I have received

- lecture support
- travel reimbursements
- equipment loans
- consulting fees
- meeting organizational support (NAVAt)

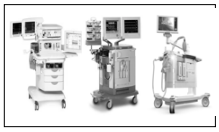
from basically all companies involved with inhaled agent delivery:

AbbVie, Acertys, Air Liquide, Allied healthcare, Armstrong Medical,
Baxter, Draeger, GE, Hospithera, Heinen und Lowenstein, Intersurgical,
Maquet, MDMS, MEDEC, Micropore, Molecular, NWS, Philips, Quantium Medical

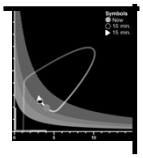
Note: this lecture may contain more examples of one anesthesia machine than another. This by no means reflects any personal preference - the choices have been made purely for didactical reasons, and also reflect my current research topics.

Target controlled
low flow anesthesia

A means to
visualize drug interactions
and guide depth



Aisys Zeus FLOW-i



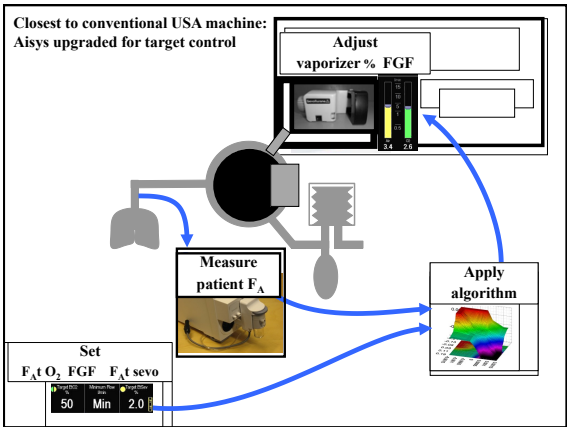
SmartPilot, Navigator
EEG derived ? Both?

Target controlled
low flow anesthesia

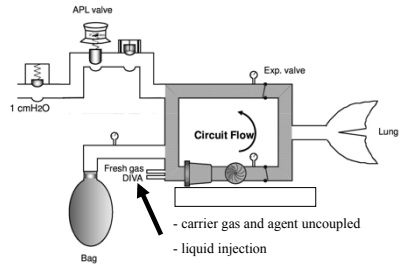
A means to
visualize drug interactions
and guide depth
(seeing context sensitive halftimes at work)

The players (others to follow)...

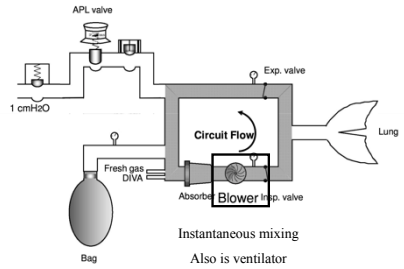
Closest to conventional USA machine:
Aisys upgraded for target control



Zeus (Draeger)



- carrier gas and agent uncoupled
- liquid injection

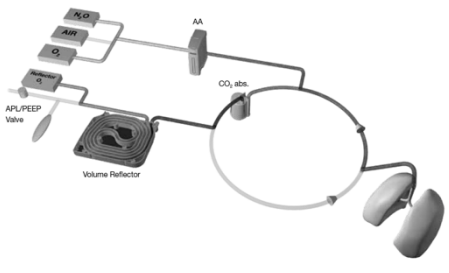


Instantaneous mixing

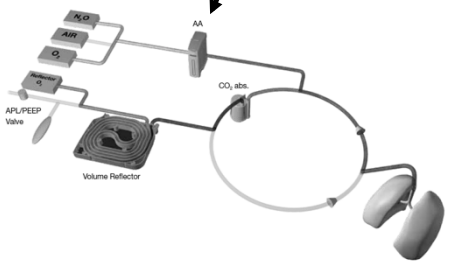
Also is ventilator

FLOW-i (Maquet)

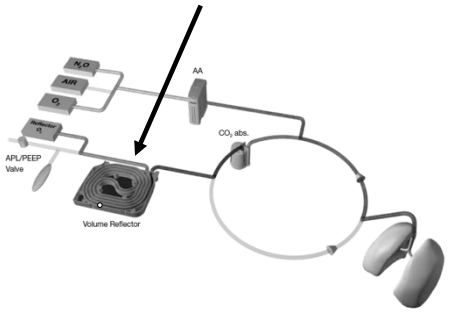
The heart of the system: carrier gas delivery systems act as ventilator



Injector



Volume reflector: physically open, functionally closed



How Technology Will Secure the Future of Inhalation Anesthesia

1. Why low flow (LFA)
2. Why target control
3. Why prediction displays
4. The smartest pilot and the really smartest pilot

How Technology Will Secure the Future of Inhalation Anesthesia

1. Why low flow (LFA)
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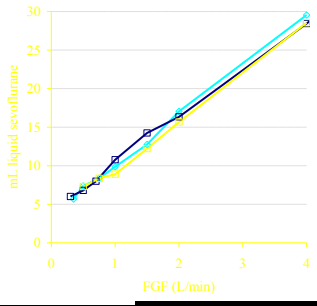
Low flow anesthesia makes sense

