# Closed Loop Control of Mechanical Ventilation : State of the Art

Rich Branson

## Why closed loop control?

- Reduce practice variation
- Enhance safety
- Respond to changes in patient condition which cannot be accomplished given staffing ratios and severity of illness
- Facilitate ventilator discontinuation
- Escalate therapy when required
- Provide standard of care regardless of environment and caregiver skill

## What is closed loop?

- Feedback control – automatic manipulation of an output variable based on the measurement of an input variable(s)
- All ventilators utilize closed loop control
- Pressure support is a simple example of closed loop control – flow is manipulated to maintain a pre-selected pressure

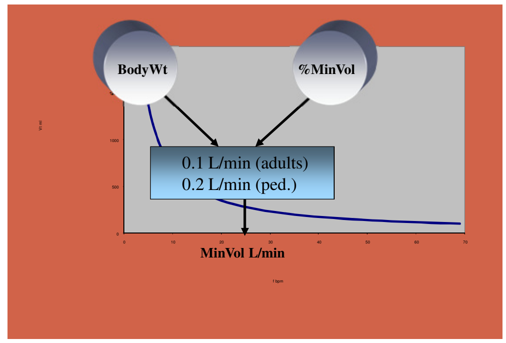
## Current State of the Art

- Mandatory minute volume (MMV)
- Adaptive pressure control (PRVC, APV, Volume control +, AutoFlow, etc)
- Adaptive support ventilation (ASV)
- AutoMode
- Proportional Assist (PAV)
- Neurally Adjusted Ventilatory Assist (NAVA)
- SmartCarePS

## On the Horizon

- Closed loop FIO2
- Closed loop FIO2/PEEP
- Complete closed loop control (Intellivent)

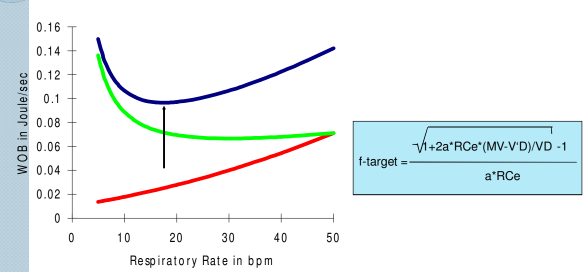
## Target Minute Ventilation

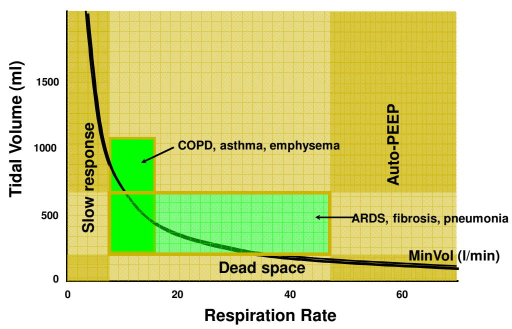



## Adaptive Support Ventilation

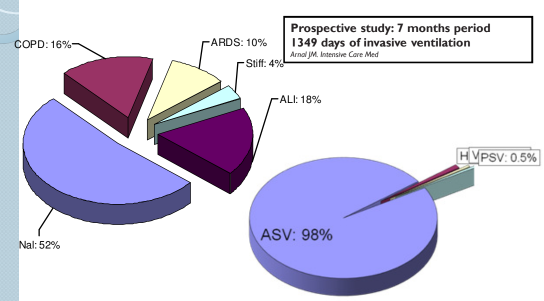
- Uses body weight and Otis' WOB formula for determining variables
- Clinician sets PEEP, $FIO_2$, and Pmax
- Ventilator algorithm chooses initial settings and modifies settings on a breath to breath basis
- Level of support determines weaning

## Calculate Optimal Breath Pattern: Minimal WOB






# ASV Performance in Different Patient Diseases




# Is ASV on Target?

**Utilization of an Automatic Mode of Ventilation (ASV) in a Mixed ICU population: Prospective Observational Study**

J-M. Arnal[a] M.D., C. Nafati[a] M.D., M. Wysocki[b] M.D., Y-S. Donati[a] M.D., I. Granier[a] M.D., J. Durand-Gasselin[a] M.D.

