subject: Rabbit
- 6 rabbits on assisted mechanical ventilation (AMV) for 3 days (flow triggered)
- 6 rabbits on controlled mechanical ventilation (CMV) for 3 days (time triggered)
- 6 rabbits (control group)

- Assessment of diaphragm electrical activity: electrode insertion during ventilation
- Measurement of diaphragm contractile property: excised diaphragm muscle
- Molecular analysis for muscle atrophy factor-box (MAF-box)



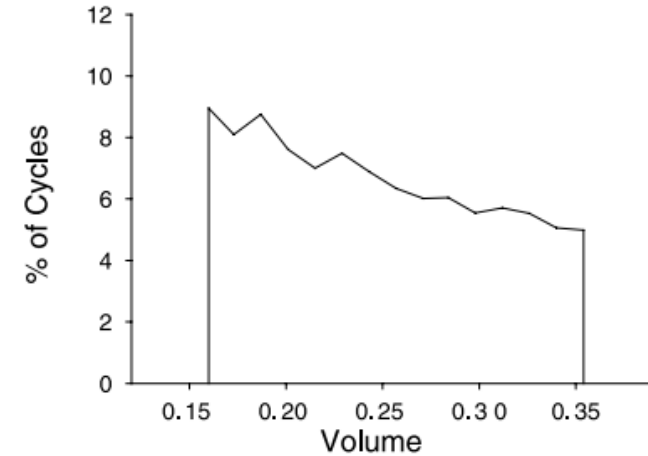
Electrical activity (in vivo)

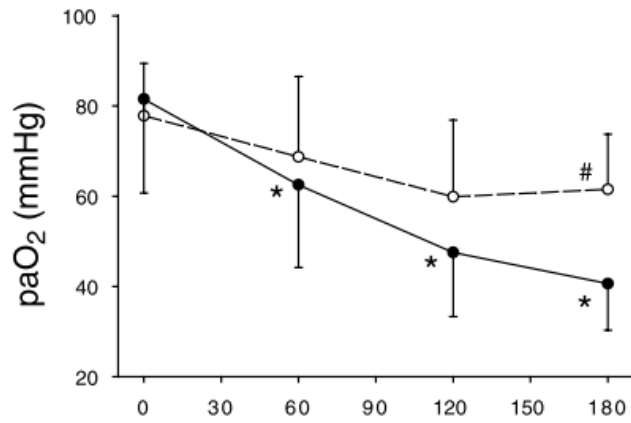
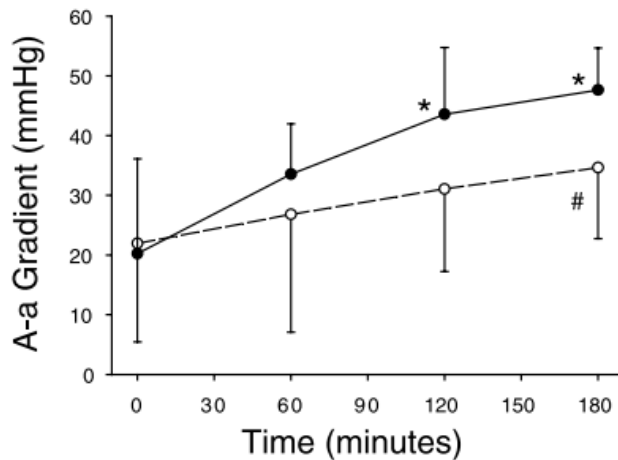


Variable ventilation induces endogenous surfactant release in normal guinea pigs

Stephen P. Arold,¹ Béla Suki,¹ Adriano M. Alencar,¹
Kenneth R. Lutchen,¹ and Edward P. Ingenito²

- Subject: Guinea pigs
 - Constant-volume ventilation (CVV): TV 5 mL/kg, RR 60/min
 - Variable ventilation (VV): mean TV 5 mL/kg, mean RR 60/min
 - Unventilated (Unvent)
-
- Whole lung lavage after 3 hours: Surfactant, Protein, Cytokine



B**D**

● CVV

○ VV

* Within group difference

Between group difference

Table 1. *BAL protein and PL content*

	<i>n</i>	PL Content	Protein Content
Unvent	5	98 ± 19	10.0 ± 3.4
CVV	6	84 ± 29	17.2 ± 3.9*
VV	5	160 ± 28†	12.0 ± 1.6

Table 2. *Surfactant PL comparison*

	PS, %	PE, %	SM, %	PC, %	PG, %
Unvent	5.7 ± 1.8	3.4 ± 0.9	1.0 ± 0.1	66.5 ± 2.6	15.1 ± 0.5
CVV	10.6 ± 1.6	9.4 ± 1.7*	3.5 ± 1.0*	56.9 ± 6.5	9.3 ± 3.7*
VV	7.9 ± 2.1	5.0 ± 1.6†	1.7 ± 0.2†	62.1 ± 7.5	16.9 ± 2.2†

Surfactant associated PL

- ✓ Increased protein content in CVV (vs Unvent)
- ✓ Increased phospholipid content in VV (vs CVV)
- ✓ Higher proportion of surfactant associated phospholipid in VV (vs CVV)

Table 3. *BAL cytokine concentrations*

	TNF-α	IL-6	MCP-1
Unvent	15 ± 1	50 ± 1	15 ± 5
CVV	160 ± 15*	1,400 ± 300*	90 ± 20*
VV	82 ± 10*†	250 ± 75*†	25 ± 10†

- ✓ Increased cytokine after mechanical ventilation
- ✓ Higher cytokine in CVV

Variable Tidal Volumes Improve Lung Protective Ventilation Strategies in Experimental Lung Injury

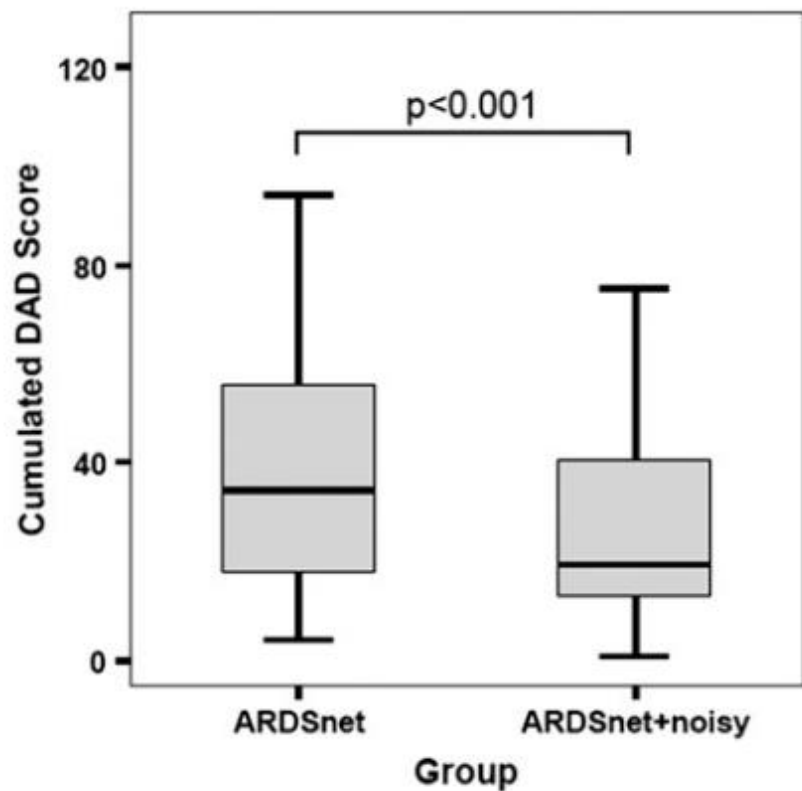
Peter M. Spieth¹, Alysson R. Carvalho¹, Paolo Pelosi², Catharina Hoehn¹, Christoph Meissner¹, Michael Kasper³, Matthias Hübler¹, Matthias von Neindorff¹, Constanze Dassow⁴, Martina Barrenschee⁴, Stefan Uhlig⁴, Thea Koch¹, and Marcelo Gama de Abreu¹

- Subject: Pig
- Model: Lung lavage induced lung injury
- ARDSnet group: PEEP 12 cmH₂O, I:E ratio 1:1, TV 6 mL/kg, FiO₂ 0.7
- ARDSnet + noisy group: breath-to-breath variation of TV (mean 6 mL/kg)

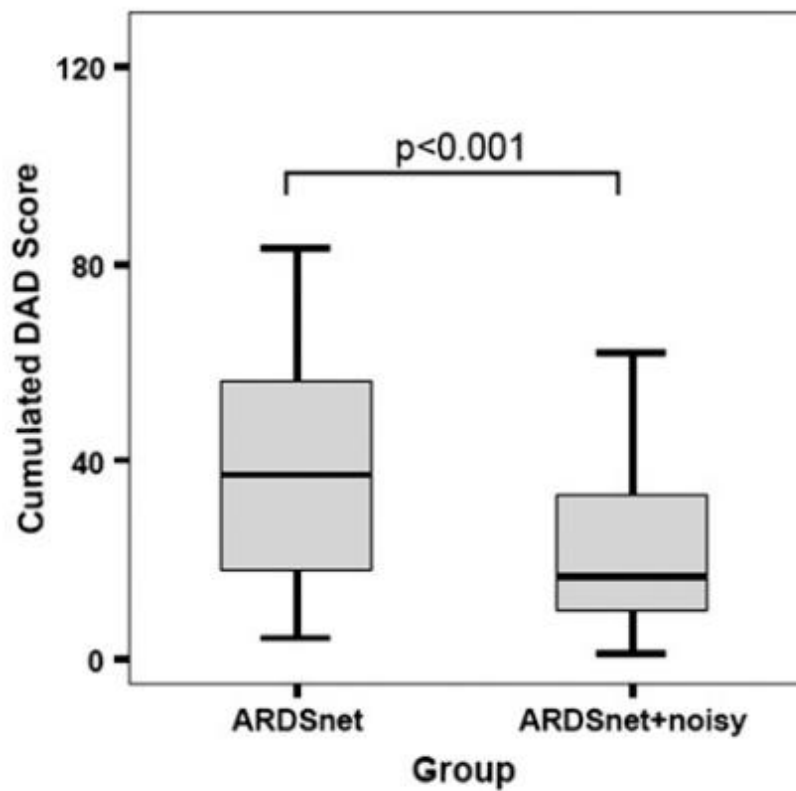
- Diffuse alveolar damage (DAD) was evaluated by blinded expert

