Optimizing Mechanical Ventilation: The Art and Science

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Objectives

- Review the components of mechanical ventilation
- Discuss options for choosing initial ventilator settings based on individual pathophysiology
- Consider ways to avoid oxygen toxicity
- Outline strategies for weaning

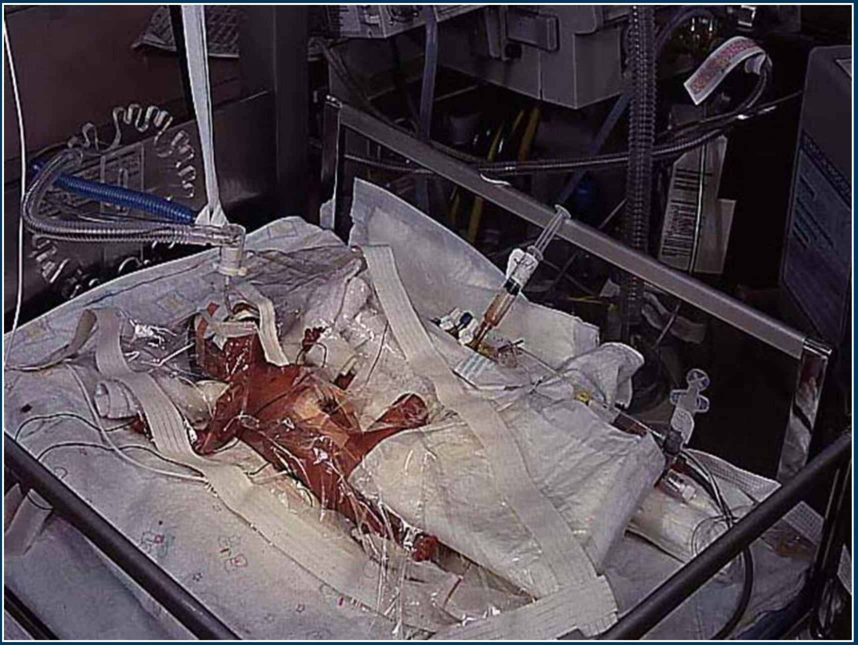
Neonatal Ventilation ca. 1975

The Baby Bird

- Flow 8-10 LPM
- PIP 20 cm H_2O
- PEEP 4 cm H_2O
- T_i 0.4 sec

It Didn't Matter…

Preterm Baby RDS



Term Baby MAS

It Didn't Matter…

Preterm Baby RDS

Term Baby MAS

Neonatal Ventilation ca. 2016

Optimizing Mechanical Ventilation: Choosing the Initial Settings

A Patient

- 25 weeks, 720 grams
- 17 y/o G_1P_0
- C/S for severe pre-eclampsia, treated with $MgSO_4$
- One dose of betamethasone to mom
- Apgar scores 2 (HR 136) and 5 (HR 140, color pink with bagging, no tone, no respiratory effort, minimal grimace)

Initial Evaluation

- ABG: 7.21/55/47
- Hgb/Hct: 14.0/43%
- Cord Mg^{++}: 5.5
- BP: 36/20 (25)

Define the Pathophysiology

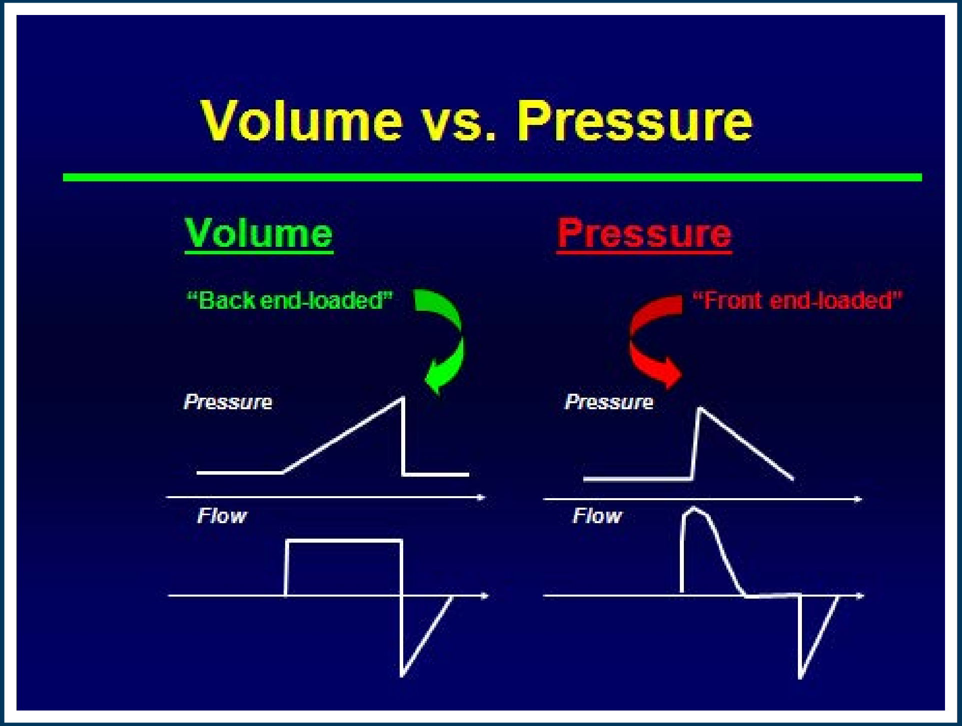
- Lung volumes?
- Compliance?
- Resistance?
- Time constant?
- Respiratory drive?
- Oxygenation?
- Ventilation?

Initial Ventilatory Options

- CPAP
- Conventional (tidal) ventilation
- High-Frequency ventilation
  - HFJV
  - HFOV

Target Variables

- Pressure
  - ➢ Pressure Limited
  - ➢ Pressure Control
- Volume



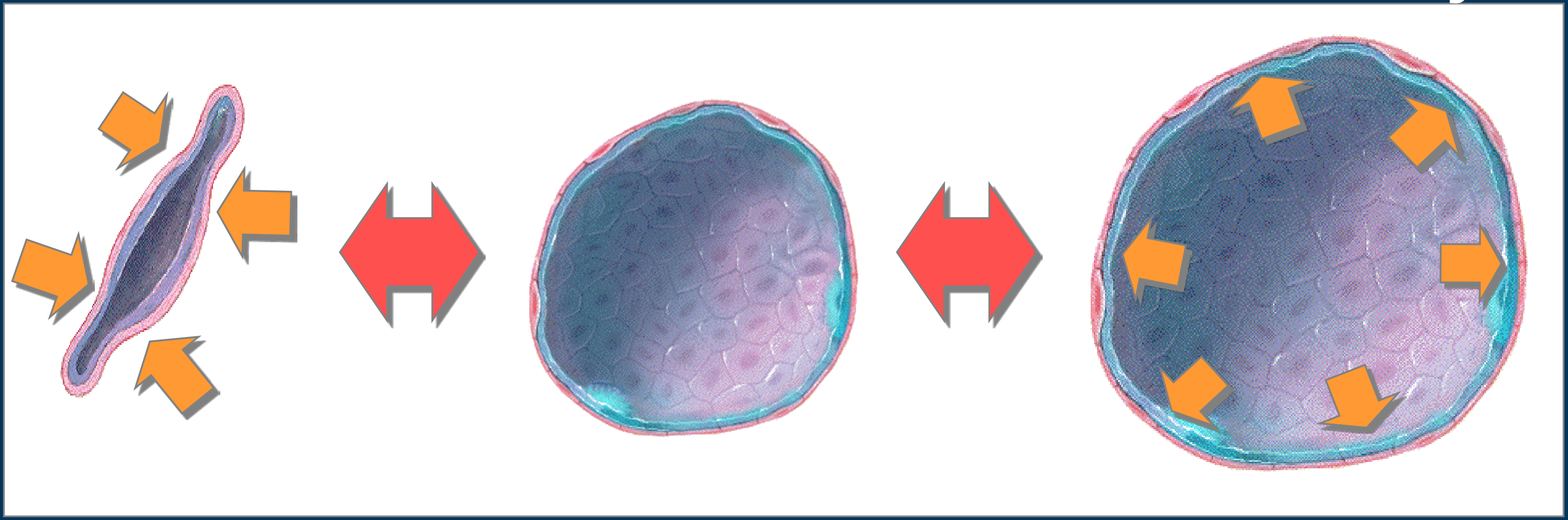
Ventilator-Induced Lung Injury

Atelectotrauma:

Repetitive alveolar opening and closing of under-recruited alveoli

Volutrauma:

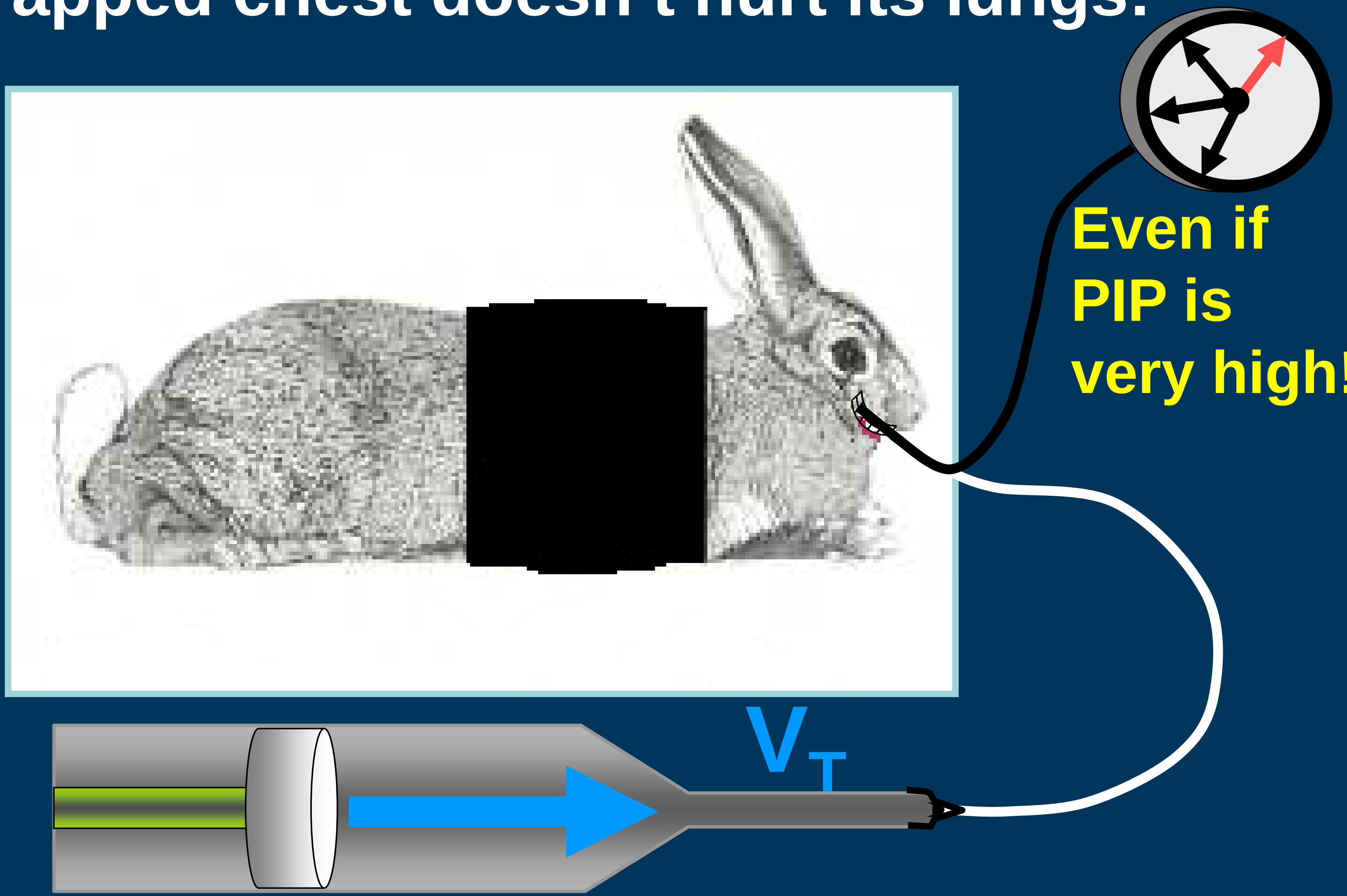
Over-distension of normally aerated alveoli from excessive volume delivery