Vt range 5.6-10.4

| | Normal lung | Obstructive lung disease | ARDS | Restrictive lung disease | Acute lung injury |
|---|---|---|---|---|---|
| %ASV | 116 ±25 | 119 ±29 NS | 131 ±25 ** | 137 ±31 ** | 130 ±29 ** |
| PEEP ($cmH_2O$) | 5.2 ±1.5 | 6 ±2.5 ** | 9 ±3.3 ** | 5 ±1.7 NS | 6.3 ±2.2 ** |
| Peak pressure ($cmH_2O$) | 22 ±6 | 24 ±7 ** | 30 ±6 ** | 27 ±6.7 ** | 25 ±6 ** |
| Vt (ml) | 516 ±131 | 585 ± 113 ** | 453 ± 112*** | 386 ± 91 ** | 503 ±109 NS |
| Ftot (C/mn) | 17 ±5 | 16 ± 6 * | 20 ± 6 ** | 23 ± 6 ** | 18 ±6 ** |
| Fspont (c/mn) | 9 ±10 | 9 ± 10 NS | 6 ± 10 ** | 13 ± 13 NS | 9 ±11 NS |
| I:E | 0.50 ±0.17 | 0.41 ±0.15 ** | 0.62 ±0.27 ** | 0.54 ± 0.24 NS | 0.48 ±0.17NS |
| RCe (s) | 0.78 ±0.28 | 1.13 ±0.70 ** | 0.55 ±0.21 ** | 0.4 ±0.15 ** | 0.70 ±0.22 ** |
| Cstat (ml/$cmH_2O$) | 46 ±23 | 56 ±25 ** | 30 ±14 ** | 22 ±10 ** | 41 ±20 ** |
| Rins ($cmH_2O$.s/l) | 16 ±7 | 16 ±10 NS | 17 ±7 NS | 14 ±9 NS | 16 ±7 NS |
| pH | 7.40 ±0.07 | 7.37 ±0.09 ** | 7.29 ±0.14 ** | 7.37 ±0.11 NS | 7.38 ±0.08 ** |
| $PaO_2/FiO_2$ | 330 ±113 | 248 ±115 ** | 140 ±48 ** | 267 ±106 ** | 215 ±61 ** |
| $PaCO_2$ (mmHg) | 40 ±7 | 44 ±11 ** | 49 ±9 ** | 45 ±9 ** | 42 ±7 ** |
| Vt/IBW (ml/Kg) | 8.3 ±1.3 | 9.3 ±2.1 ** | 6.8 ±1.2 ** | 7.0 ±1.1 ** | 8.1 ±1.2 NS |

# ASV European Multicenter Study

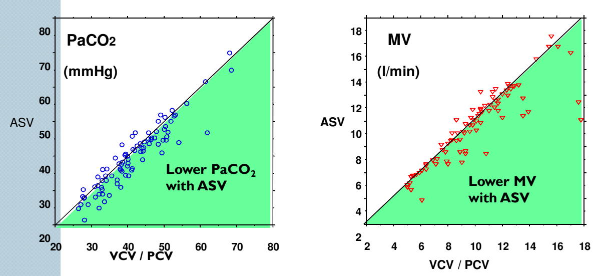
86 patients (+ 1 drop out for respiratory instability)
59 males, 27 females
Age (years): 63 (range 28-85)
Actual Body Weight (Kg): 78 Kg (range 44 - 179)
Ideal Body Weight (Kg): 66 Kg (range 43 - 85)

**Respiratory Disease:**
- Normal lungs 30%
- Restricted 34%
- Obstructed 36%

**Conventional ventilation:**
- VCV 60%
- PCV 40%

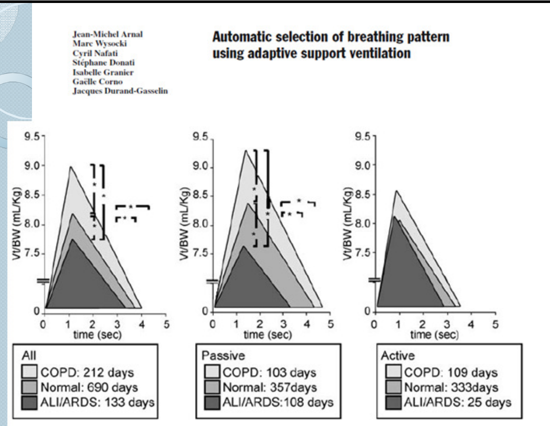
**Humidification:**
- HH 76%
- HME 24%

## Results - PaCO2 & MV

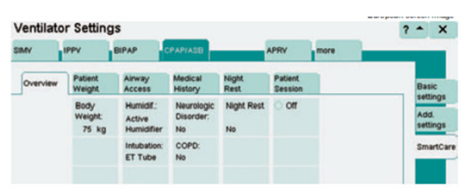



## SmartCare (NeoGanesh)

- Pressure support ventilation
- Input :frequency, Vt, PetCO2 – Zone of acceptable ventilation
- Output: Pressure
- Adjustments every 2-5 minutes
- 12<f<28 b/min, Vt – 300 mL, PetCo2 < 55 mmHg
- If PSV is stable – suggests a SBT