- P/F ratio after lung injury < 200

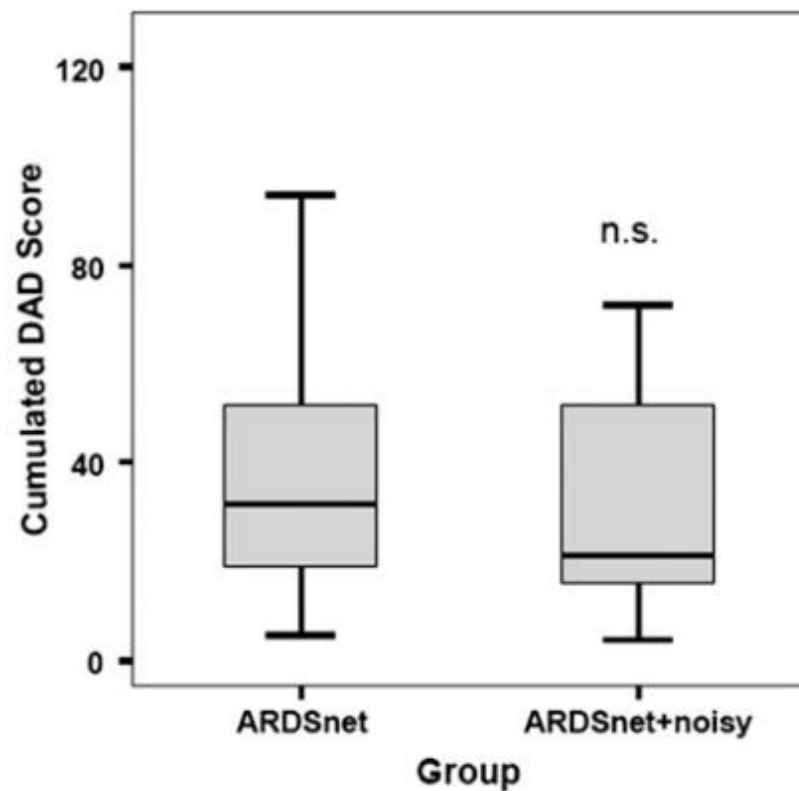
Overall



Dependent



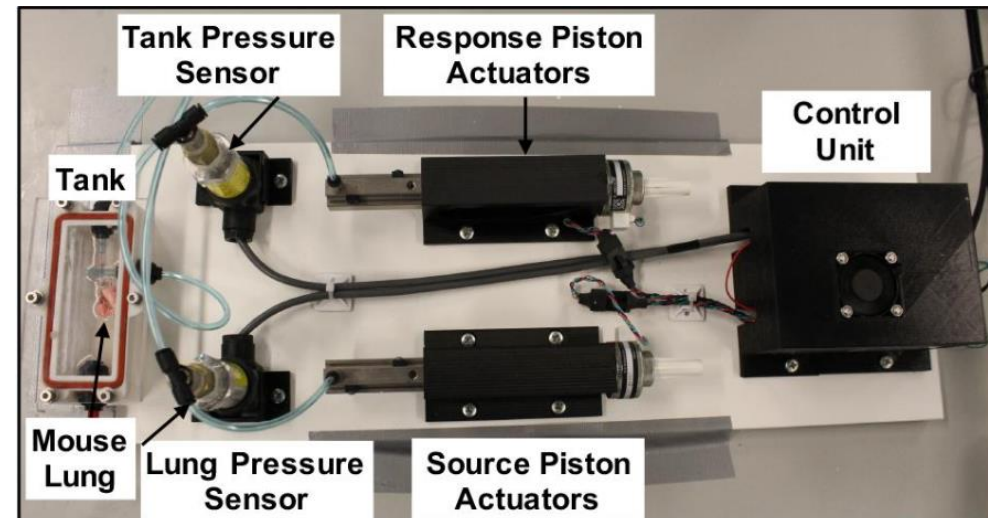
Non-dependent

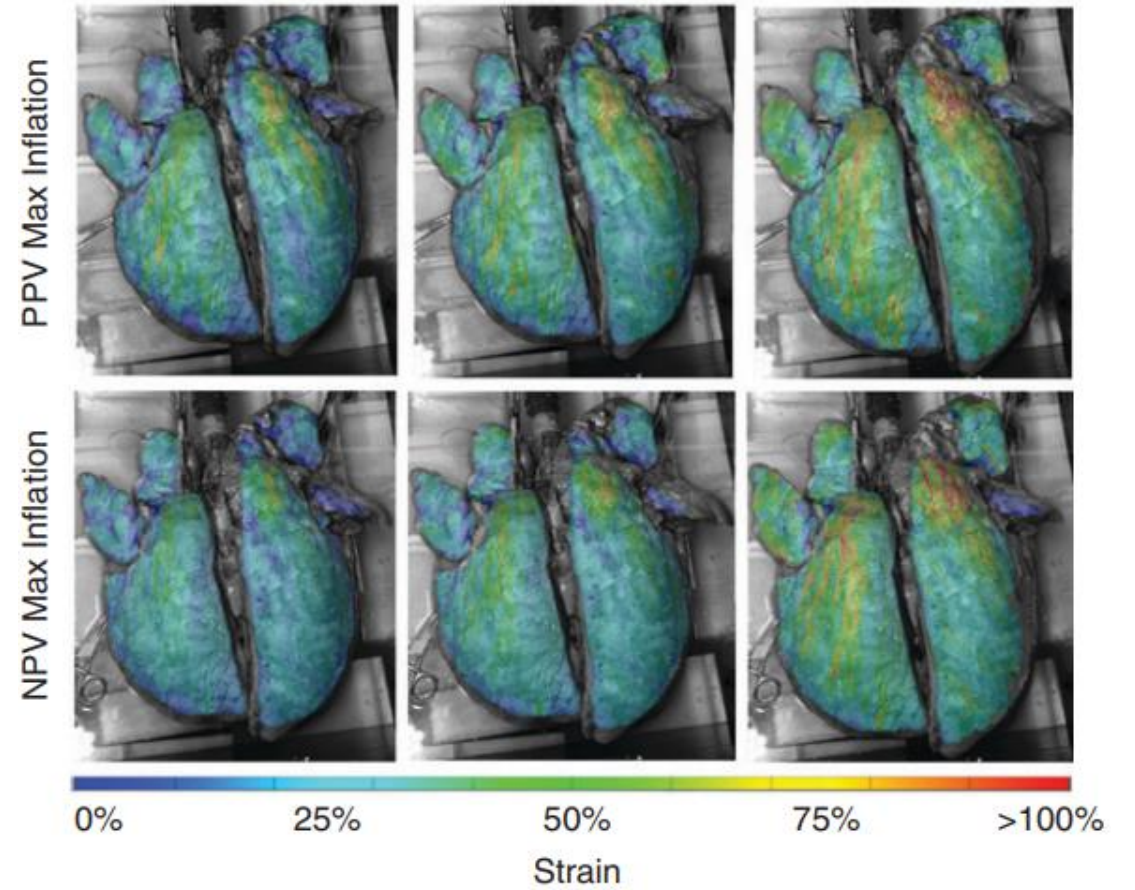
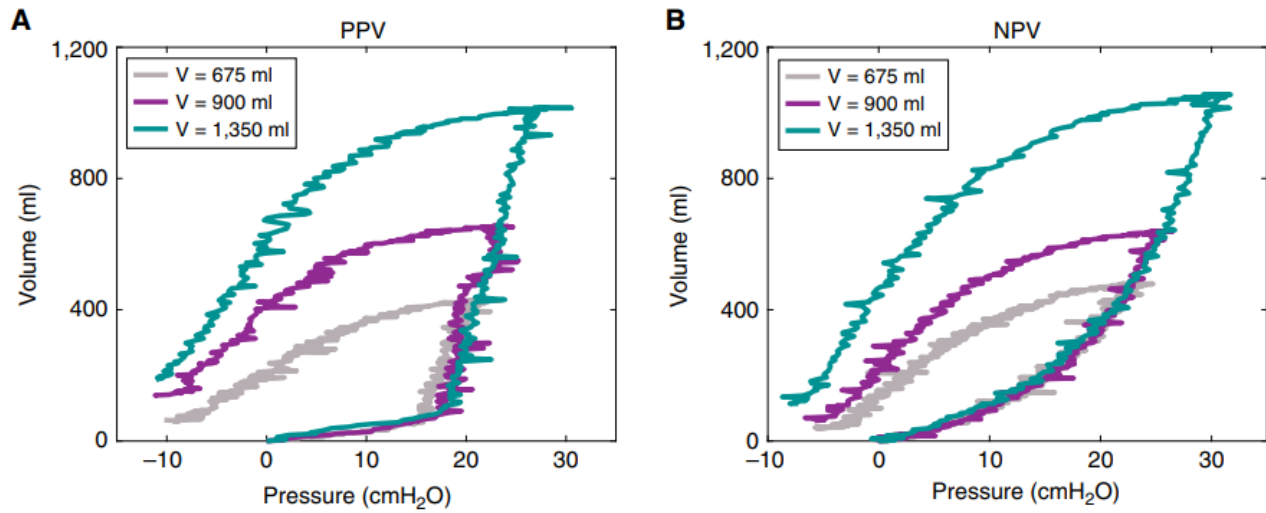


Positive- and Negative-Pressure Ventilation Characterized by Local and Global Pulmonary Mechanics

Samaneh Sattari^{1*}, Crystal A. Mariano^{1*}, Ware G. Kuschner², Hossein Taheri³, Jason H. T. Bates⁴, and Mona Eskandari^{1,5,6}