- less waste
- less pollution
- less costs
- heat & humidity

Sevo usage 5 - 60 min (F_A = 1.8%)



The CAEQ of sevo with the ADU®: De Cooman S, data on file

Aisys: De Cang, ESA 2014 Annual meeting, abstract 3AP1-7

FLOW-i: Carette R,et al. Maquet ESA grant 2014, in writing

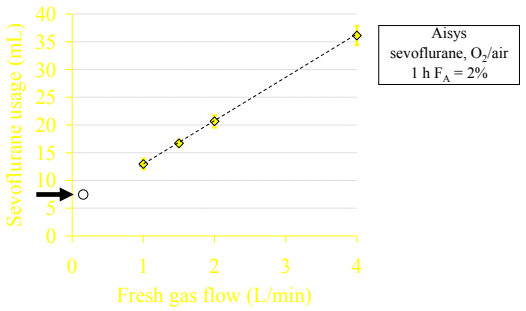
How low can you go?

Minimum we need?

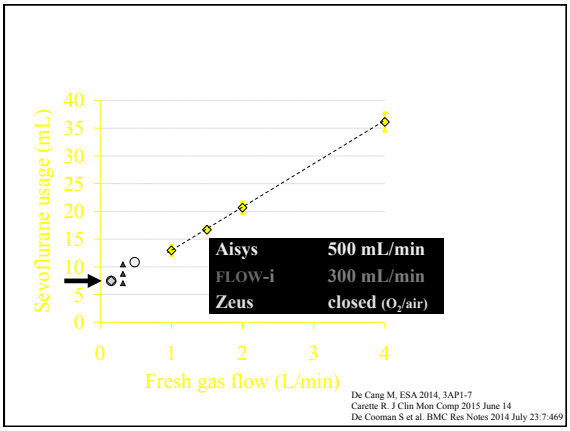
O_2 uptake	180 (37) mL/min	
N_2O uptake	200 100 ~~m~~L/min (10' 1h) →	
Desflurane (6% F_A, 1h)	12.5 mL liquid	10.3 mL by patient 2.2 mL circuit + lungs
Sevoflurane (2% F_A, 1h)	7.0 mL liquid	6.0 mL by patient 1.0 mL circuit + lungs

Robinson G et al. J Appl Physiol 2004:97:960-66
De Cooman S et al. BMC Res Notes 2014 July 23:7:469
Severinghaus J. J Clin Invest 1954;33:1183-9
Hendrickx J et al. Anest Analg 1997;84:413-8
Hendrickx J et al. Br J Anaesth 1998;81:495-501

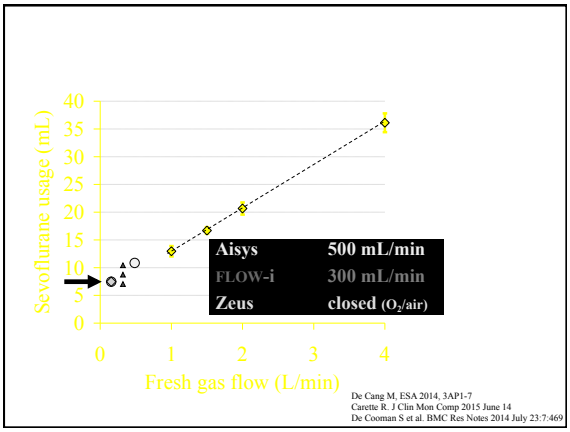
Lowest you can go



De Cang M, ESA 2014, 3AP1-7
Hendrickx J et al. Br J Anaesth 1998;81:495



De Cang M, ESA 2014, 3AP1-7
Carette R. J Clin Mon Comp 2015 June 14
De Cooman S et al. BMC Res Notes 2014 July 23:7:469



De Cang M, ESA 2014, 3AP1-7
Carette R. J Clin Mon Comp 2015 June 14
De Cooman S et al. BMC Res Notes 2014 July 23:7:469

Low flow anesthesia makes sense

- less waste
- less pollution
- less costs
- heat & humidity

All agents impede infrared radiation to outer space (GWP)

Global effect = 1 coal fired power plant
= 1 million passenger cars

Table 1. Summary of Radiative Properties, Atmospheric Lifetimes, and Global Warming Potentials for Nitrous Oxide and the Halogenated Anesthetic Gases

Compound	Atmospheric lifetime (y)	Radiative efficiency (W m^{-2} ppb^{-1})	GWP 20-y time horizon	GWP 100-y time horizon	GWP 500-y time horizon	Ozone depletion potential
Nitrous oxide, N_2O	114[8]	0.00303[8]	289[8]	298[8]	153[8]	0.017[17]
Halothane, $CF_3CHClBr$	1.0[8]	0.165[a]	190[a]	50[a,b]	20[a]	0.4[a,c]
Enflurane, $CHFClCF_2OCF_2H$	4.3[8]	0.447[a]	2370[a]	680[a,d]	210[a]	0.01[a,c]
Isoflurane, $CF_3CHClOCHF_2$	3.2[13]	0.453[13]	1800[13]	510[13]	160[13]	0.01[a,c]
Desflurane, $CF_3CHFOCHF_2$	14[3]	0.469[13]	6810[3]	2540[3]	130[3]	0[a,c]
Sevoflurane, $(CF_3)_2CHOCH_2F$	1.1[3]	0.351[13]	440[3]	130[3]	40[3]	0[a,c]