## SmartCare PS



## A Multicenter Randomized Trial of Computer-driven Protocolized Weaning from Mechanical Ventilation

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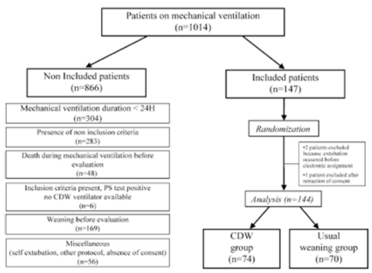


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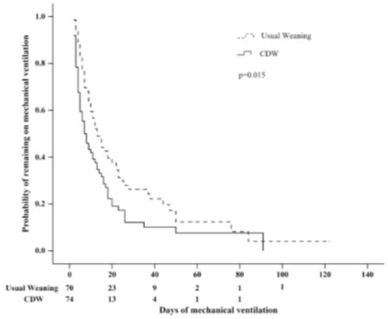


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TABLE 3. COMPLICATIONS OF MECHANICAL VENTILATION

| Complication | CDW Group (*n* = 74) | Usual Weaning Group (*n* = 70) | p Value |
|---|---|---|---|
| Reintubation within 72 h | 12 (16) | 16 (23) | 0.40 |
| Any reintubation | 17 (23) | 23 (33) | 0.20 |
| Need for noninvasive ventilation | 14 (19) | 26 (37) | 0.02 |
| Self-extubation | 8 (11) | 7 (10) | 0.99 |
| Tracheostomy | 12 (16) | 13 (19) | 0.83 |
| Mechanical ventilation duration for > 14 d | 12 (16) | 20 (29) | 0.11 |
| Mechanical ventilation duration for > 21 d | 5 (7) | 11 (16) | 0.11 |

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# Automated Weaning

TABLE 2. COMPARISON OF OUTCOME BETWEEN STUDY GROUPS

| Outcome | CDW Group (*n* = 74) | Usual Weaning Group (*n* = 70) | p Value |
|---|---|---|---|
| Time to first extubation* | 2.00 (1.75–6.25) | 4.00 (2.00–8.25) | 0.02 |
| Duration of mechanical ventilation until first extubation* | 6.50 (3.00–12.25) | 9.00 (5.75–16.00) | 0.03 |
| Time to successful extubation† | 3.00 (2.00–8.00) | 5.00 (2.00–12.00) | 0.01 |
| Total duration of mechanical ventilation† | 7.50 (4.00–16.00) | 12.00 (7.00–26.00) | 0.003 |
| Intensive care length of stay | 12.00 (6.00–22.00) | 15.50 (9.00–33.00) | 0.02 |
| Hospital length of stay | 30.00 (17.00–54.75) | 35.00 (21.00–60.25) | 0.22 |

ISSUES

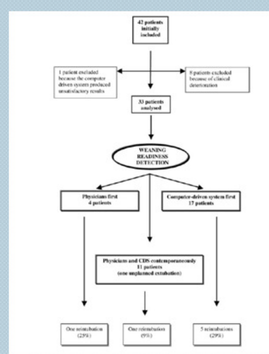
- Multicenter trial (5 sites)
- Four sites had protocols
- Not all sites used spontaneous breathing trials
- Compliance with protocols was not determined
- Success can be the result of the comparator

Lellouche F AJRCCM 2006;174:894-900

# AUTOMATED WEANING

- Improved matching of ventilator output to patient need
- Reducing practice variation
- Complimenting clinician knowledge
- Early detection of weaning readiness

Bouadma L ICM 2005;31:1446-1450




# Background

- Oxygen represents 20%-30% of the weight of supplies for transport.
- Liquid oxygen provides the greatest volume but has storage, position, and off gassing issues.
- Cylinders are heavy and carry an explosive risk.
- Reducing oxygen usage has potential advantages.

# Automated Weaning

| | MMV | ASV | SmartCare |
|---|---|---|---|
| Principle | Rate or PS to meet MV | Wt based VT/VE Exp time constant to set I:E | PS to maintain pt comfort – f, VT, ETCO2 |
| Breath type | VC-CMV, PS | Dual control SIMV/PS | PS |
| Set Variable | f and MV | MV/Pmax | None |
| Adaptation | 7.5-10.0 sec | Breath to Breath | 2-5 mins |
| Mode | CMV, SIMV, PS | SIMV+PS | PS |
| Automated SBT | No | No | Yes |

Burns KE ICM 2008;34:1757-1765

# Study Goals

- Closed loop control of inspired oxygen concentration ($FiO_2$) using arterial oxygen saturation ($SpO_2$) can
  - Reduce oxygen usage during transport.
  - Reduce the number of low $SpO_2$ conditions.
  - Provide normoxemia vs. hyperoxemia.