- Subject: Pig
- Ex vivo lung inflation
- Custom-designed, volume-controlled, airtight pressure–volume ventilation system
- Positive-pressure ventilation (PPV)
- - inflation volume (6, 8, 12 mL/kg)
- Negative-pressure ventilation (NPV)
- - transpulmonary pressure matched to PPV





- ✓ Global TV and transpulmonary pressure are similar
- ✓ Different path of lung inflation & deflation
- ✓ Homogeneous and smaller regional strain during NPV

Clinical evidence

Spontaneous Breathing in Early Acute Respiratory Distress Syndrome: Insights From the Large Observational Study to UNDERstand the Global Impact of Severe Acute Respiratory Failure Study*

- Design: Secondary analysis of a prospective, observational, multicenter study (LUNG SAFE)
- Patients: ARDS and at least 2 days of invasive mechanical ventilation
 - - Controlled (C): controlled mode + no SB activity (set RR = actual RR)
 - - SB: mode without mandatory breath (ex, PSV) or assist control mode + actual RR > set RR
- Intervention: Spontaneous breathing
- Comparator: Passive ventilation
- Outcomes: Ventilator free-day, Mortality → Adjusted by logistic regression

	P/F ratio ≥ 150		P/F ratio < 150	
	SB (N = 584)	C (N = 324)	SB (N = 432)	C (N = 416)
SOFA	9.0 \pm 3.7	10.0 \pm 3.6	10.4 \pm 3.7	11.1 \pm 4.2
Non-pulmonary SOFA	6.4 \pm 3.8	7.3 \pm 3.7	6.7 \pm 3.7	7.3 \pm 4.1
FiO ₂	0.4 (0.4–0.5)	0.5 (0.4–0.6)	0.6 (0.6–0.8)	0.7 (0.6–0.8)
TV (mL/kg)	7.9 \pm 1.8	7.6 \pm 1.5	7.8 \pm 1.7	7.5 \pm 1.5
PEEP	7.4 \pm 2.6	8.0 \pm 2.7	8.8 \pm 2.8	9.5 \pm 3.3
VFD	16.0 (0.0–23.0)	10.5 (0.0–21.0)	12.0 (0.0–21.0)	0.0 (0.0–18.0)
ICU mortality	168 (28.8)	115 (35.5)	149 (34.5)	173 (41.6)
Hospital mortality	206 (35.5)	135 (41.7)	171 (39.6)	184 (44.7)

Effect of No SB

	P/F ratio ≥ 150		P/F ratio < 150	
	OR (95% CI)	P value	OR (95% CI)	P value
ICU mortality	1.17 (0.92-1.49)	0.208	1.05 (0.72-1.52)	0.806
Hospital mortality	1.13 (0.92-1.50)	0.298	1.16 (0.86-1.56)	0.346

Early Neuromuscular Blockade in the Acute Respiratory
Distress Syndrome

The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network*

- Design: Multicenter, unblinded, randomized trial (ROSE trial)
- Patients: ARDS (PF ratio < 150, PEEP \geq 8 cmH₂O, Less than 48 hours)
- Intervention: NMB with deep sedation (RASS -5 ~ -4, cisatracurium 37.5 mg/h for 48 hours)
- Control: Light sedation (RASS -1 ~ 0)
- Outcomes: In-hospital death from any cause at 90 days

- Protocol
- - High PEEP strategy

FiO2	0.3	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.5	0.5	0.5	0.6	0.7	0.8	0.8	0.9	1.0	1.0
PEEP	5	5	6	8	10	12	14	16	16	18	20	20	20	20	22	22	22	24

- - Conservative fluid strategy
- - NMB can be stopped when weaning criteria met ($FiO_2 \leq 0.4$, $PEEP \leq 8\text{cmH}_2\text{O}$)
- - NMB bolus can be administered when plateau pressure $> 32\text{ cmH}_2\text{O}$ despite other measure
- Sample size calculation: 1408 patients (mortality 27% vs 35%, power 90%)
- After second interim analysis: 1006 patients included and study stopped

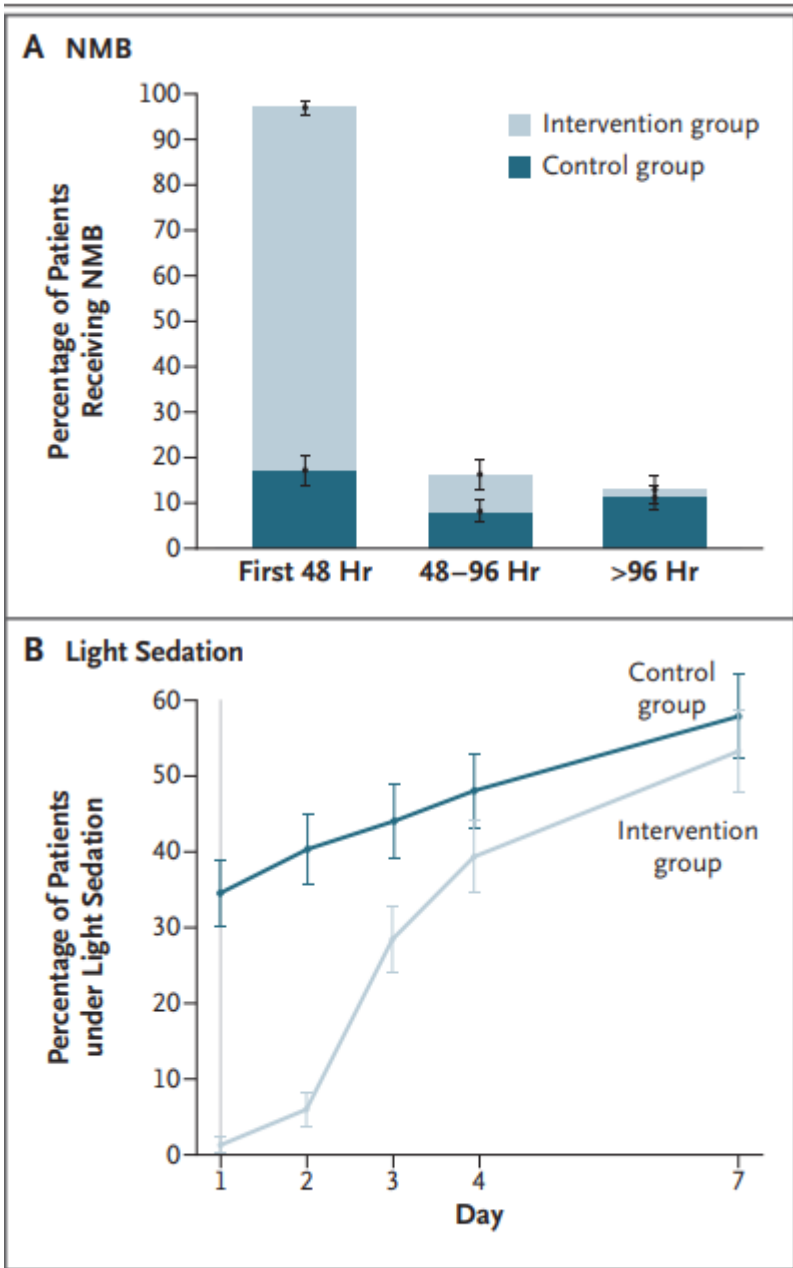
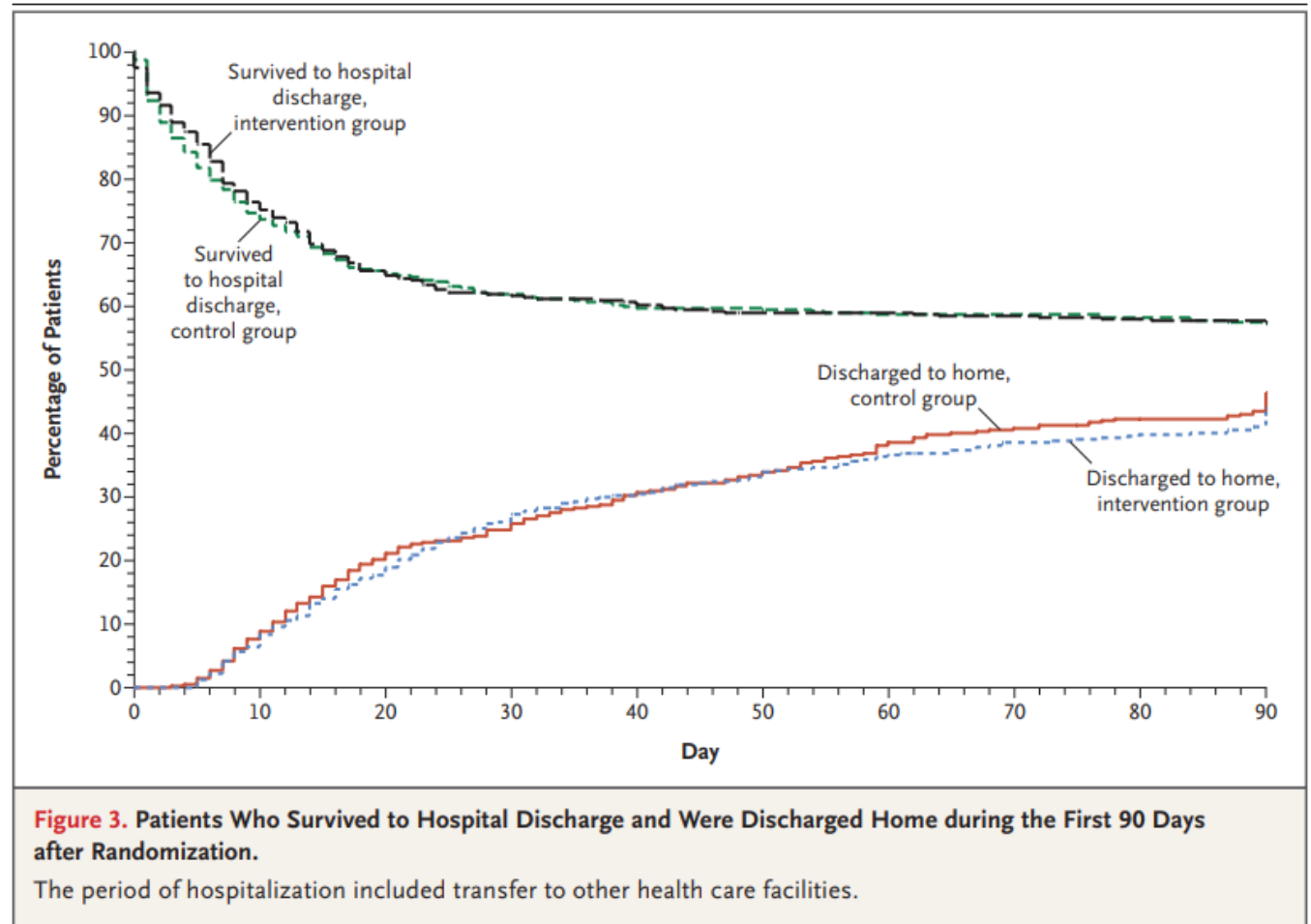


Figure 2. Neuromuscular Blockade and Sedation.