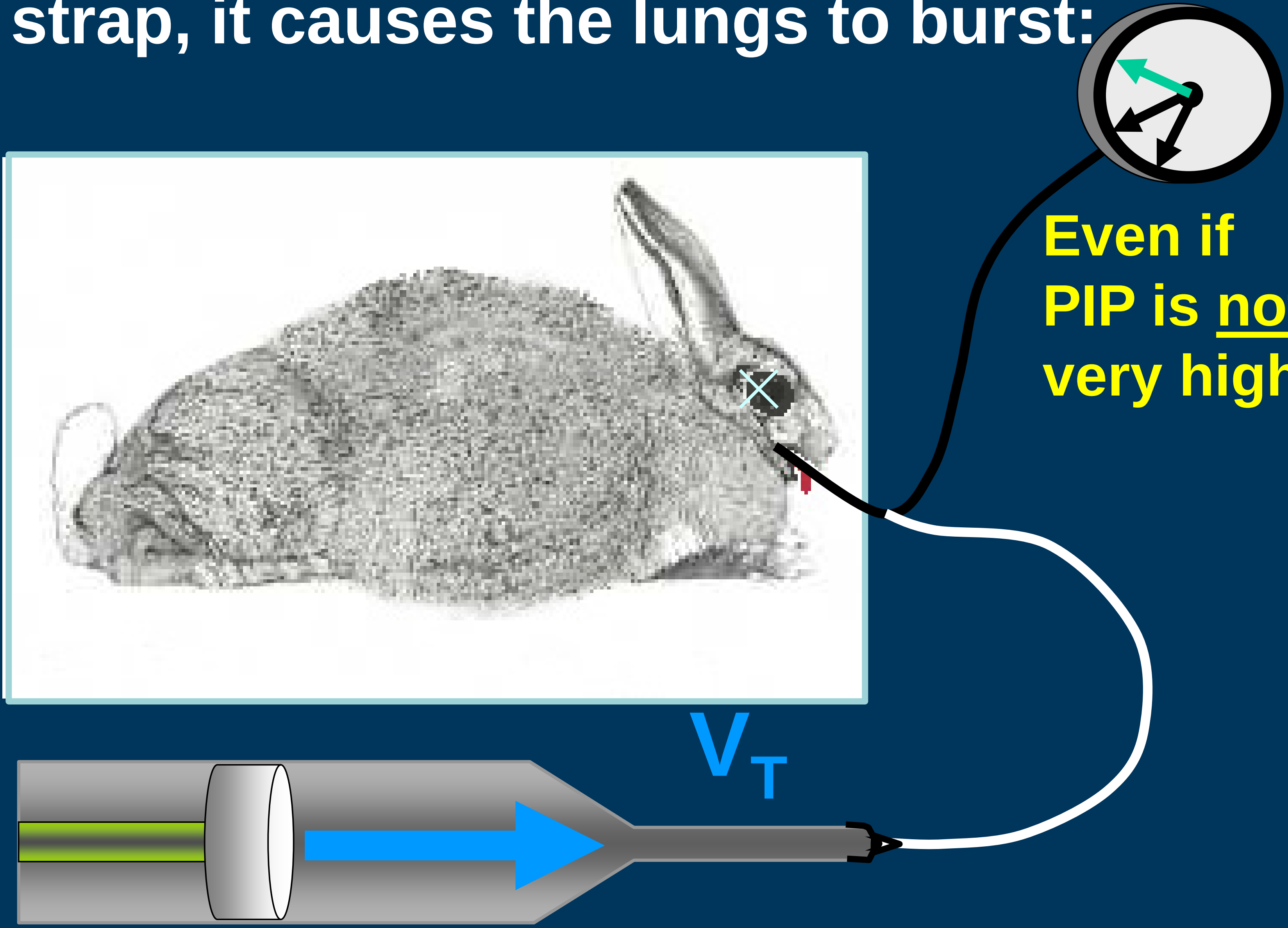
Hernandez et al (1989) and Dreyfus et al (1998)

- Demonstrated severe acute lung injury occurred in small animals using large V_T
- When the chest cavity was bound and the lungs exposed to high pressures, the acute lung injury markers were much lower than the injury that ensued once the binding was removed
- Excessive V_T -and not high pressure- is primarily responsible for lung injury

A large V_T injected into a critter with a strapped chest doesn't hurt its lungs:



If one pushes in that same V_T without the strap, it causes the lungs to burst:

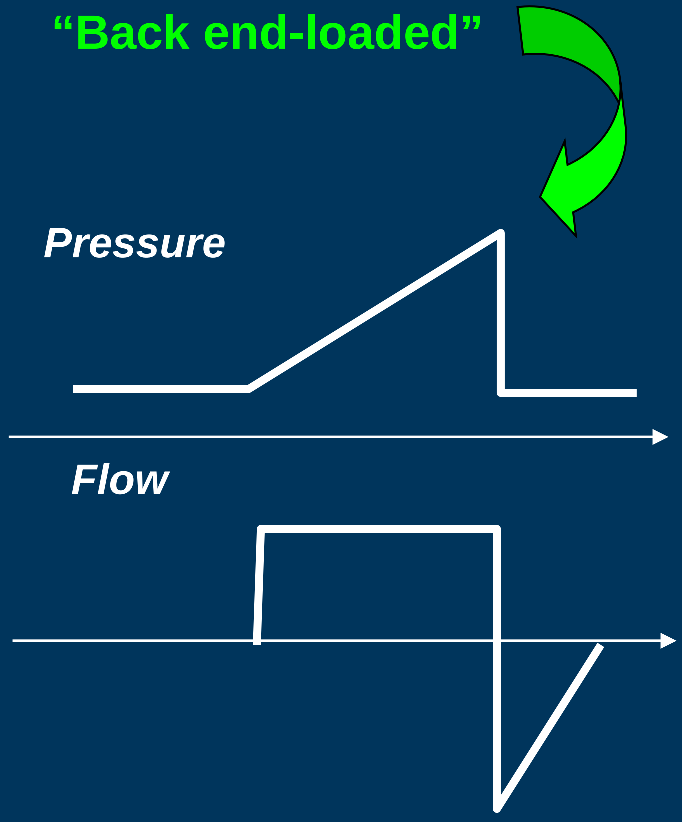


Even if PIP is not very high!

Volume vs. Pressure

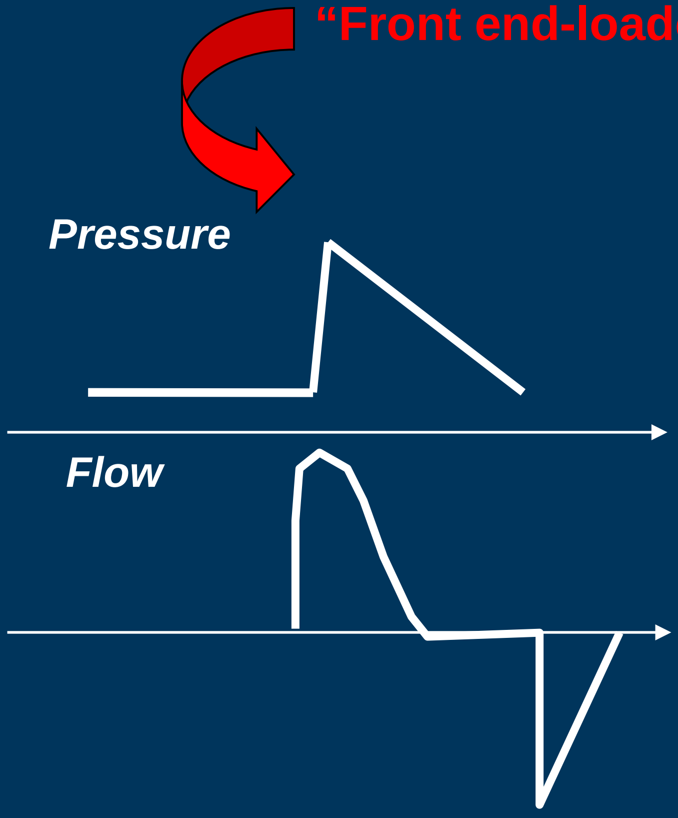
Volume

"Back end-loaded"



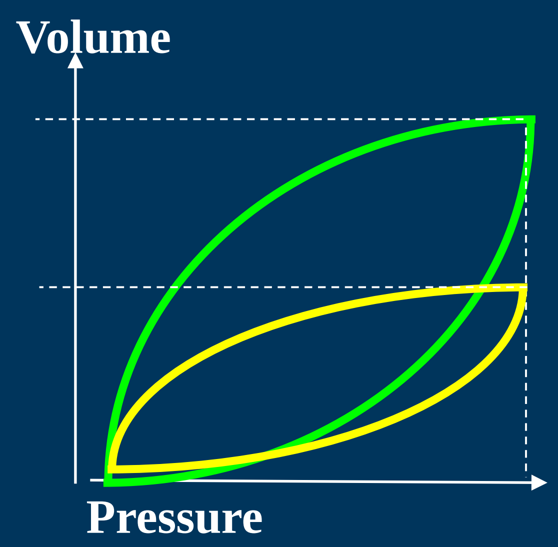
Pressure

"Front end-loaded"

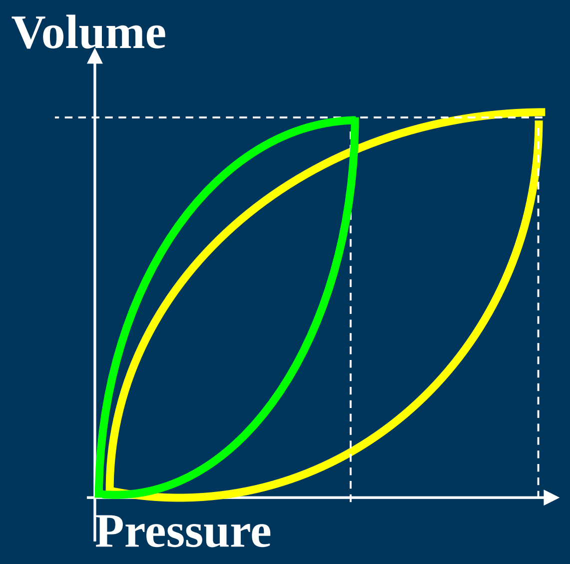


Pressure vs. Volume
(Control variables)