## Clinical Implications

- Reduced oxygen usage will reduce the weight and cube of required oxygen stores.
- Prevention of hypoxemia will improve outcome (a single episode of hypoxemia in closed head injury is associated with negative outcomes.)
- Closed loop can provide appropriate oxygenation for the patient from injury to definitive care.

## Description

- $FiO_2$ automatically adjusted based on $SpO_2$, $SpO_2$-target difference and trends in $SpO_2$.
- $SpO_2$ target is 94% (adjustable).
- If $SpO_2 \leq 88\%$, $FiO_2$ increases to 1.0.
- A combination of fine and coarse control.
- If $SpO_2$ signal is lost, $FiO_2$ remains constant.
- If $FiO_2$ increases > 10%, an alert is provided.

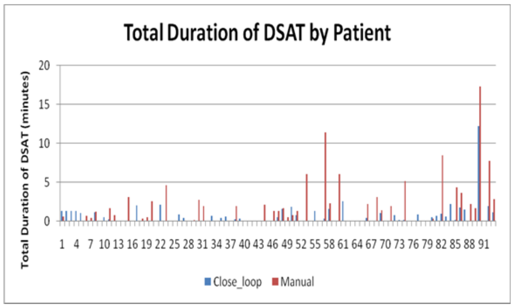
## Safety & Efficacy

- Safety – Prevention of hypoxemia ($SaO_2 \leq$ 88%)
- Efficacy – Ability of controller to maintain $SaO_2$ target (94% ± 2%)
- Oxygen conservation

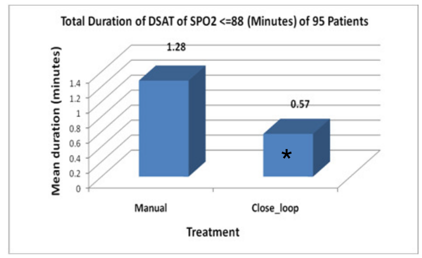
## Closed Loop $FiO_2$/$SpO_2$

- *Total enrollment n = 95*
- *Gender 84 men, 16 women*
- *Ethnicity 73 Caucasian, 21 African-American, 1 Asian*
- *Mean age - 35.3 ± 11.7*
- *Mean Glasgow Coma Score – 10.8 ± 3.9*
- *Mean Injury Severity Score – 34 ± 13*
- *Mean APACHE II – 20 ± 7*