	NMB + deep sedation (N = 501)	Light sedation (N = 505)	P value
Tidal volume (mL/kg)	6.3±0.9	6.3±0.9	
FiO ₂	0.8±0.2	0.8±0.2	
PEEP (cmH ₂ O)	12.6±3.6	12.5±3.6	
PF ratio	98.7±27.9	99.5±27.9	
Cisracurium use	488 (97.4%)	86 (17%)	
Cisracurium dose (mg)	1807 (1706-1815)	38 (14-200)	
90-day mortality	213 (42.5±2.2%)	216 (42.8±2.2%)	0.93
PF ratio < 120	42.5±2.6%	42.2±2.6%	n-s
PF ratio ≥ 120	42.4±4.2%	44.2±4.1%	n-s
Serious cardiovascular event	14 (2.8%)	4 (0.8%)	0.02
Barotrauma	20 (4.3%)	32 (6.3%)	0.12
Pneumothorax (first 2 days)	8 (1.6%)	10 (2.0%)	0.81

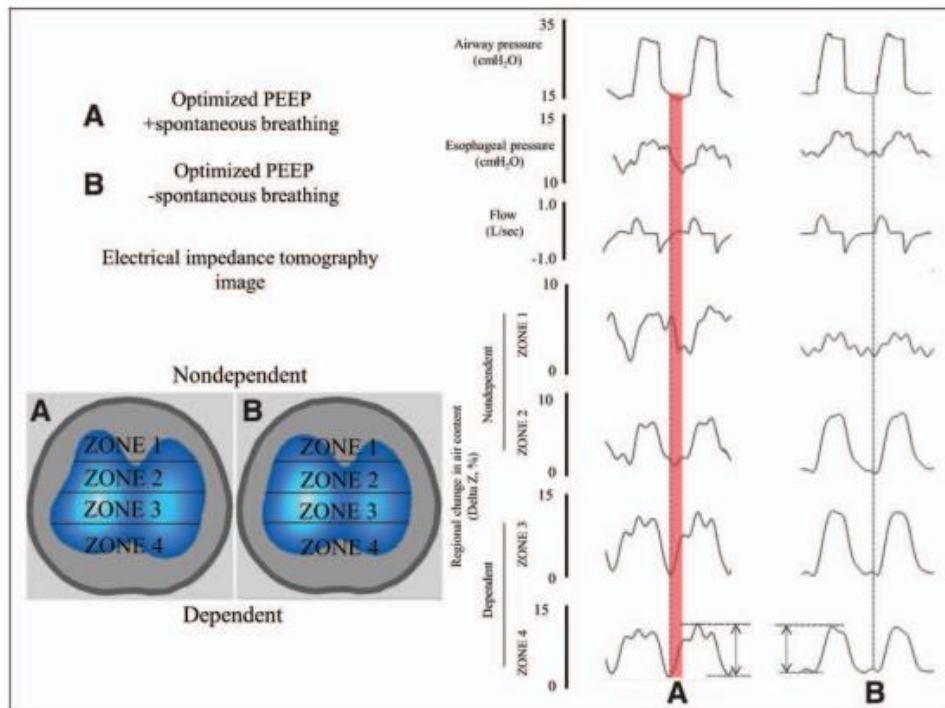
Possible strategies to facilitate spontaneous breathing

Spontaneous Effort During Mechanical Ventilation: Maximal Injury With Less Positive End-Expiratory Pressure*

Takeshi Yoshida, MD, PhD^{1,2}; Rollin Roldan, MD^{1,3}; Marcelo A. Beraldo, PhD^{1,4}; Vinicius Torsani, PhD¹;
Susimeire Gomes, PhD¹; Roberta R. De Santis, MD¹; Eduardo L. V. Costa, MD^{1,5}; Mauro R. Tucci, MD¹;
Raul G. Lima, PhD⁶; Brian P. Kavanagh, MD⁷; Marcelo B. P. Amato, MD, PhD¹

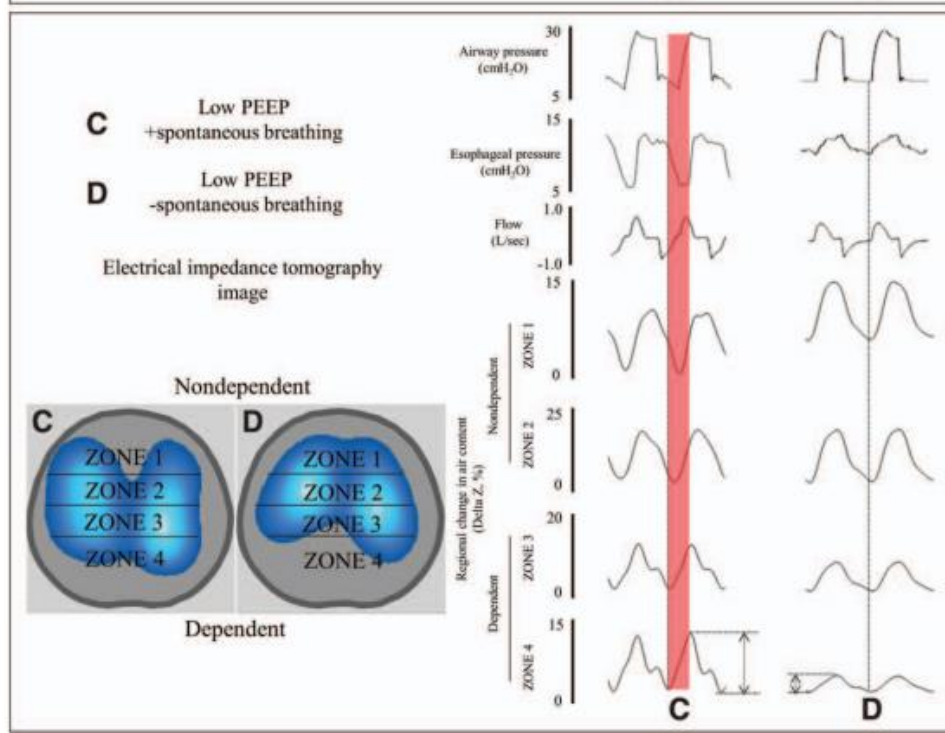
- Subject: Pig
- Model: Injurious ventilation induced lung injury
- Pressure control mode (I:E ratio 1:2, TV 6~7 mL/kg, FiO₂ 1.0)
- - Optimum PEEP ± spontaneous breathing
- - Low PEEP ± spontaneous breathing
- - Optimum PEEP: open-lung PEEP estimated by electrical impedance tomography
- - Low PEEP: open-lung PEEP minus 10 cmH₂O