Pressure Targeted



Volume Targeted

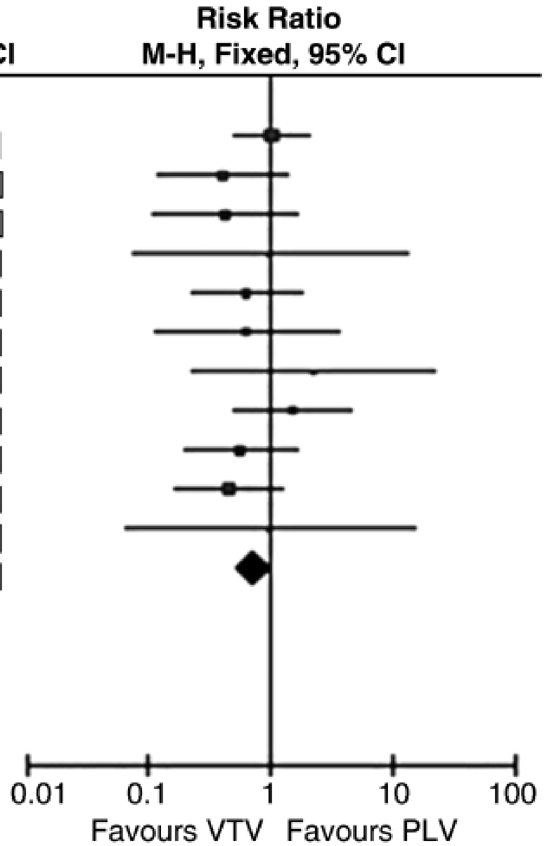


Mortality

Study or Subgroup	VTV Events	VTV Total	PLV Events	PLV Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 Incidence of death						
D'Angio CT2005	13	104	13	107	21.1%	1.03 [0.50, 2.11]
Duman N2012	3	23	7	22	11.8%	0.41 [0.12, 1.39]
Guven S2013	3	42	5	30	9.6%	0.43 [0.11, 1.66]
Keszler M2004	1	9	1	9	1.6%	1.00 [0.07, 13.64]
Lista G2004	5	30	6	23	11.2%	0.64 [0.22, 1.84]
Liu CQ2011	2	31	3	30	5.0%	0.65 [0.12, 3.59]
Nafday SM2005	2	16	1	18	1.5%	2.25 [0.22, 22.53]
Piotrowski A2007	7	30	4	26	7.1%	1.52 [0.50, 4.60]
Piotrowski A1997	4	27	8	31	12.3%	0.57 [0.19, 1.70]
Singh J2006	5	57	10	52	17.2%	0.46 [0.17, 1.25]
Sinha SK1997	1	25	1	25	1.6%	1.00 [0.07, 15.12]
Subtotal (95% CI)		**394**		**373**	**100.0%**	**0.73 [0.51, 1.05]**
Total events	46		59			

Heterogeneity: $Chi^2 = 6.13$, $df = 10$ ($P = 0.80$); $I^2 = 0\%$

Test for overall effect: $Z = 1.71$ ($P = 0.09$)



Peng WS, et al. Arch Dis Child Fetal Neonatal Ed 2014;99:F158–F165

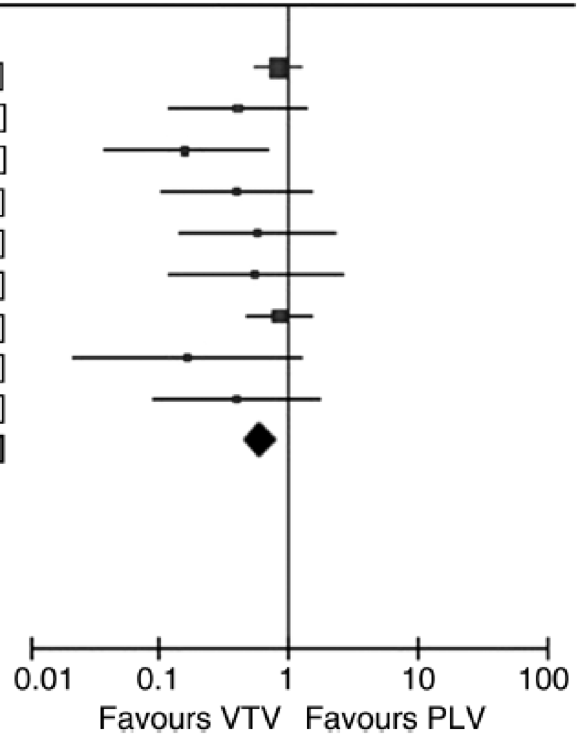
Incidence of BPD

Study or Subgroup	VTV Events	VTV Total	PLV Events	PLV Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.1 Incidence of BPD						
D'Angio CT2005	27	93	32	92	35.0%	0.83 [0.55, 1.27]
Duman N2012	3	23	7	22	7.8%	0.41 [0.12, 1.39]
Guven S2013	2	42	9	30	11.4%	0.16 [0.04, 0.68]
Keszler M2004	2	9	5	9	5.4%	0.40 [0.10, 1.55]
Lista G2004	3	30	4	23	4.9%	0.57 [0.14, 2.32]
Nafday SM2005	2	16	4	18	4.1%	0.56 [0.12, 2.67]
Singh J2006	16	57	17	52	19.3%	0.86 [0.49, 1.52]
Sinha SK1997	1	25	6	25	6.5%	0.17 [0.02, 1.29]
Zhou XJ2007	2	15	5	15	5.4%	0.40 [0.09, 1.75]
Subtotal (95% CI)		**310**		**286**	**100.0%**	**0.61 [0.46, 0.82]**
Total events	58		89			

Heterogeneity: $Chi^2 = 9.37$, df =8 (P = 0.31); $I^2 = 15\%$

Test for overall effect: Z = 3.36 (P = 0.0008)

Risk Ratio M-H, Fixed, 95% CI



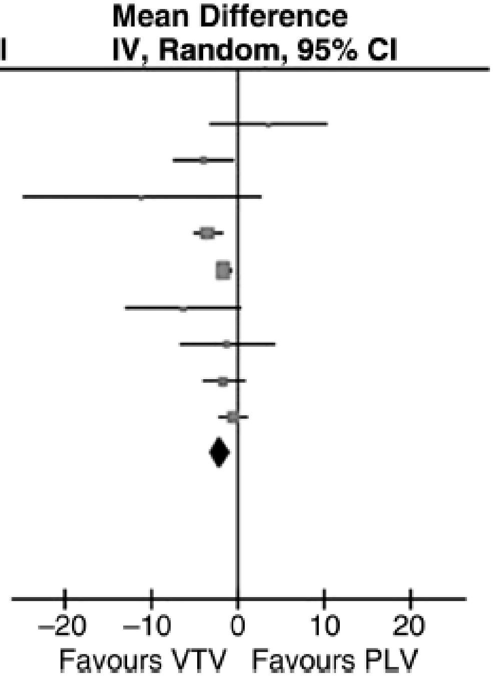
Peng WS, et al. Arch Dis Child Fetal Neonatal Ed 2014;99:F158–F165

Duration of Ventilation

Study or Subgroup	VTV Mean	VTV SD	VTV Total	PLV Mean	PLV SD	PLV Total	Weight	Mean Difference IV, Random, 95% CI
1.3.1 length of mechanical ventilation								
D'Angio CT2005	27.6	23.8	90	24	22.4	94	2.7%	3.60 [–3.08, 10.28]
Guven S2013	3.02	6.76	42	6.93	7.81	30	8.2%	–3.91 [–7.37, –0.45]
Keszler M2004	4.5	7.3	8	15.6	18.4	8	0.7%	–11.10 [–24.82, 2.62]
Lista G2004	8.8	3	30	12.3	3	23	19.8%	–3.50 [–5.13, –1.87]
Liu CQ2011	4.792	1.125	31	6.458	1.917	30	28.6%	–1.67 [–2.46, –0.87]
Piotrowski A1997	6.7	4.9	23	13	15	22	2.8%	–6.30 [–12.88, 0.28]
Singh J2006	8.4	12.6	52	9.7	14	42	3.9%	–1.30 [–6.75, 4.15]
Sinha SK1997	5.1	2.7	25	6.7	5.6	25	13.2%	–1.60 [–4.04, 0.84]
Zhou XJ2007	9.3	2.1	15	9.8	2.3	15	20.3%	–0.50 [–2.08, 1.08]
Subtotal (95% CI)			**316**			**289**	**100.0%**	**–2.00 [–3.14, –0.86]**

Heterogeneity: $Tau^2 = 1.02$; $Chi^2 = 14.45$, df = 8 (P = 0.07); $I^2 = 45\%$

Test for overall effect: Z = 3.44 (P = 0.0006)

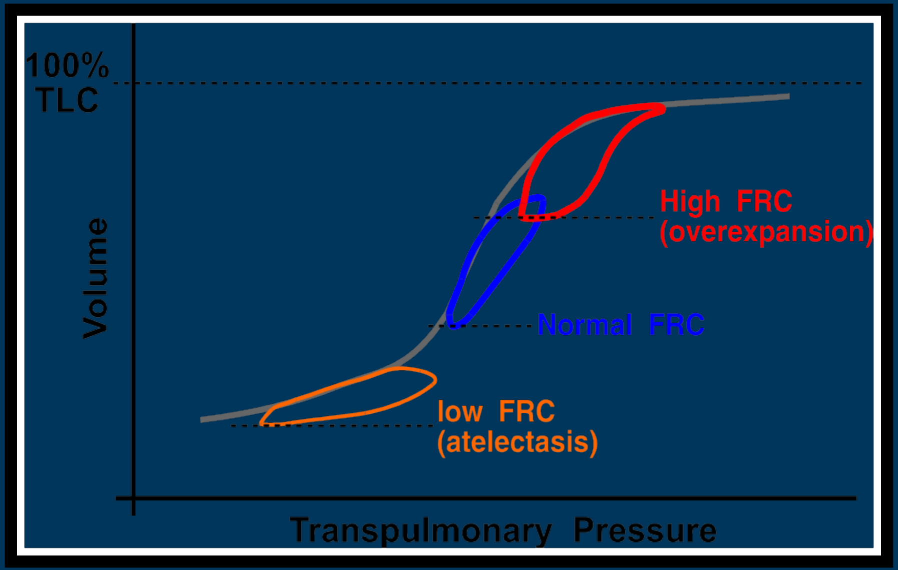


VTV reduced the incidence of BPD, duration of mechanical ventilation, failure of primarily assigned ventilatory mode, grades 3/4 IVH, PVL and air leaks compared to PLV modes. **[Peng, IBID]**