## Duration of Desaturation per Patient

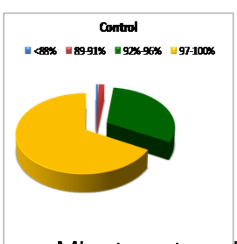


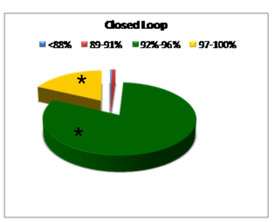

## Hypoxemia




*p = 0.0017

## Closed Loop $FiO_2/SpO_2$



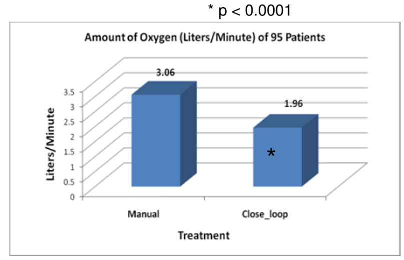




Minutes at each level of oxygen saturation

*p < 0.0001

## Closed Loop $FiO_2/SpO_2$

* p < 0.0001



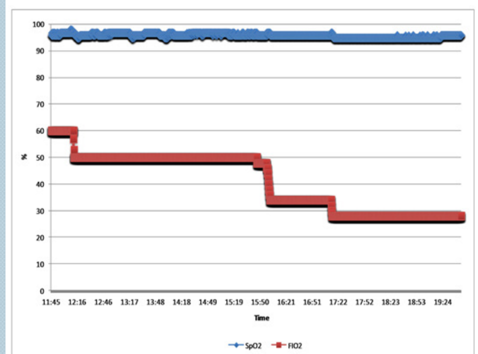

Oxygen conservation

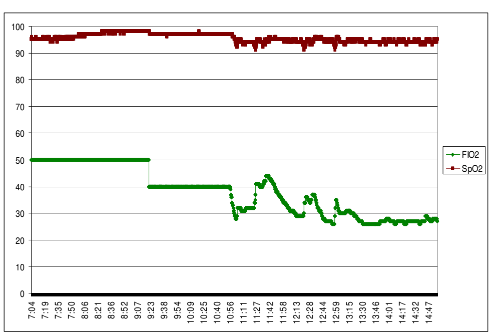
Closed loop 0.02-5.9 L/min

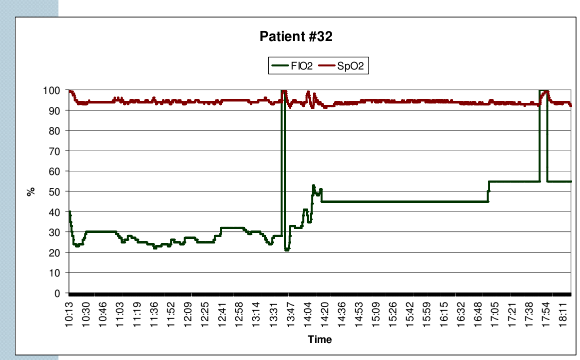
Manual 0.9-7.7 L/min

## $FiO_2$ Changes

- Closed loop 95.2 changes per 4-h period
- Control 4.4 changes per 4-h period
- 95 ± 49 vs. 4.46 ± 2 ($p < 0.0001$)



## Closed Loop FIO2 in Neonates

- Hypoxemia and hyperoxemia have known severe consequences in the newborn
- Ideal environment for closed loop control
- NICU staff cannot keep up with the number of changes required to maintain normoxemia
- Current investigations of a PID controller designed by Claure known as CLiO

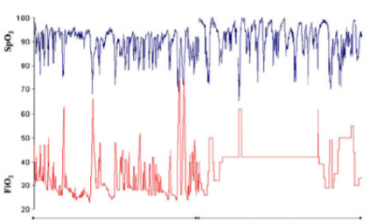
## Closed Loop FIO2 in Neonates

### Automated Adjustment of Inspired Oxygen in Preterm Infants with Frequent Fluctuations in Oxygenation: A Pilot Clinical Trial

Nelson Claure, MSc, PhD, Carmen D'Ugard, RRT, and Eduardo Bancalari, MD

**Objective** To assess the efficacy of a system for automated fraction of inspired oxygen ($FiO_2$) adjustment in maintaining oxygen saturation ($SpO_2$) within an intended range in preterm infants with spontaneous fluctuations in $SpO_2$.
**Study design** Sixteen infants (gestational age, 24.9 ± 1.4 weeks; birth weight, 678 ± 144 g; age, 33 ± 15 days) with frequent hypoxemia episodes underwent two 4-hour periods of $FiO_2$ adjustment by clinical personnel (routine) and the automated system (automated).
**Results** Compared with the routine period, the percent time within intended $SpO_2$ range (88%-95%) increased during the automated period (58% ± 10% versus 42% ± 9%; $P < .001$), whereas the percent time with $SpO_2$ higher than the intended range and ≥98% were reduced (9% ± 10% versus 31% ± 8% [$P < .001$] and 3% ± 5% versus 16% ± 9% [$P < .001$], respectively). Percent time with $SpO_2 < 88\%$ increased during the automated period (33% ± 7% versus 27% ± 9%; $P = .003$) because of more frequent episodes, whereas the time with $SpO_2 < 75\%$ did not differ. The 4-hour median $FiO_2$ was lower during the automated period (29% ± 4% versus 34% ± 5%; $P < .001$).
**Conclusion** Automated $FiO_2$ adjustment improved maintenance of $SpO_2$ within the intended range and reduced hyperoxemia and $FiO_2$. These findings should be examined in longer periods with standard clinical conditions and, eventually, in the context of randomized trials powered to detect clinically important effects on outcome. (*J Pediatr 2009;155:640-5*).

## Closed Loop FIO2 in Neonates




## Closed Loop FIO2 in Neonates

**Table I.** Time within or outside the intended $SpO_2$ range, and time in severe hypoxemia or hyperoxemia

| | Routine | Automated | *P* value |
|---|---|---|---|
| $SpO_2$ 88%-95 % (% of time) | 42 ± 9 | 58 ± 10 | <.001 |
| $SpO_2$ > 95 % (% of time) | 31 ± 8 | 9 ± 10 | <.001 |
| $SpO_2$ ≥ 98% (% of time) | 16 ± 9 | 3 ± 5 | <.001 |
| $SpO_2$ < 88% (% of time) | 27 ± 9 | 33 ± 7 | .003 |
| $SpO_2$ < 85% (% of time) | 22 ± 8 | 25 ± 7 | .1 |
| $SpO_2$ < 75% (% of time) | 6.6 ± 5.6 | 4.6 ± 3.4 | .114 |
| $SpO_2$ < 70% (% of time) | 2.5 (0.5-4.1) | 1.1 (0.2-1.7) | .005 |

Data in mean ± SD or median (25th-75th percentile).