- P/F ratio after lung injury = 125
- PEEP: 16.9 (16.7) cmH₂O vs 6.5 (6.1) cmH₂O



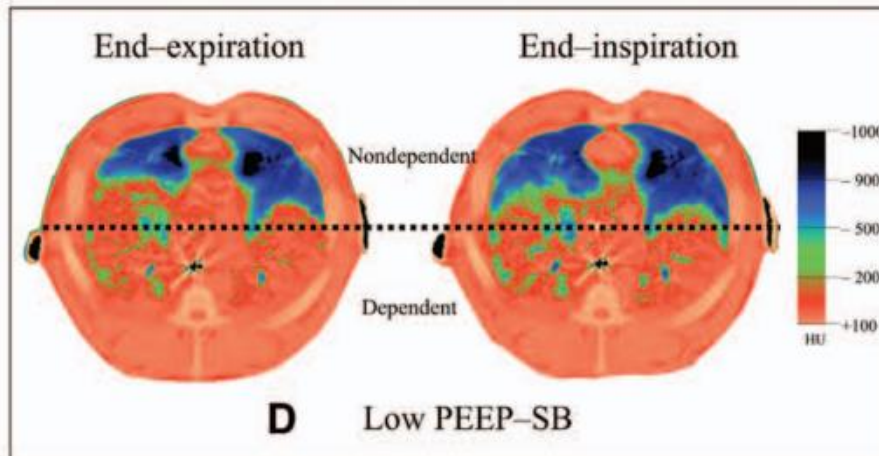
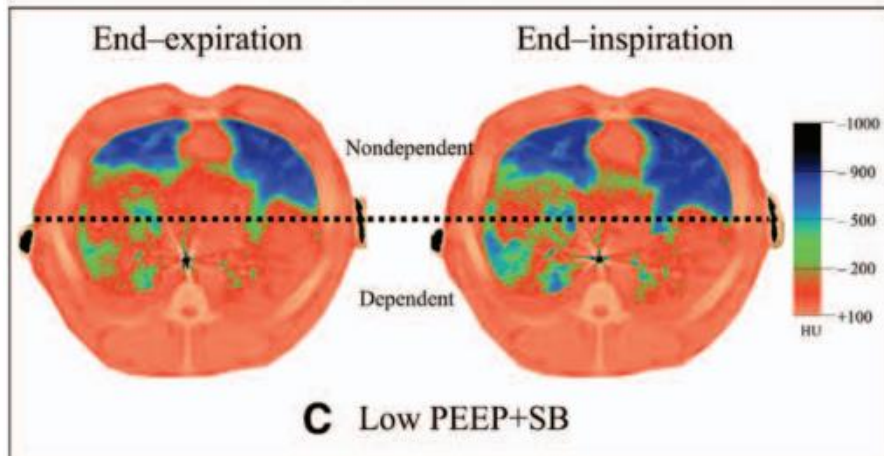
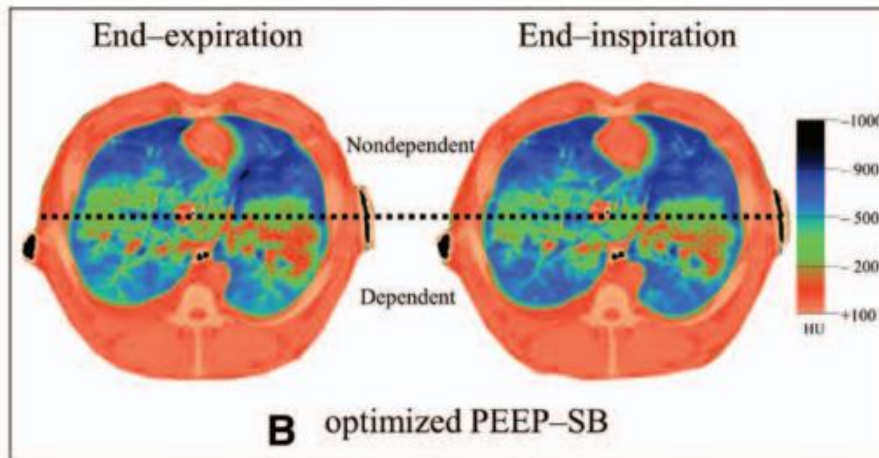
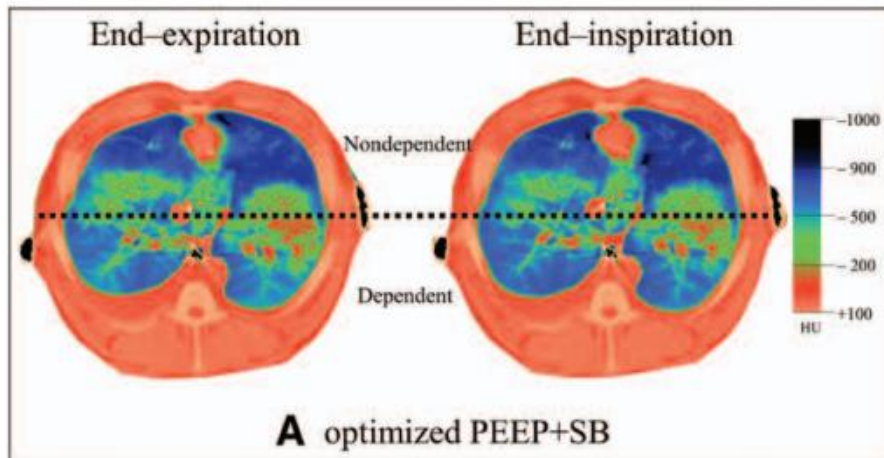
✓ Similar distribution of ventilation regardless of SB in optimum PEEP

✓ Shorter duration of pendelluft (red bar)



✓ Different distribution of ventilation according to presence or absence of SB in low PEEP

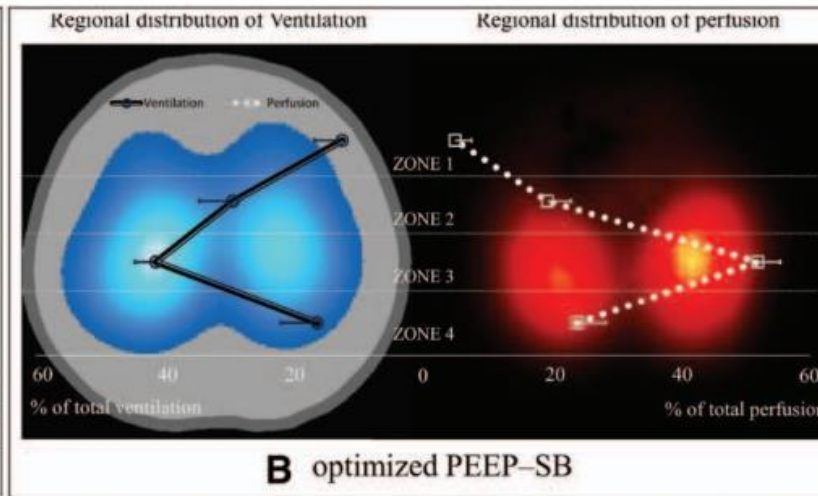
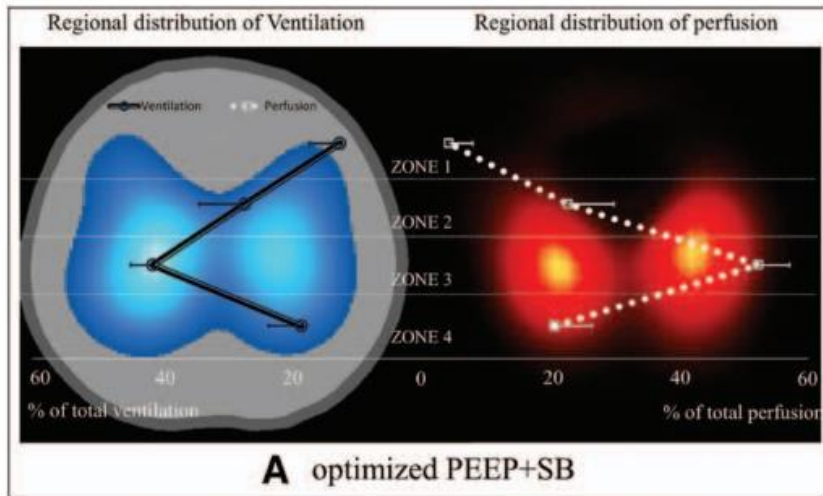
✓ Longer duration of pendelluft (red bar)



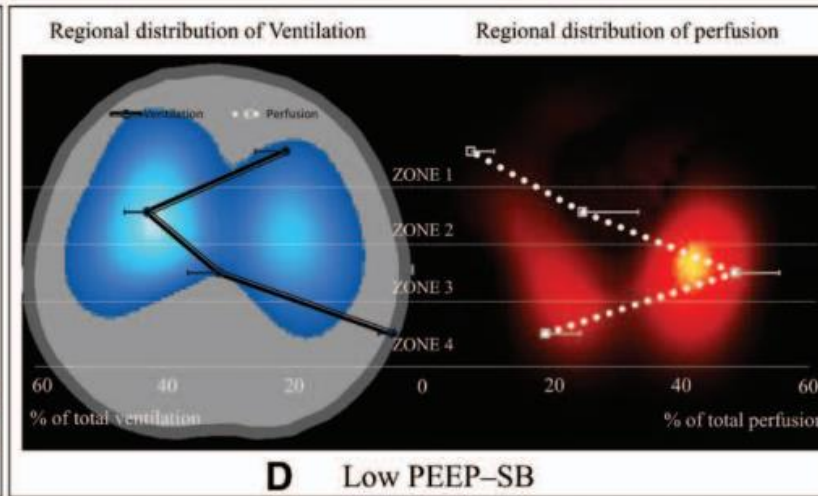
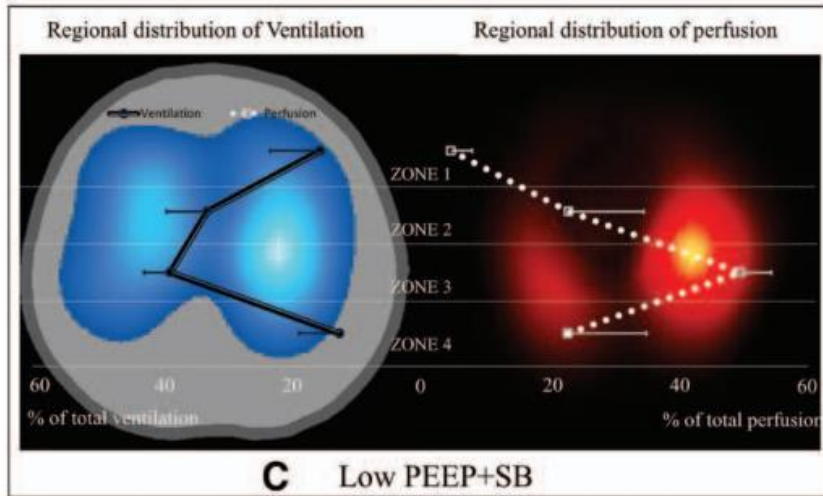
✓ No tidal recruitment in optimum PEEP