Fetal Neonatal Ed 2014;99:F158–F165

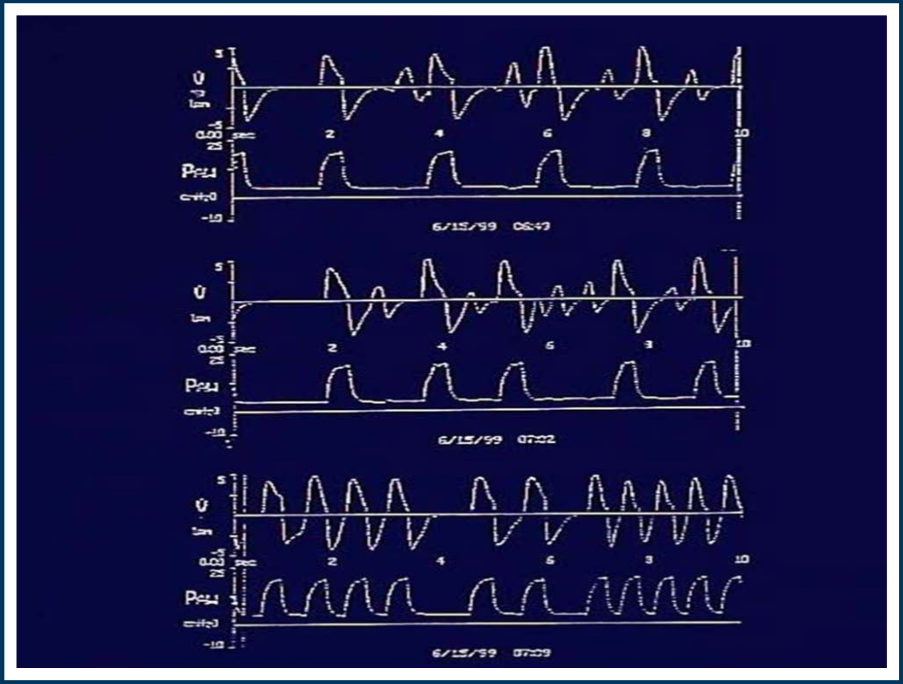
Volume Targeting

- Adjust pressure or volume to provide 4-7 mL/kg
- Avoid both hyperinflation and underinflation
- A happy baby will breathe at 40-60 bpm



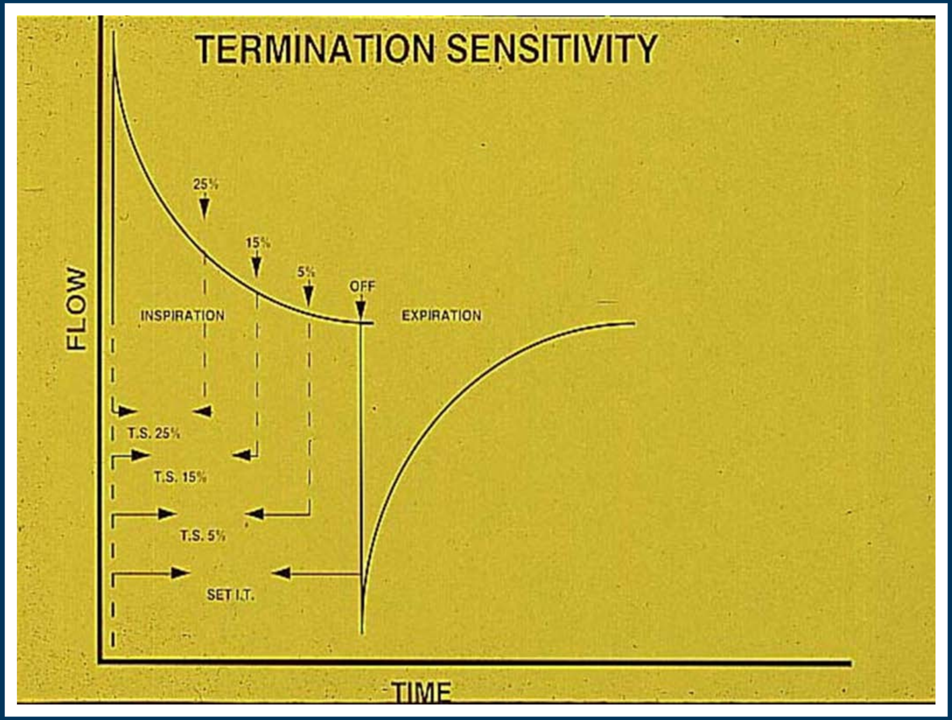
Mode

- IMV
- SIMV
- Assist/Control



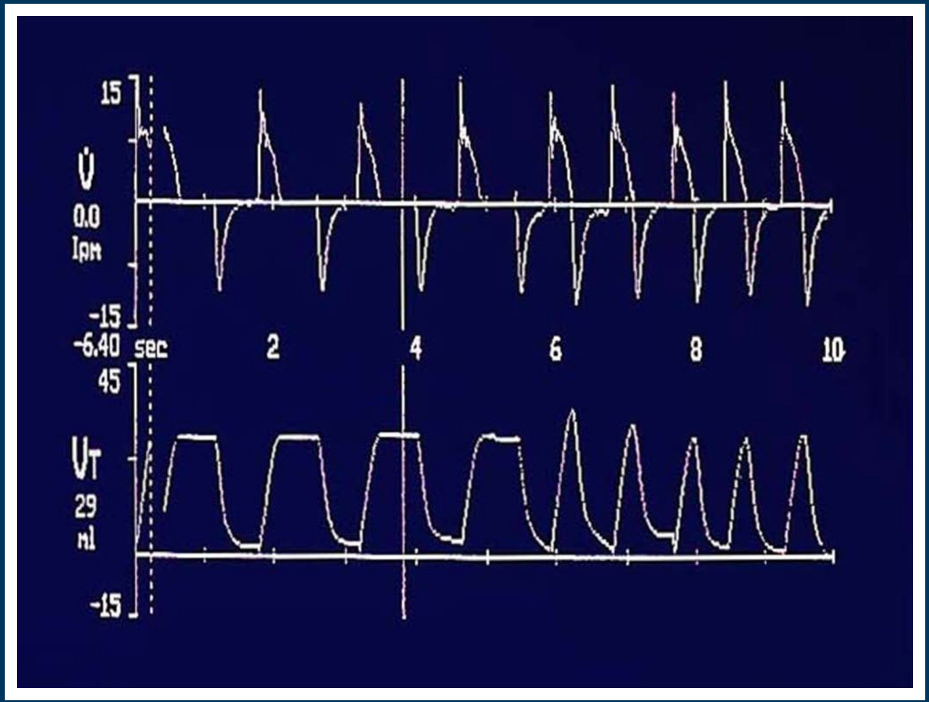
Cycling

- Time
- Flow



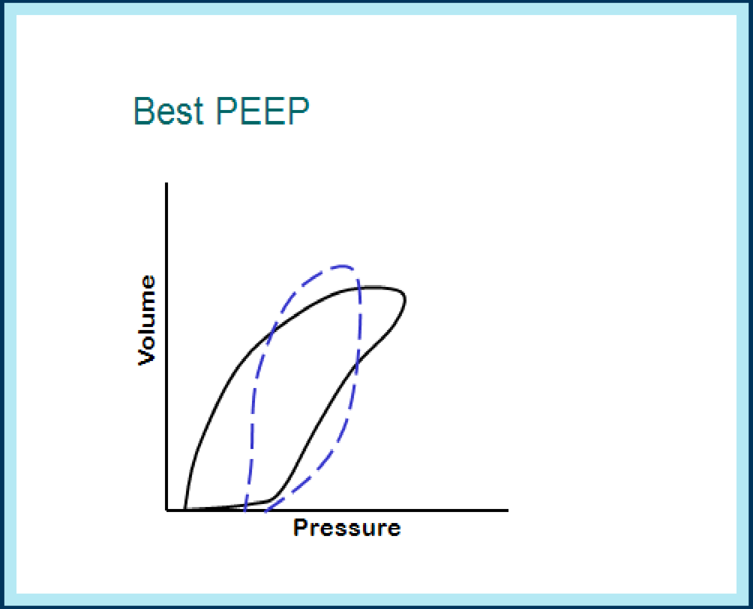
Inspiratory Time

- Time Constant
- I:E ratio
- Gas trapping



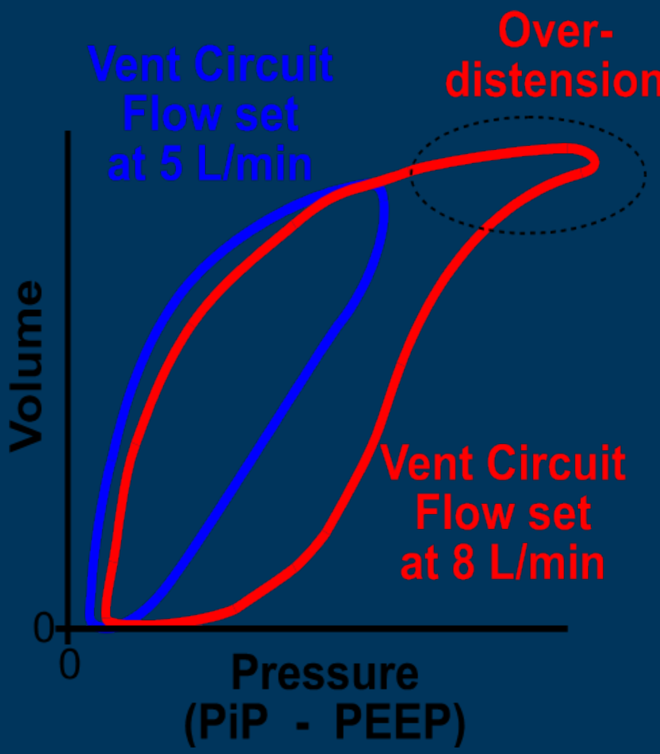
PEEP

- One size does not fit all
- Optimize inflation
- Find best compliance



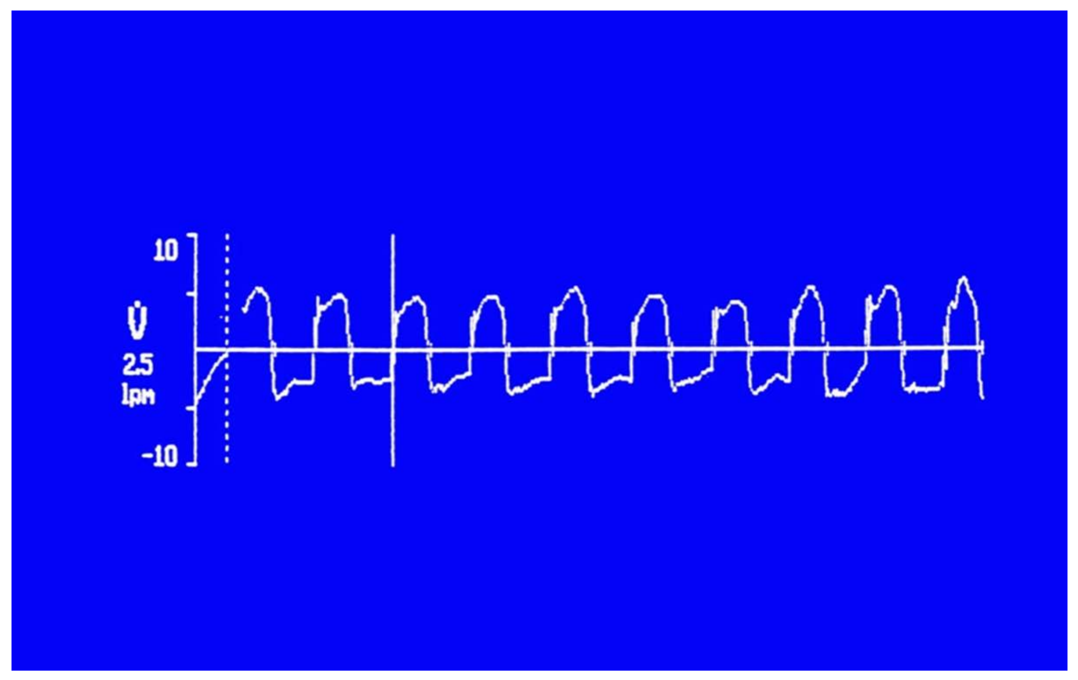
Flow

- Avoid rheotrauma
- If too high
  - ➢ Turbulence
  - ➢ Inadvertent PEEP
- If too low
  - ➢ Flow starvation
  - ➢ Inability to reach PIP or desired Vt