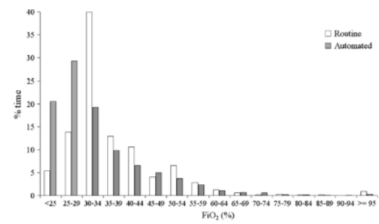
## Closed Loop FIO2 in Neonates

**Table II. Frequency and duration of episodes of hypoxemia and bradycardia**

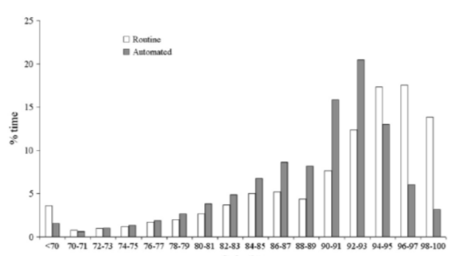
| Type of Episode | Routine | Automated | *P* value |
|---|---|---|---|
| **$SpO_2$ < 88%, ≥10 s** | | | |
| Episodes/hour | 15 ± 5 | 23 ± 5 | .001 |
| Episode duration (seconds) | 59 ± 16 | 52 ± 12 | .136 |
| **$SpO_2$ < 75 %, ≥10 seconds** | | | |
| Episodes/hour | 5.1 ± 3.5 | 4.8 ± 3.7 | .79 |
| Episode duration (seconds) | 32 (23-39) | 24 (16-27) | .013 |
| **$SpO_2$ < 85%, >120 s** (# of episodes per 4 hours) | 5.5 ± 3.8 | 2.5 ± 3.0 | .022 |
| **$SpO_2$ < 75%, >60 s** (# of episodes per 4 hours) | 3.9 ± 3.3 | 2.0 ± 2.8 | .022 |
| **Heart rate < 100 beats/min, ≥10 s** (# of episodes per 4 hours) | 2.0 (0.3-3.8) | 1.0 (0.0-2.0) | .01 |

Episodes of hypoxemia with $SpO_2$ < 75 % are a subset of those with $SpO_2$ < 88 %. Data in mean ± S.D. or median ($25^{th}$–$75^{th}$ percentile).

## Closed Loop FIO2 in Neonates



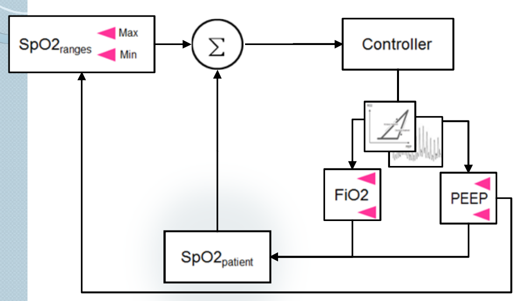

## Closed Loop FIO2 in Neonates




## Future

- Continued development
- Regulatory pathway? 510k or PMA?
- Thermostat for oxygen
- Regulatory burden may never be recovered
- How much would you be willing to pay for that?

# IntelliVent®: Oxygenation controller




# IntelliVent: PEEP / FIO2 combinations

**OXYGENATION GOAL: $PaO^2$ 55-80 mmHg or $SpO^2$ 88-95%**

**IntelliVent- user set PEEP limit so don't automatically ramp up to ARDSnet PEEP ranges**
**Lower/PEEP higher FIO2 used when increasing PEEP/FIO2**
**Higher PEEP table used when decreasing therapy (PEEP/FIO2).**
**FIO2's higher than table will start to wean q30 minutes if SpO2 in range**

ARDSnet

NIH NHLBI ARDS Clinical Network
Mechanical Ventilation Protocol Summary

**INCLUSION CRITERIA: Acute onset of**
1. $PaO_2/FiO_2 \leq 300$ (corrected for altitude)
2. Bilateral (patchy, diffuse, or homogeneous) infiltrates consistent with pulmonary edema
3. No clinical evidence of left atrial hypertension

**OXYGENATION GOAL: $PaO_2$ 55-80 mmHg or $SpO_2$ 88-95%**
Use a minimum PEEP of 5 cm $H_2O$. Consider use of incremental $FiO_2$/PEEP combinations such as shown below (not required) to achieve goal.