✓ Tidal recruitment in low PEEP with SB

✓ No tidal recruitment in low PEEP without SB, BUT dependent atelectasis



✓ Perfect V/Q matching in optimum PEEP regardless of SB



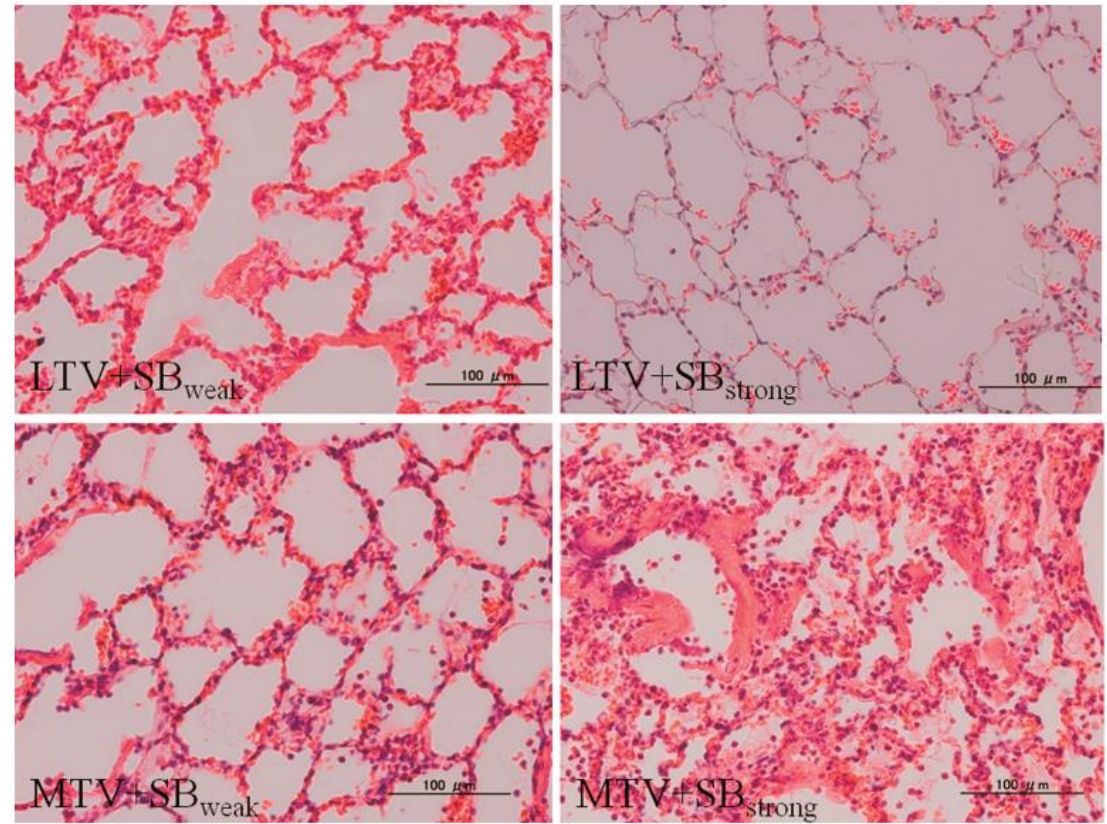
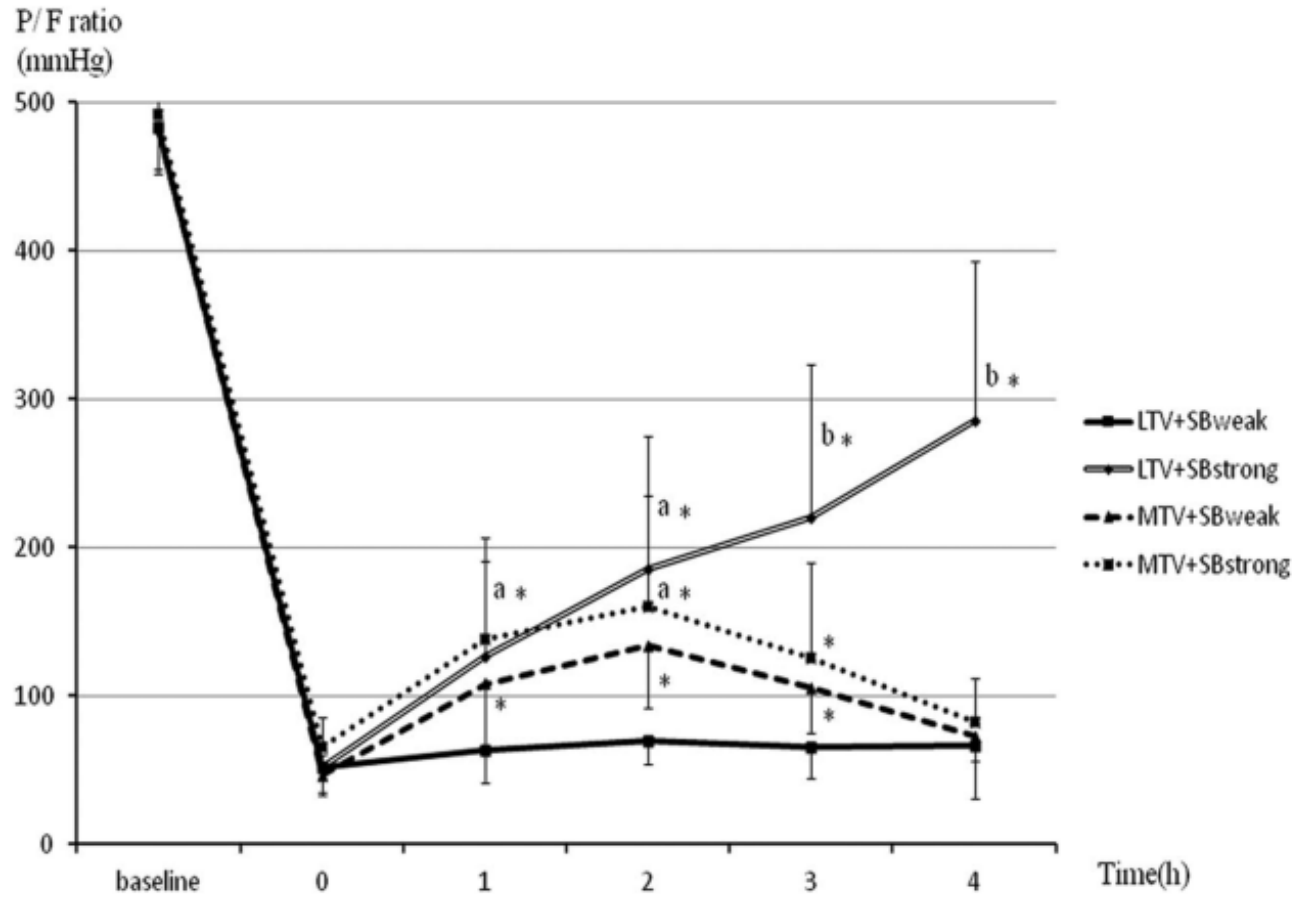
✓ Poor V/Q matching in low PEEP without SB

✓ Improved V/Q matching in low PEEP with SB, BUT poorer than optimum PEEP

Spontaneous breathing during lung-protective ventilation in an experimental acute lung injury model: High transpulmonary pressure associated with strong spontaneous breathing effort may worsen lung injury*

Takeshi Yoshida, MD; Akinori Uchiyama, MD, PhD; Nariaki Matsuura, MD, PhD;
Takashi Mashimo, MD, PhD; Yuji Fujino, MD, PhD

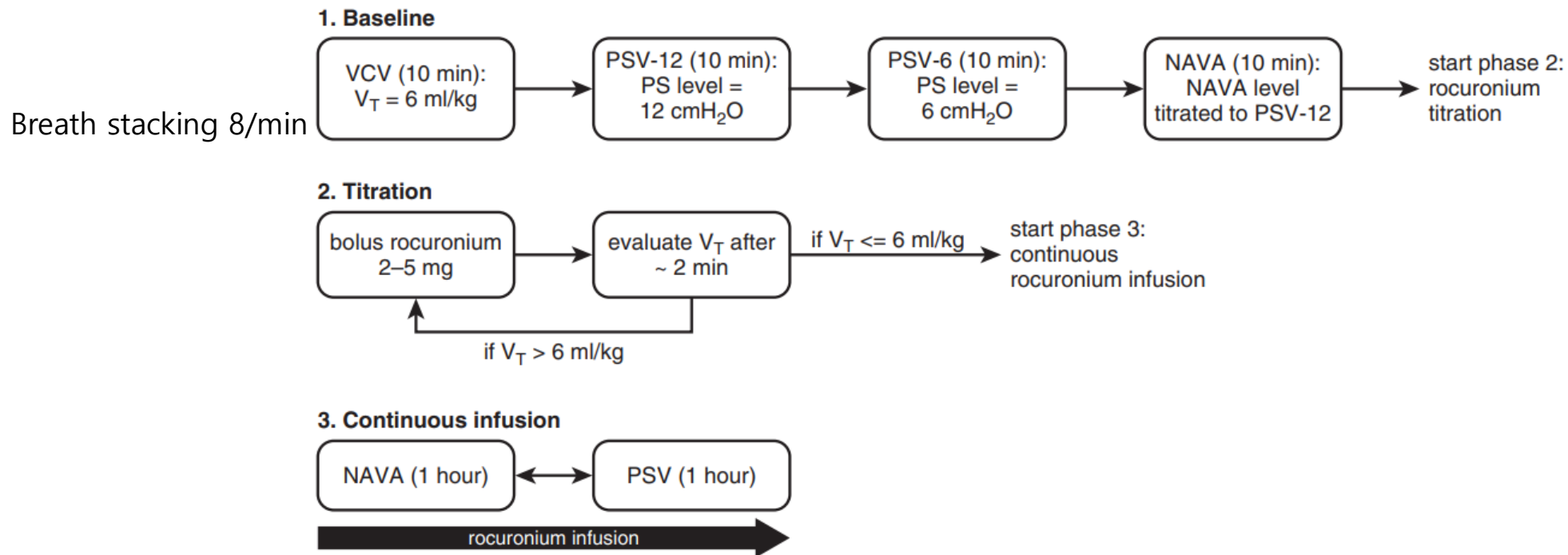
- Subject: Rabbit
- Model: Lung lavage induced lung injury
- Low TV with weak or strong SB (PEEP 8cmH₂O, I:E ratio 1:2, TV 6 mL/kg, FiO₂ 1.0)
- Moderate TV with weak or strong SB (PEEP 8cmH₂O, I:E ratio 1:2, TV 7~9 mL/kg, FiO₂ 1.0)
- Weak or Strong SB (P_{0.1} 2cmH₂O)
- P/F ratio after lung injury < 100