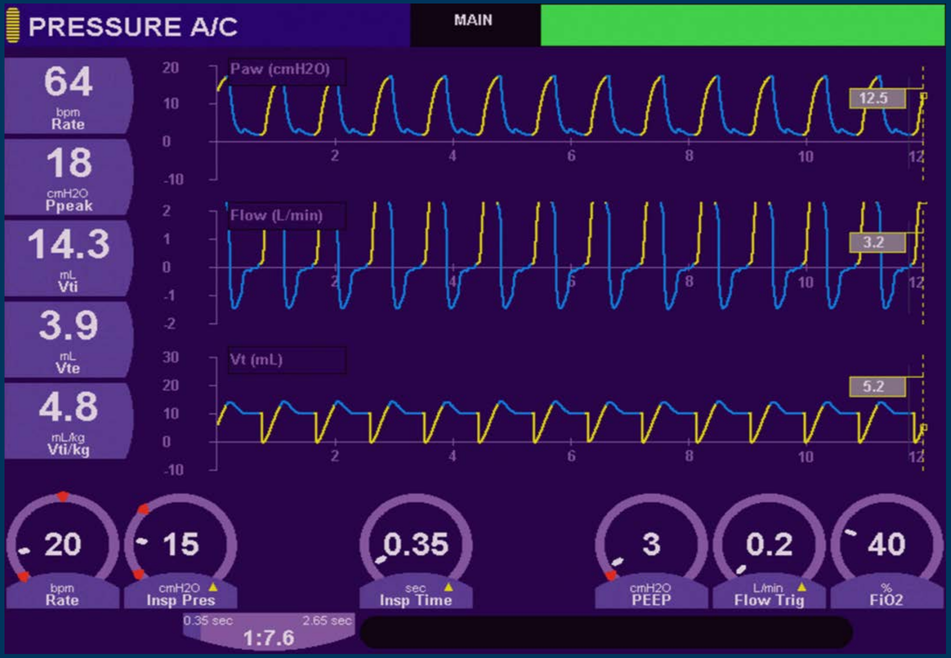
Rate

- Encourage spontaneous breathing
- Provide adequate safety net
- Follow minute ventilation, if possible



Trigger

- Set at lowest level that avoids autocycling



Oxygen Therapy:
Can We Get It Right?

Introduction

Oxygen

- An integral part of all respiratory support
- One of the most commonly used drugs in the neonatal intensive care unit

Introduction

Goal of Oxygen Therapy:

- To achieve adequate delivery of oxygen to the tissues without creating oxygen toxicity

The Controversy

- The recent trials of oxygen therapy suggest that lower SpO2 can reduce severe retinopathy of prematurity (ROP), but is associated with a higher mortality.
- Babies often display wide fluctuations in SpO2
- How can we better control both oxygen delivery and limit these fluctuations?

Closed-Loop Control of Oxygenation

Background

- Most preterm infants exhibit spontaneous fluctuations in SpO_2.
- Preterm infants often require supplemental oxygen, increasing risk of:
  - Retinopathy of prematurity
  - Lung injury
  - Oxidative stress injury
  - Necrotizing enterocolitis

Background

- **Delayed responses to these fluctuations result in hyperoxemic and hypoxemic episodes, as well as:**
  - **Increased risk of impaired oxygen delivery**
  - **Increased risk of ROP and chronic lung disease**

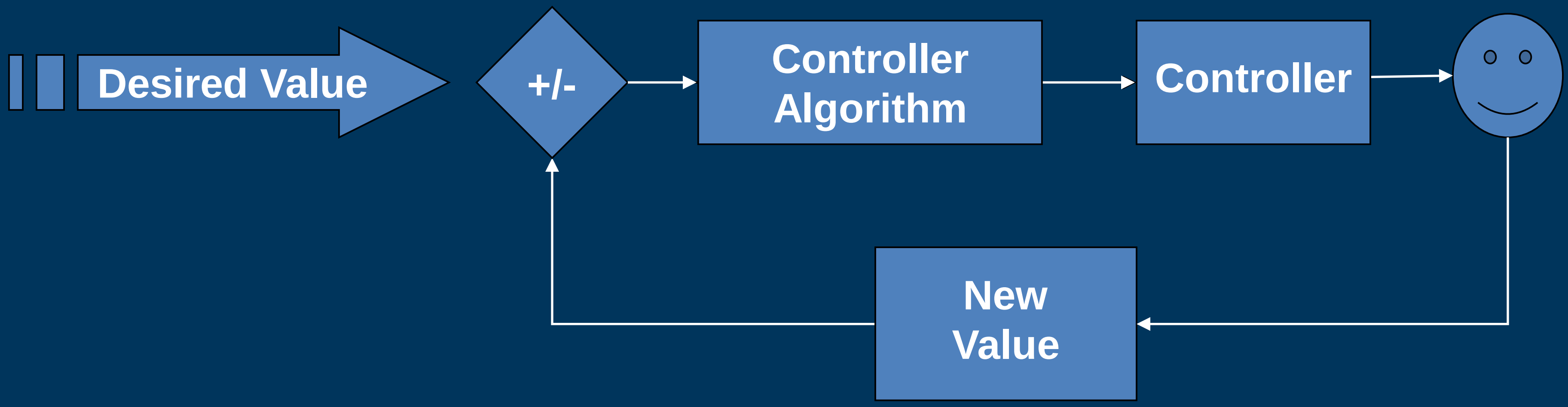
Background

- Only about 50% of the time, is SpO_2 within the desired range.
  - Laptook et al (J Perinatol 2006)
    - N=74, 1 center, 19 months
    - 27% below, 58% within, 15% above
  - Hagadorn et al (Pediatrics 2006)
    - N=84, 14 centers (3 countries), 8 months
    - 16% below, 48% within, 36% above

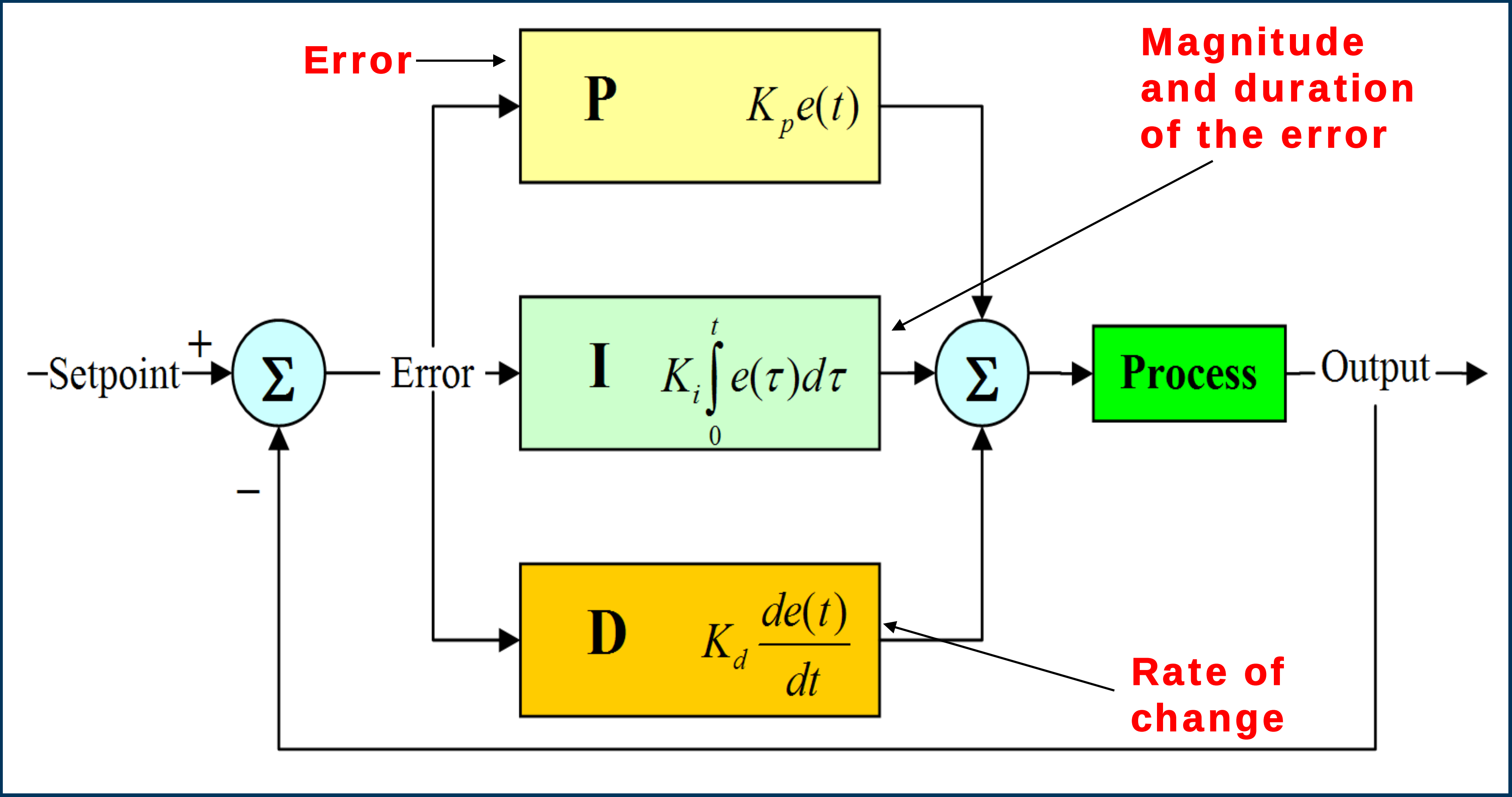
“The computer allows you to make mistakes faster than any other invention, with the possible exception of handguns and alcohol.”