**Lower PEEP/higher FiO2**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **$FiO_2$** | 0.3 | 0.4 | 0.4 | 0.5 | 0.5 | 0.6 | 0.7 | 0.7 |
| **PEEP** | 5 | 5 | 8 | 8 | 10 | 10 | 10 | 12 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **$FiO_2$** | 0.7 | 0.8 | 0.9 | 0.9 | 0.9 | 1.0 |
| **PEEP** | 14 | 14 | 14 | 16 | 18 | 18-24 |

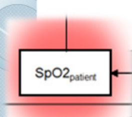
**Higher PEEP/lower FiO2**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **$FiO_2$** | 0.3 | 0.3 | 0.3 | 0.3 | 0.3 | 0.4 | 0.4 | 0.5 |
| **PEEP** | 5 | 8 | 10 | 12 | 14 | 14 | 16 | 16 |

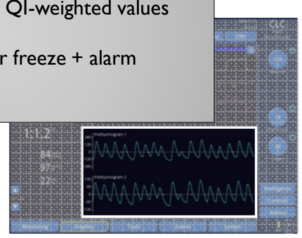
| | | | | | | |
|---|---|---|---|---|---|---|
| **$FiO_2$** | 0.5 | 0.5-0.8 | 0.8 | 0.9 | 1.0 | 1.0 |
| **PEEP** | 18 | 20 | 22 | 22 | 22 | 24 |

http://www.ardsnet.org/

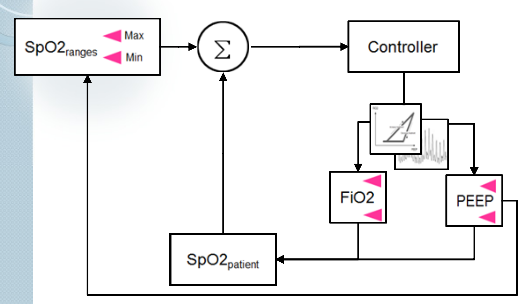
# IntelliVent®: Sensors/Signals



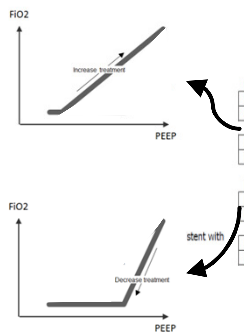

- Plethysmogram inspection
- Sensor reliability - QI derived
"SpO2" = 15 last QI-weighted values
- 2 sensors possible
- No "SpO2" = controller freeze + alarm



# IntelliVent: Oxygenation controller



## IntelliVent: Oxygenation controller: PEEP/FiO2




Lower PEEP/higher FiO2

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| $FiO_2$ | 0.3 | 0.4 | 0.4 | 0.5 | 0.5 | 0.6 | 0.7 | 0.7 |
| PEEP | 5 | 5 | 8 | 8 | 10 | 10 | 10 | 12 |

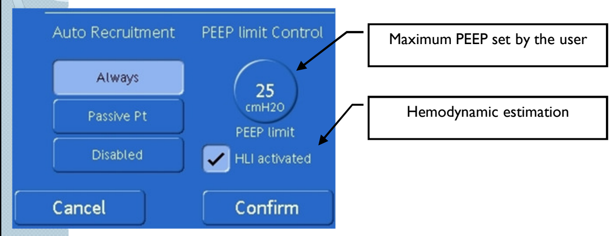
| | | | | | | |
|---|---|---|---|---|---|---|
| $FiO_2$ | 0.7 | 0.8 | 0.9 | 0.9 | 0.9 | 1.0 |
| PEEP | 14 | 14 | 14 | 16 | 18 | 18-24 |

Higher PEEP/lower FiO2

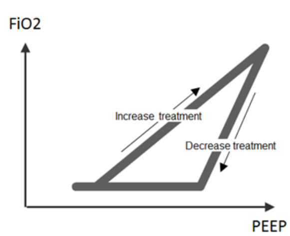
| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| $FiO_2$ | 0.3 | 0.3 | 0.3 | 0.3 | 0.3 | 0.4 | 0.4 | 0.5 |
| PEEP | 5 | 8 | 10 | 12 | 14 | 14 | 16 | 16 |

| | | | | | | |
|---|---|---|---|---|---|---|
| $FiO_2$ | 0.5 | 0.5-0.8 | 0.8 | 0.9 | 1.0 | 1.0 |
| PEEP | 18 | 20 | 22 | 22 | 22 | 24 |

## IntelliVent: Oxygenation controller: PEEP limit




## IntelliVent Oxygenation controller: PEEP/FiO2



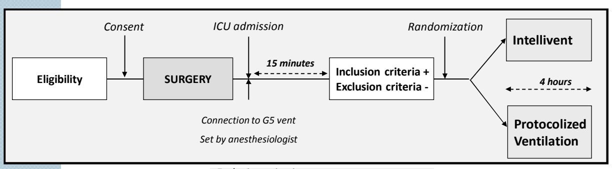

## PEEP/FIO2 rate of change

| Action | action definition |
|---|---|
| Decrease FiO2 stepwise | Decrease FiO2 by 5% of current FiO2 every 60s, minimal step size 1% |
| Increase FiO2 stepwise | Increase FiO2 by 10% of current FiO2 every 30s, minimal step size 1% |
| Decrease PEEP stepwise | Decrease PEEP every 360s (if quickly: 30s) by 2 cmH2O |
| Increase PEEP stepwise | Increase PEEP every 360s, Recruitment maneuver if last maneuver has been >= 6 min ago and PEEP step is >= 2 cmH2O |