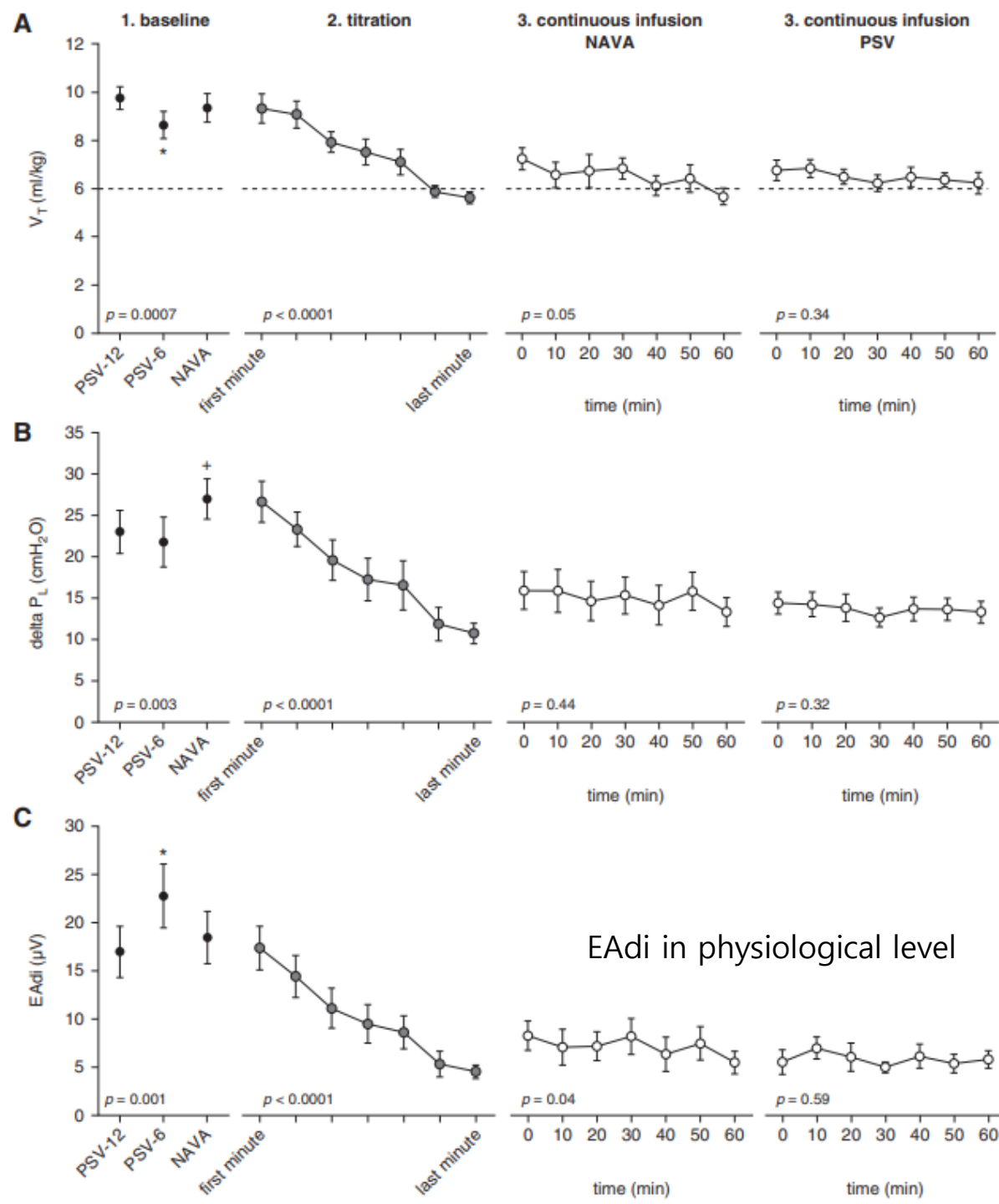


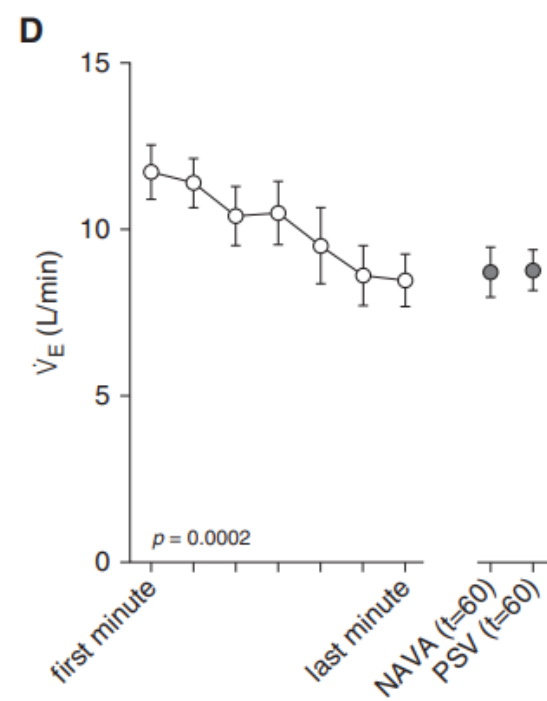
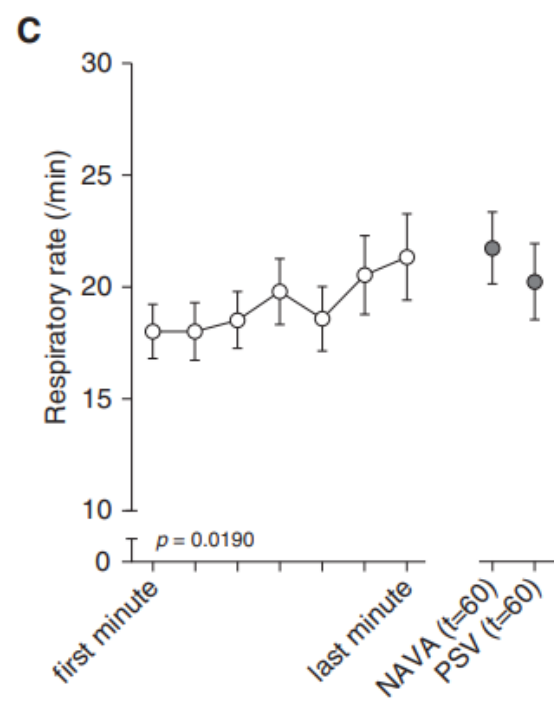
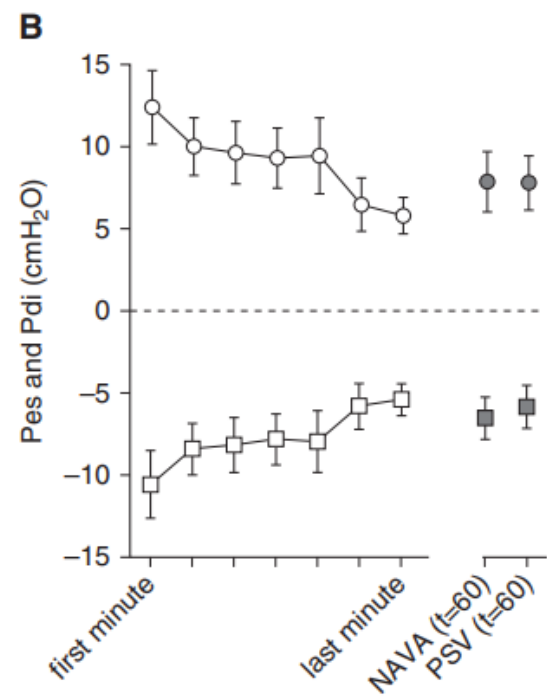
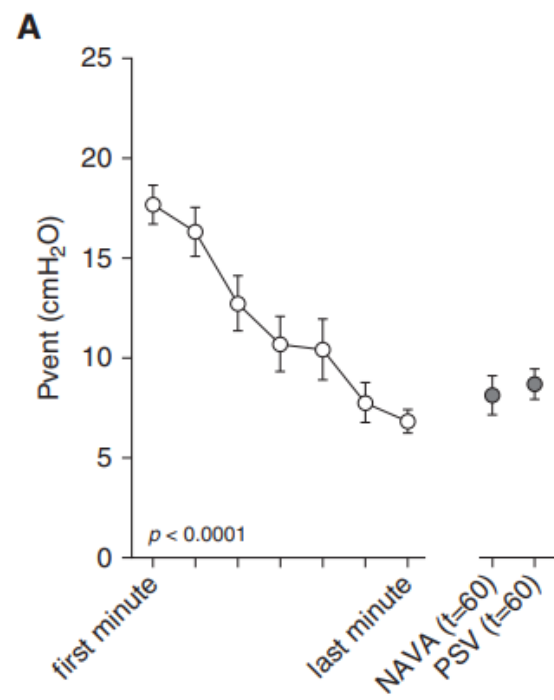
✓ Low TV with strong SB improves oxygenation and histology

Spontaneous Breathing in Early Acute Respiratory Distress Syndrome: Insights From the Large Observational Study to UNDERstand the Global Impact of Severe Acute Respiratory Failure Study*


- Design: Proof-of-concept study
- Patients: ARDS patients. PSV mode (PS = 12cmH₂O, TV > 8mL/kg)