- Mitch Ratcliffe

Closed-Loop



Closed-Loop



Proportion – Integral - Derivative

Closed-Loop Control

- **Goal**
  - **Minimize time out of target SpO_2 range, especially high SpO_2**
  - **Reduce modulation of SpO_2**

Algorithm Goals

- Normoxemia
  - Minimize change in SPO_2
  - Gradually wean FIO_2
- Hypoxemia
  - Rapidly increase FIO_2 to bring SPO_2 in bounds
    - Reduce FIO_2 as SpO_2 approaches target.
- Hyperoxemia
  - Minimize the further increase in SPO_2
  - Gradually wean FIO_2

CLiO$_2$ Pilot Trial Summary

- **In ventilated infants with frequent episodes of hypoxemia, automated regulation of FiO$_2$ in comparison to routine care:**
  - **Increased time within intended SpO$_2$ range**
  - **Reduced severe hyper- and hypoxemia**
  - **Reduced the fraction of inspired O$_2$**
  - **Reduced manual interventions**

Claure, et al, J Pediatr (2009) 155: 640-5

Automated Adjustment of Inspired Oxygen in Mechanically Ventilated Preterm Infants: A Multicenter Crossover Trial

N. Claure [1], E. Bancalari [1], C. D'Ugard [1], L. Nelin [2], M. Stein [2], R. Ramanathan [3], R. Hernandez [3], S.M. Donn [4], M. Becker [4] and T. Bachman [5].

[1] University of Miami
[2] Ohio State University
[3] University of Southern California
[4] University of Michigan
[5] California State University

Hypotheses

- **In ventilated preterm infants with frequent fluctuations in oxygenation, automated FiO_2 adjustment is more effective than standard care in maintaining SpO_2 within the intended range <u>under routine clinical conditions</u>**

Hypotheses

- **Automated FiO_2 adjustment reduces severe hyper- and hypoxemia, supplemental O_2 and the number of manual FiO_2 adjustments**

Objective

- **To evaluate the efficacy and safety of automated FiO_2 adjustment in maintaining SpO_2 within the intended range in preterm infants with frequent spontaneous episodes of hypoxemia in the standard clinical setting in a multicenter crossover trial**

Study Approval

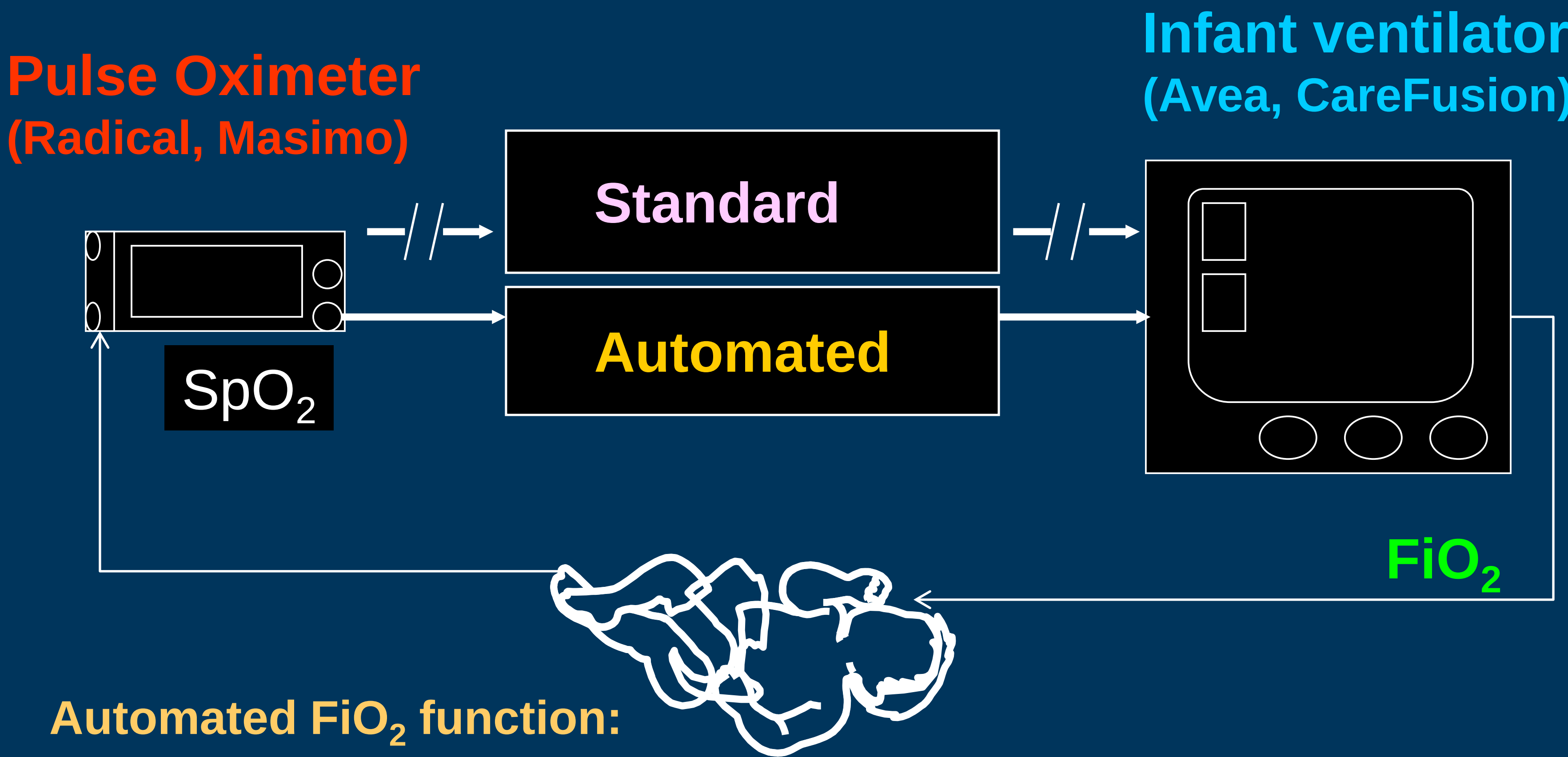
- **Approved by the each institution's IRB**
- **Conducted under approval for use of the "Automated FiO_2 Adjustment Function" of the Avea infant ventilator as an investigational device by the US FDA (G060031/S009)**
- **Written informed parental consent**

Eligibility

- Preterm infants on supplemental O_2 and mechanical ventilation
- Frequent spontaneous episodes of hypoxemia ($SpO_2 < 80\%$, $\geq$ 4 episodes per 8 hrs., during previous 24 hrs.)
- Hemodynamically stable
- Absence of major congenital anomalies
- Absence of seizure activity
- Absence of ongoing sepsis or meningitis

Study Protocol

- Two consecutive periods:
  - 24 hrs. with FiO_2 adjusted routinely by clinical staff (Standard)
  - 24 hrs. of automated FiO_2 adjustment (Automated)
- Sequence assigned by random blocks per center
- The intended SpO_2 range for both periods was 87 - 93%



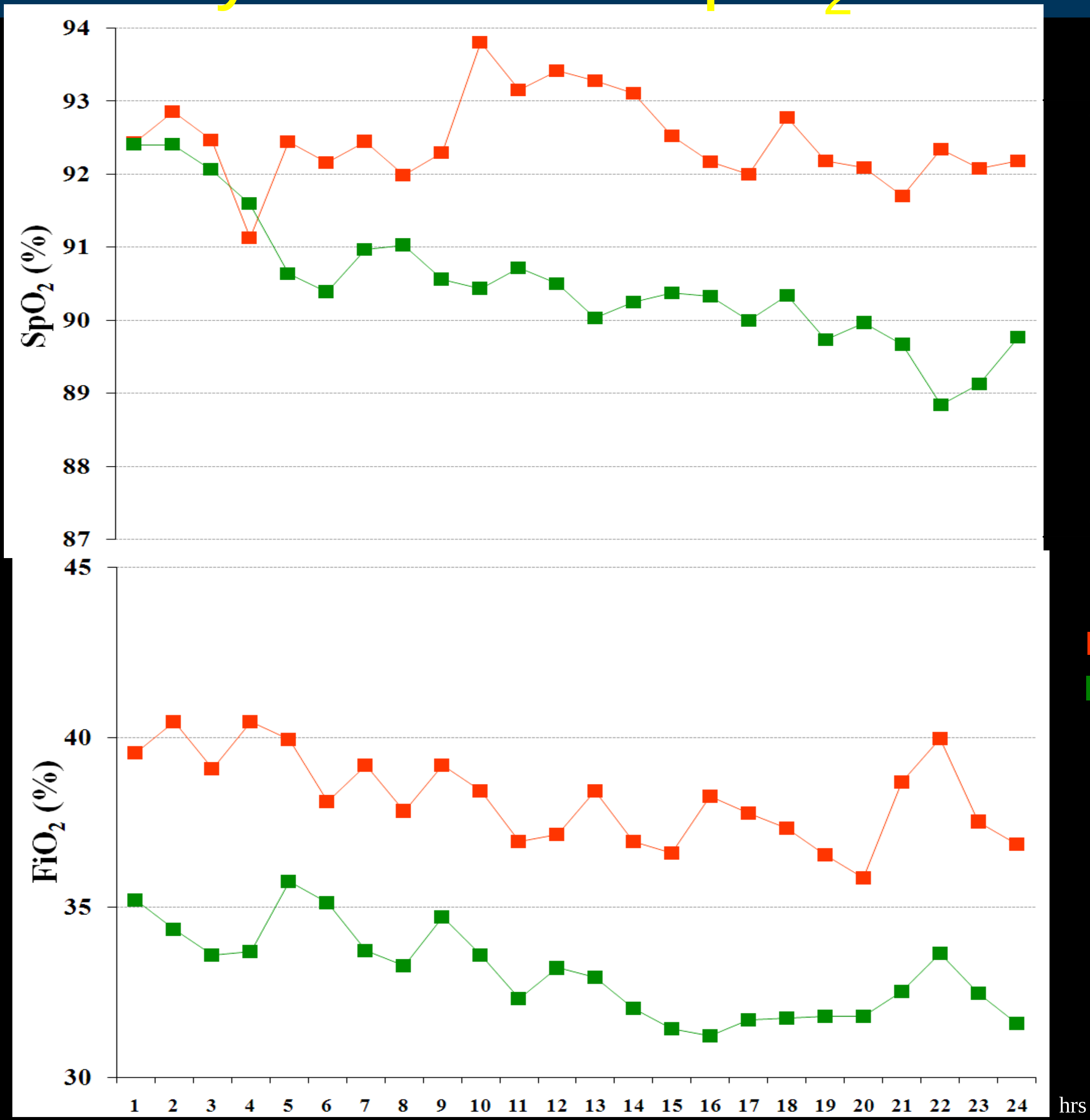
Automated FiO_2 function:

- FiO_2 is ↑ or ↓ step-wise if SpO_2 is < or > the intended range
- Magnitude and frequency of FiO_2 adjustments are determined by:
  - difference between SpO_2 and intended range
  - time outside range
  - trend in SpO_2
  - basal FiO_2
- Basal FiO_2 is adjusted gradually to keep SpO_2 within range

Study Population

Birth weight:	**671 ± 156 g**
Gestational age:	**25 ± 2 w**
Postnatal age:	**26 ± 15 d**
Rate:	**27 ± 10 bpm**
PIP:	**22 ± 6 cm H_2O**
PEEP:	**6 ± 1 cm H_2O**
PSV:	**8 ± 2 cm H_2O**
FiO_2:	**37 ± 11 %**

Hourly Median SpO_2 and FiO_2

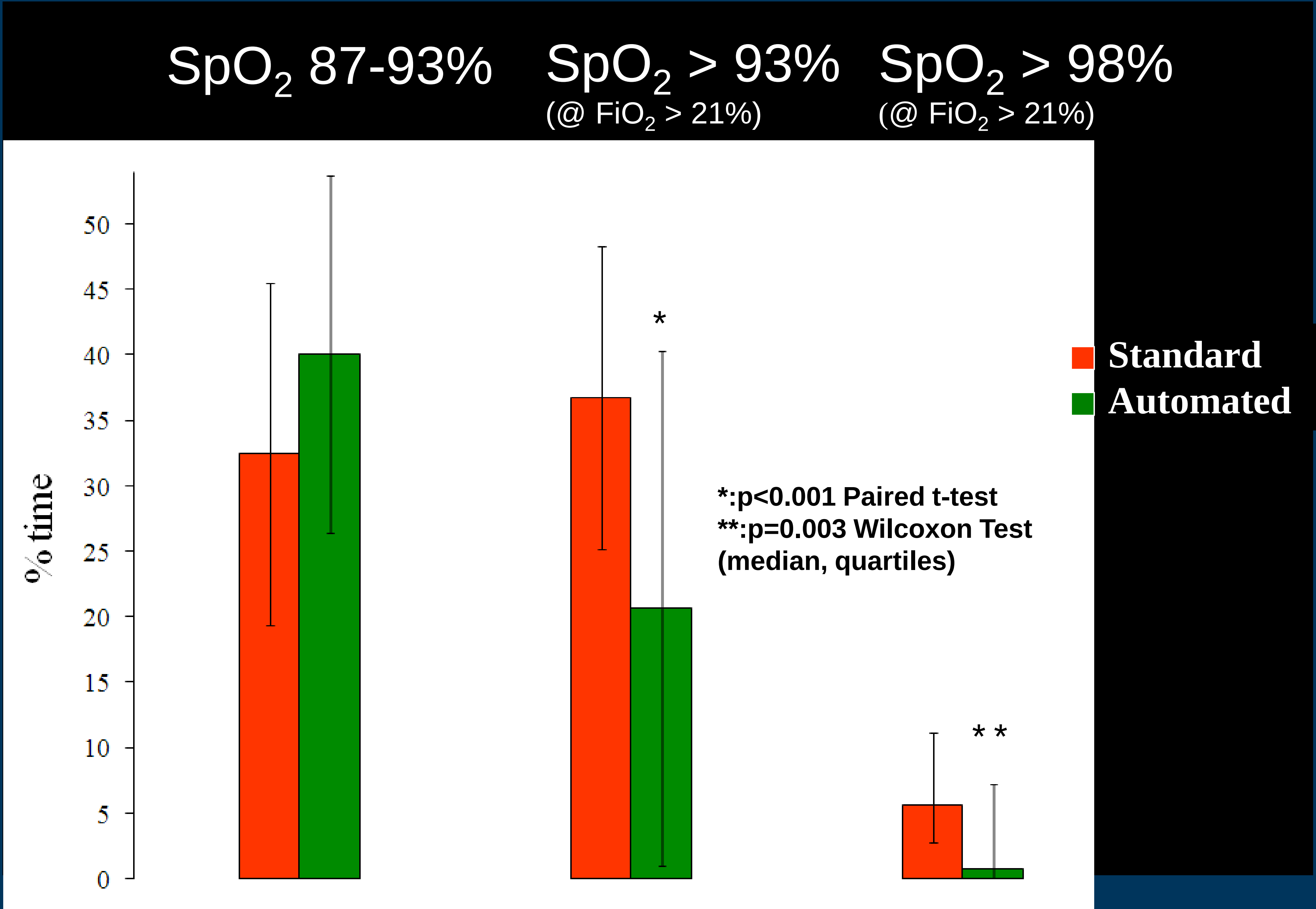


Intended range

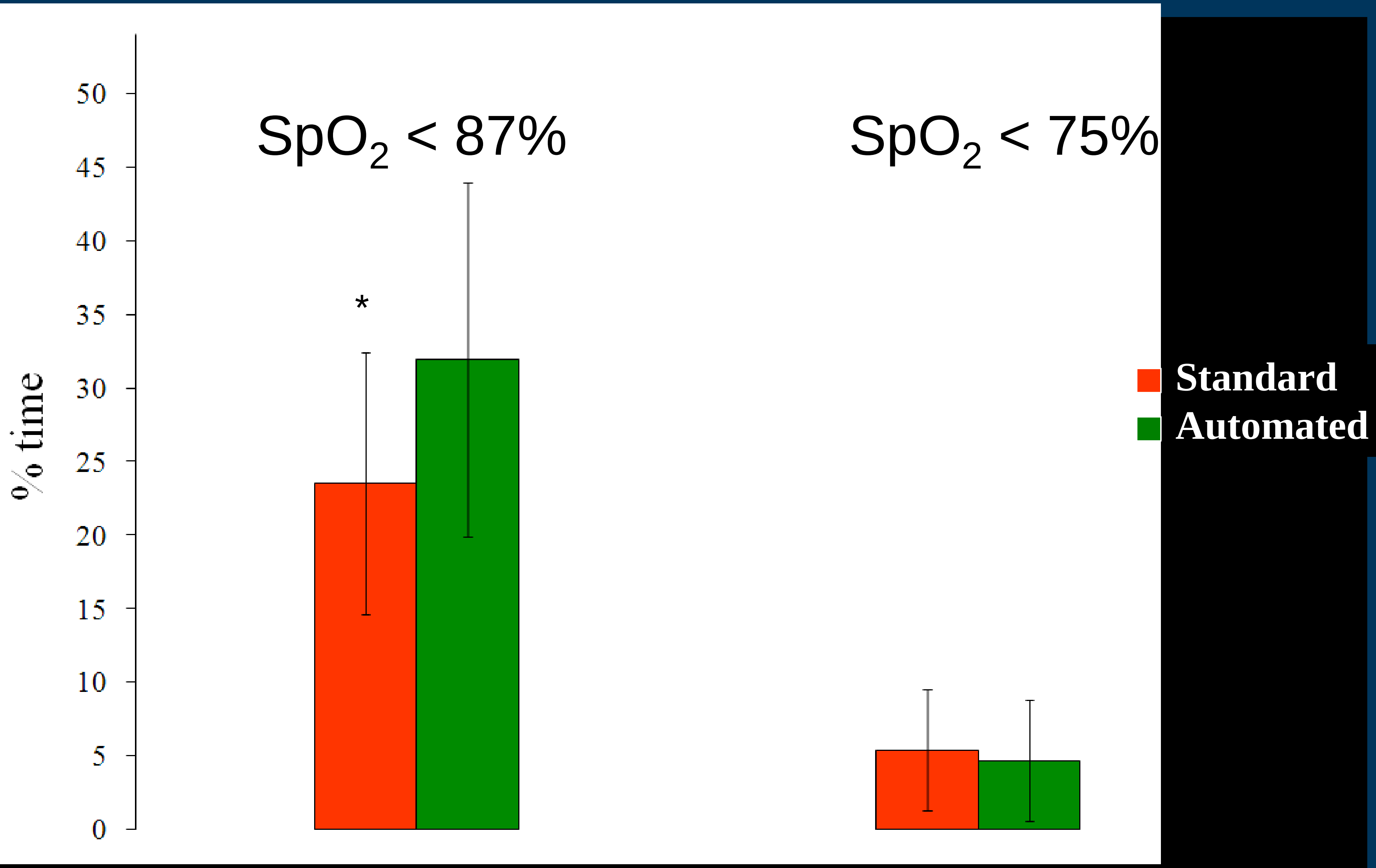
Standard
Automated

*:p<0.05 Two way RM ANOVA

Time Within or Above Intended Range

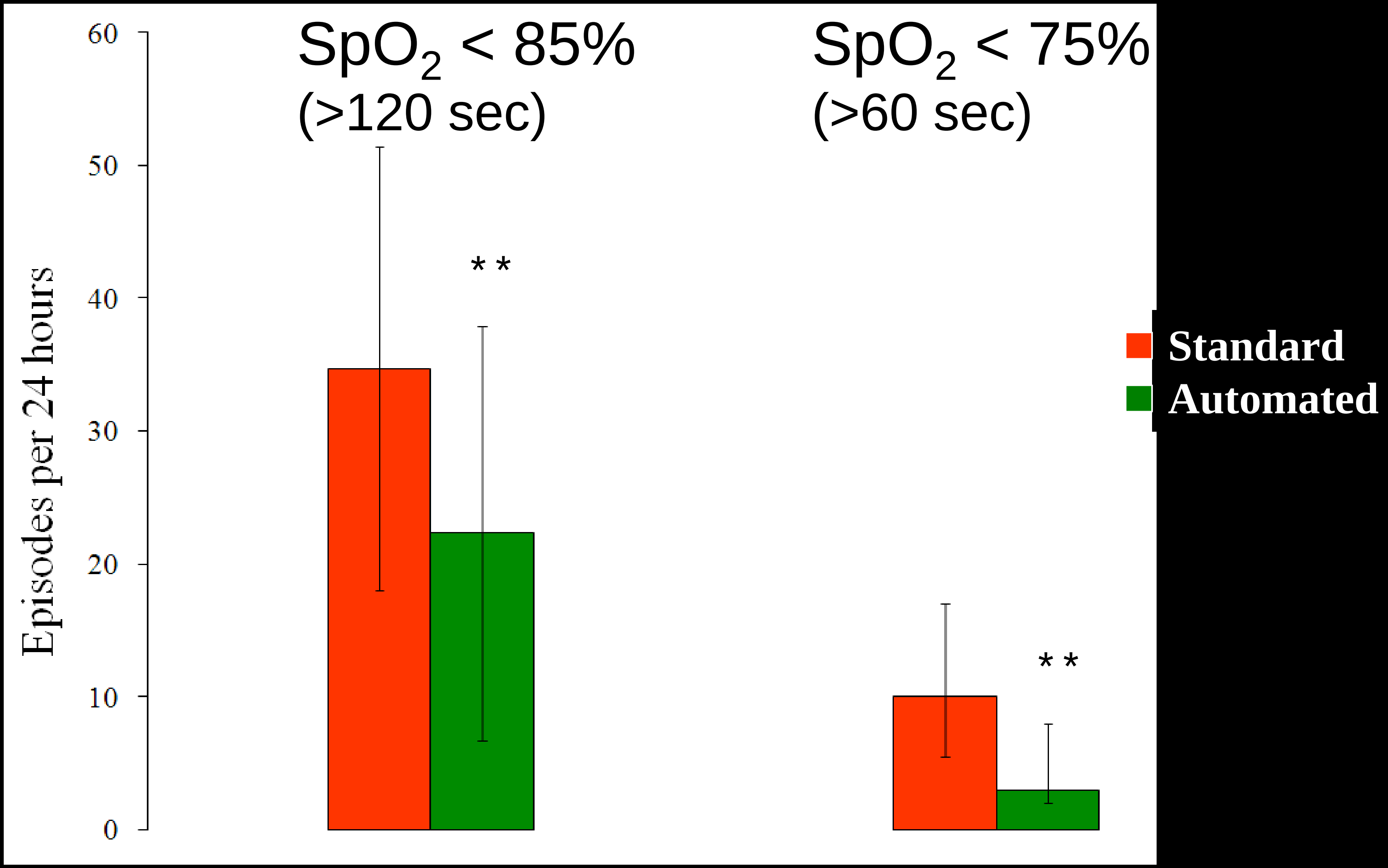


Time Below Intended Range



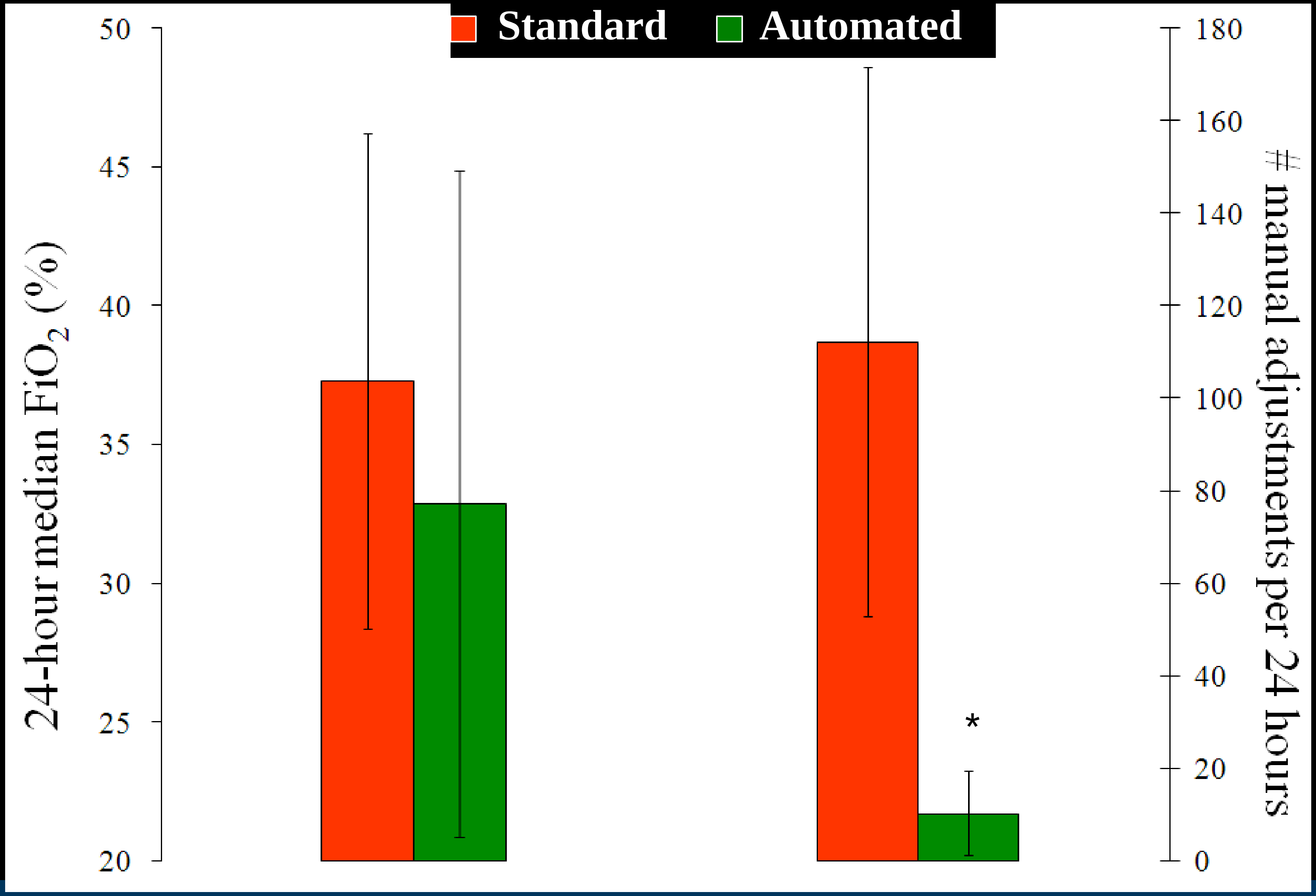
*:p<0.001 Paired t-test (mean±SD)

Prolonged Episodes Below Intended Range



**:p=0.001 Wilcoxon Signed Rank Test (median and 25th – 75th percentile)

24 Hr Median FiO_2 and Manual Adjustments



*:p<0.001 Paired t-test (mean±SD)

Conclusions

These data from a group of preterm infants with frequent fluctuations in SpO_2, obtained under standard clinical conditions, showed that:

Automated FiO_2 adjustment

- **improved maintenance of SpO_2 within the intended range**
- **reduced hyperoxemia, supplemental O_2, and staff workload**

Conclusions

- **The increased number of mild episodes with SpO_2 below the intended range is likely related to FiO_2 weaning and avoidance of hyperoxemia.**

Limitations

- Automated FiO_2 should not be a substitute for more appropriate observations or interventions