**Note- if PEEP and FIO2 are changing, then FIO2 changes with PEEP, e.g. q 6 minutes**

## Conventional versus IntelliVent in post cardiac surgery

Inclusion Criteria:
- Hemodynamic stability
  - < 3 red-cell Tf units within last 15 min
  - Epi or norepinephrine below < 1 mg/h
  - Bleeding <100 ml within last 15 min
- No anuria



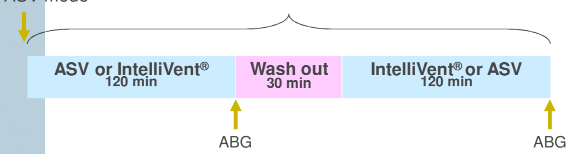

Exclusion criteria:
- Unexpected surgical procedure
- Major complication during surgery
- Early extubation expected (< 1 hour)
- Broncho-pleural fistula
- Study ventilator not available

Recordings:
- Data from the ventilator
- Manual interventions
- Time w optimal ventilation

Lellouche F, Am J Respir Crit Care Med 181;2010:A6035

## Prospective cross over controlled trial in Med-ICU

Inclusion
Consent
Baseline
ASV mode



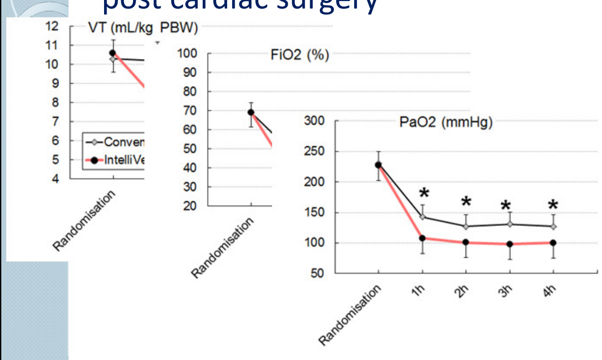

Continuous clinical monitoring (Invasive BP)

Continuous recording: Ventilation, SpO2, EtCO2

Respiratory mechanics – ABG

**Arnal JM, Am J Respir Crit Care Med 181;2010:A3004**

## Conventional versus IntelliVent in post cardiac surgery




Lellouche F, Am J Respir Crit Care Med 181;2010:A6035

## Pulmonary conditions

**19 normal lungs patients:**
- 12 coma: stroke, head trauma, meningitis…
- 7 septic shock

**31 ALI/ARDS patients:**
- 20 pulmonary injury: CAP, aspiration, chest trauma, post surgery pneumonia
- 11 extrapulmonary injury: septic shock, pancreatitis

**Arnal JM, Am J Respir Crit Care Med 181;2010:A3004**

# Ventilation

| All patients (n= 50) | ASV | IntelliVent® | p |
|---|---|---|---|
| Cstat (mL/cmH$_2$0) | 40 ± 16 | 37 ± 12 | 0,191 |
| Rinsp (cmH$_2$O/L/s) | 17 ± 4 | 17 ± 5 | 0,970 |
| RCexp | 0,7 ± 0,1 | 0,6 ± 0,1 | 0,343 |
| %MV (%) | 128 ± 27 | 114 ± 29 | 0,003 |
| **$V_T$/PBW (mL/kg)** | **8,4 + 0,8** | **8,1 + 0,8** | **0,003** |
| RR (breath/min) | 15 ± 3 | 14 ± 3 | <0,001 |
| Ppeak (cmH$_2$0) | 29 ± 8 | 26 ± 6 | <0,001 |
| **Pplat (cmH$_2$0)** | **24 + 6** | **22 + 6** | **0,016** |
| PEEP (cmH$_2$O) | 10 ± 4 | 9 ± 5 | 0,015 |
| FiO$_2$ (%) | 45 ± 18 | 37 ± 13 | <0,001 |
| pH | 7,30 ± 0,08 | 7,28 ± 0,10 | 0,078 |
| PaO$_2$ (mmHg) | 102 ± 34 | 91 ± 24 | 0,064 |
| PaO$_2$/FiO$_2$ (mmHg) | 250 ± 107 | 263 ± 94 | 0,124 |
| PaCO$_2$ (mmHg) | 38 ± 7 | 41 ± 10 | 0,024 |
| EtCO$_2$ (mmHg) | 39 ± 6 | 42 ± 6 | 0,002 |
| SaO$_2$ (%) | 96 ± 3 | 95 ± 4 | 0,018 |

**Arnal JM, Am J Respir Crit Care Med 181;2010:A3004**