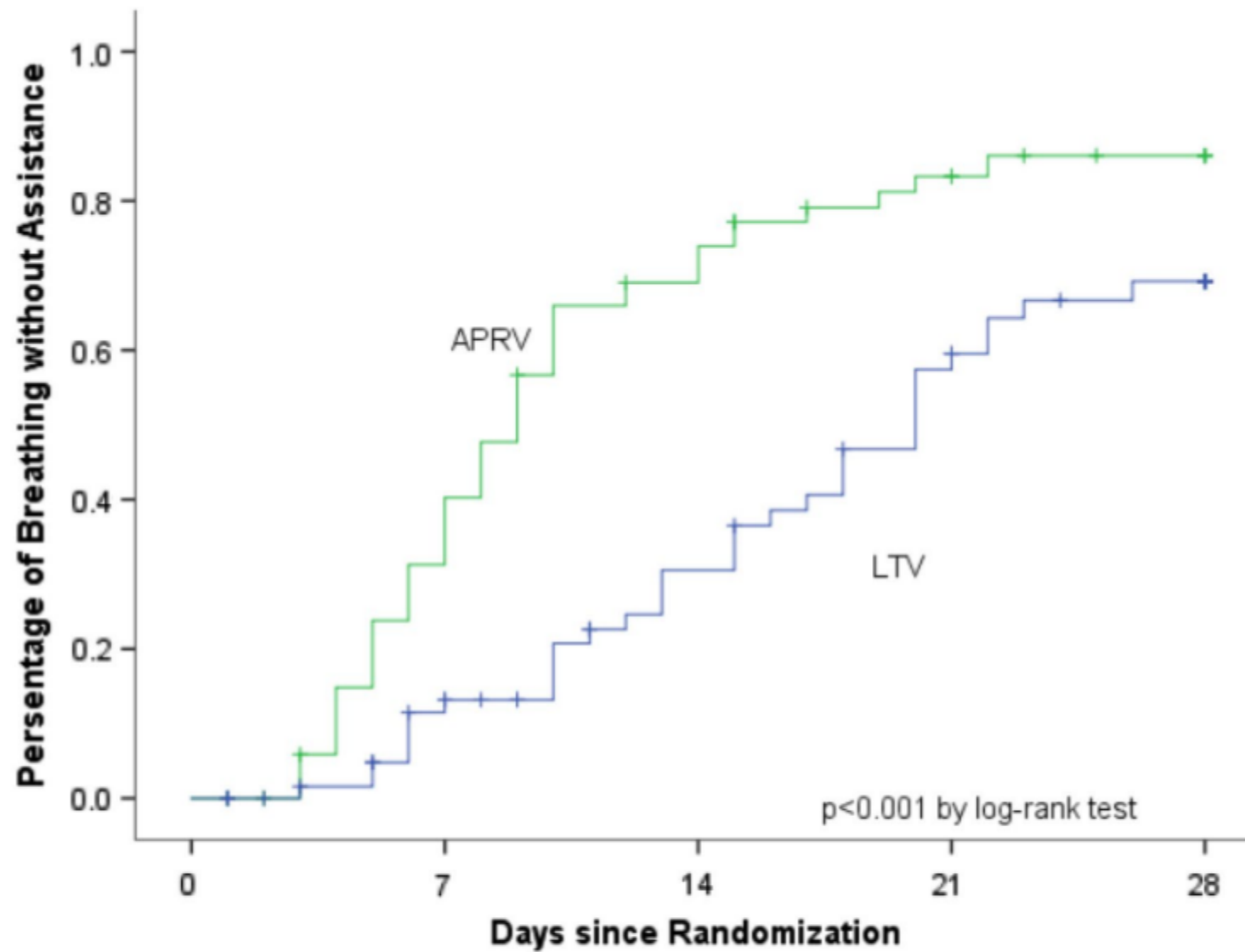




Early application of airway pressure release ventilation may reduce the duration of mechanical ventilation in acute respiratory distress syndrome

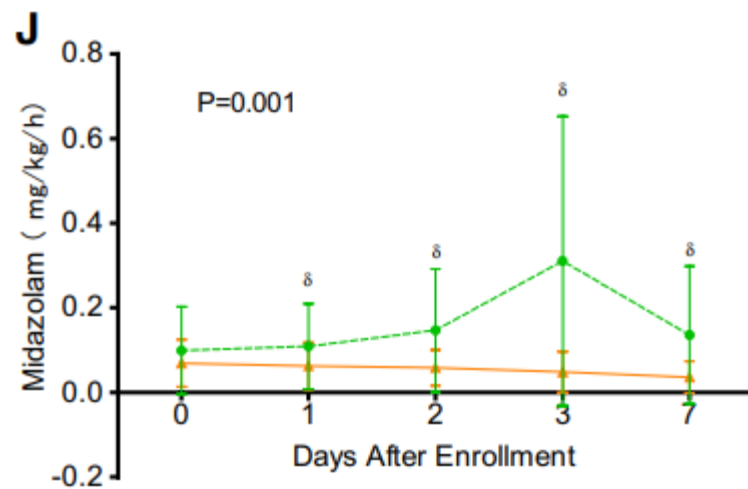
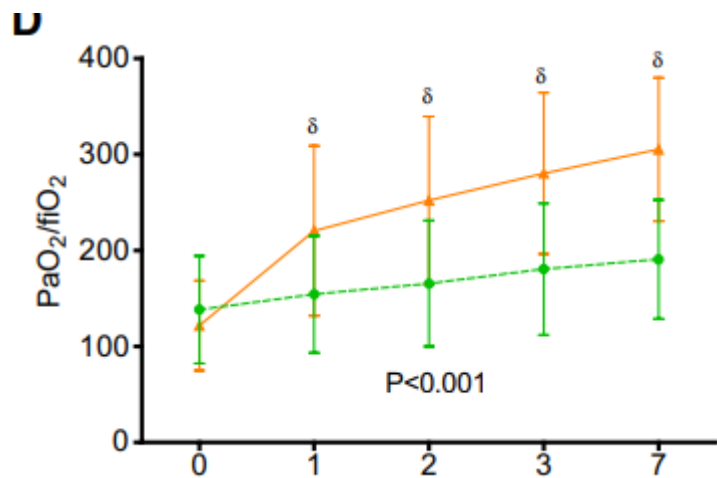
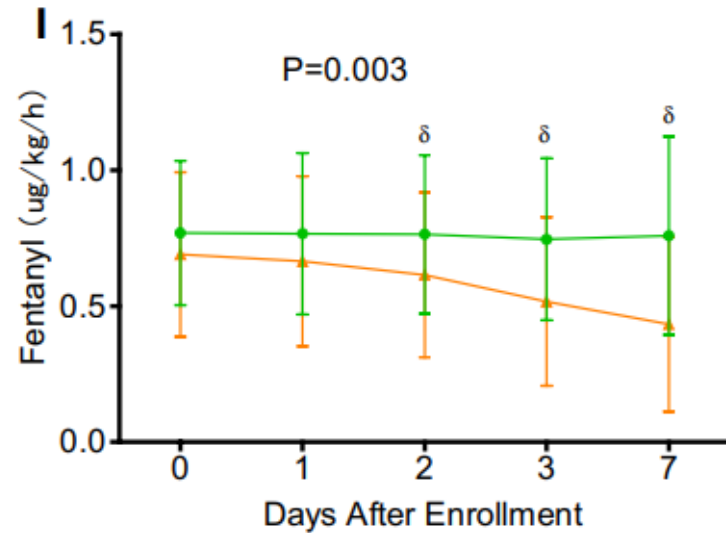
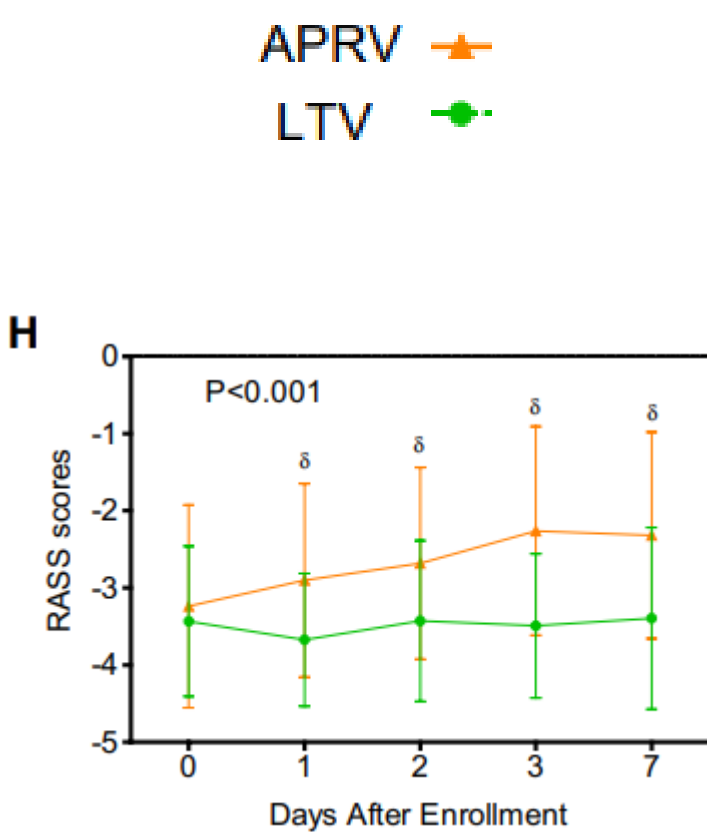
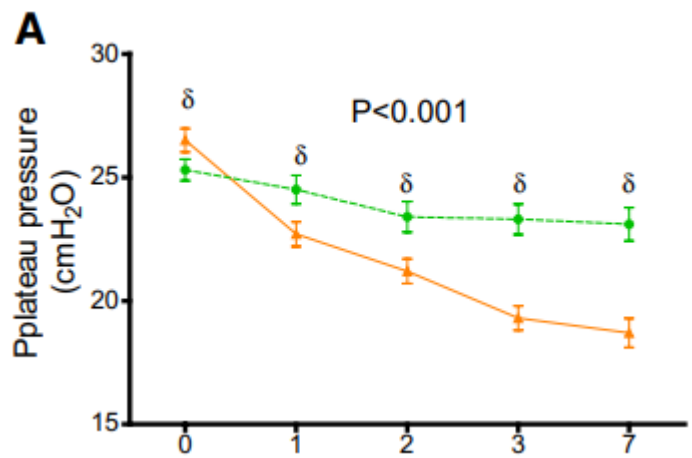
Yongfang Zhou, Xiaodong Jin, Yinxia Lv, Peng Wang, Yunqing Yang, Guopeng Liang, Bo Wang and Yan Kang^{*} 

- Design: Single center, unblinded, randomized controlled trial
- Patients: ARDS with PF ratio ≤ 250 , IMV less than 48 hours
- Before randomization, volume control mode with plateau pressure $< 30\text{cmH}_2\text{O}$
- Control(low tidal ventilation): TV 6 mL/kg (4~8), ARDSnet protocol
- Intervention(APRV): P_{high} (previous plateau) P_{low} (5cmH₂O), spontaneous minute ventilation (30% of total)
- Outcome: 28-day ventilator free day



No. at risk

APRV	71	46	19	8	3
LTV	67	52	35	20	12



Summary

- Lung recruitment
 - V/Q matching
 - Pulmonary hemodynamics
 - Surfactant release with less cytokine release
 - Homogeneous regional strain
-
- Ventilator-free day
-
- High PEEP
 - Low tidal volume with partial neuromuscular block
 - APRV mode

THANK



YOU