- Automated FiO_2 may give an excessive sense of confidence and lead to reduce attentiveness

Limitations

- **Automated FiO_2 is dependent on pulse oximetry accuracy**
- **Observed differences in this study may be relative to the effectiveness of standard care**
- **Physiologic consequences of different targeted SpO_2 ranges should be taken in consideration**


1 3 5
2 4 R

WEANING INFANTS FROM MECHANICAL VENTILATION

Weaning

The process of transferring the work of breathing from the ventilator to the baby.

Weaning

- Weaning- or at least the consideration to wean- should begin as soon as a baby is intubated.

Weaning and Extubation

- Still largely determined by personal preferences
- Tends to be experiential or anecdotal
- Very little clinical data

Weaning is a Dynamic Process

- Changing disease and/or patient status
- Interaction between heart and lungs (e.g., PDA)
- Caloric intake vs. expenditure
- Relationship between central control of breathing and respiratory muscles

Physiologic Essentials for Extubation

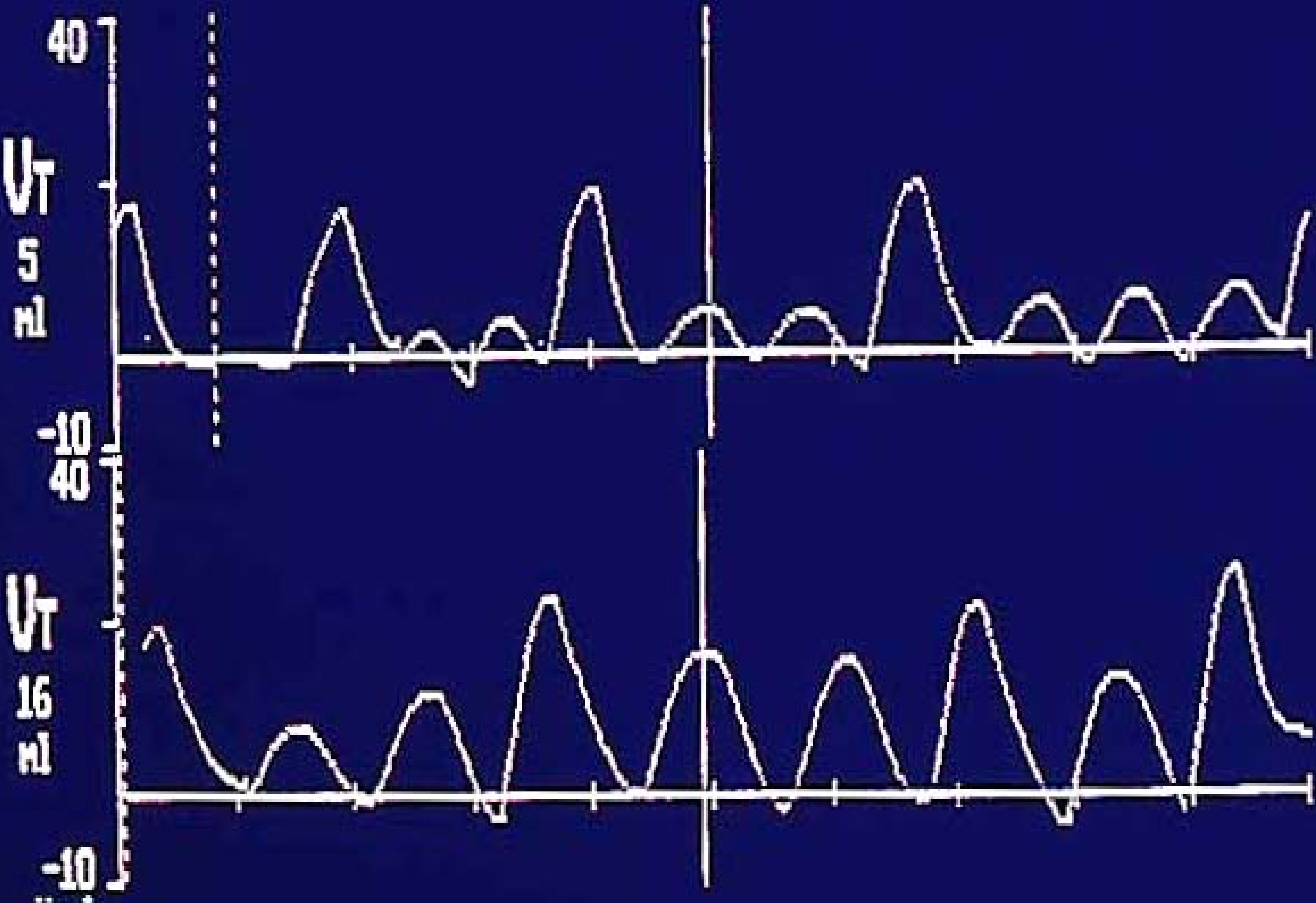
- Reliable respiratory drive
- Neuromuscular competence
- Reduction in respiratory system load

Impediments to Successful Weaning

- Infection
- Neurologic dysfunction
- Neuromuscular incompetence
- Inadequate caloric intake
- Excessive fat/CHO intake

Impediments to Successful Weaning

- Electrolyte imbalance
- Metabolic alkalosis
- Congestive heart failure
- Anemia
- Pharmacologic agents



40
VT
5
ml
-10
40
VT
16
ml
-10

"The biggest reason for failure to wean is failure to wean."

-Donn