Sulbaek Andersen MP. Anesth Analg 2012;114:1081-5

All agents impede infrared radiation to outer space (GWP)

Global effect = 1 coal fired power plant
= 1 million passenger cars

Table 1. Summary of Radiative Properties, Atmospheric Lifetimes, and Global Warming Potentials for Nitrous Oxide and the Halogenated Anesthetic Gases

Low flow = waste reduction by 90%
Feldman J. (2012) Anesth Analg 114:1093-1101

Sulbaek Andersen MP. Anesth Analg 2012;114:1081-5

Low flow anesthesia makes sense

- less waste
- less pollution
- less costs
- heat & humidity

complex

combined cost agent + CO_2 absorber does continue to decrease with ↓FGF

Low flow anesthesia makes sense

- less waste
- less pollution
- less costs
- heat & humidity CO_2 - CO_2 absorbent reaction
  = exothermic, H_2O producing
  = no need for HME, only filter

Anthony Wilkes
www.NAVAt.org 2015

Low flow anesthesia makes sense

- less waste
- less pollution
- less costs
- heat & humidity

Then why

- the hesitancy to use low flow fresh gas flows (FGF) ?
- the intuitive use of 1.5 - 2 L/min FGF ?
- the ill defined fear of FGF << 1L/min ?

Teaching alone does not work...

	Baseline	After being taught to use lower FGF	And 6 months later...
	Preintervention Period (N = 2031)	Postintervention Period (N = 2242)	Delayed Follow-up Period (N = 2056)
Flow (l/min)			
Mean ± SD	2.4 ± 1.1	1.8 ± 1.1	1.9 ± 1.1
25th, 50th, 75th percentiles	2.0, 2.0, 3.0	1.0, 1.7, 2.0	1.0, 2.0, 2.5
≤1 l/min (%)	270 (13%)	656 (29%)*	585 (29%)*†
≤2 l/min (%)	1081 (53%)	1736 (77%)*	1483 (72%)*†
Flow (l/min)			
Isoflurane	2.4 ± 1.0	1.8 ± 0.9*	2.0 ± 1.0*‡
Desflurane	2.0 ± 1.1	1.3 ± 1.0*	1.4 ± 1.0*
Sevoflurane	2.7 ± 1.1	2.2 ± 0.9*	2.4 ± 1.0*†

Body SC, Fanikos J, DePeiro D, Philip JH, Segal BS.
Anesthesiology 1999;90:1171-5

Compound A ?

Hard to believe this continues to be an issue

Sevoflurane used routinely with closed-circuit anesthesia

If medicolegal issue: use Amsorb Plus, SpiraLith, LithoLyme

The reasons for the hesitancy to use FGF << 1L/min explain why we need target control delivery of agents and O_2

How Technology Will Secure the Future of Inhalation Anesthesia

1. Why low flow (LFA)

2. Why target control
   - LFA more convenient, less distraction
   - conventional LFA teaching = inconsistent use
   - safety agent
     O_2

3. Why prediction displays (drug interactions, times)

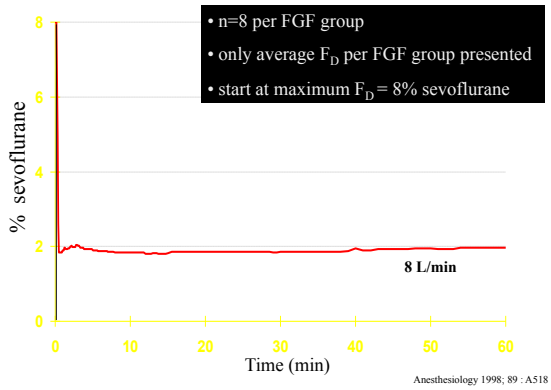
4. The smartest pilot and the really smartest pilot

Clinical Example

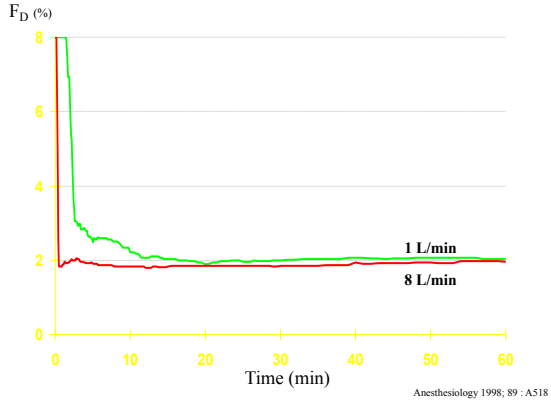
How to adjust vaporizer setting (F_D)
to maintain sevoflurane F_A at 1.3%
with FGF from 0.3 to 8 L/min O_2/N_2O
with conventional machine (ADU®)?

Hendrickx J, Van Zundert A, et al. Anesthesiology 1998; 89 : A518

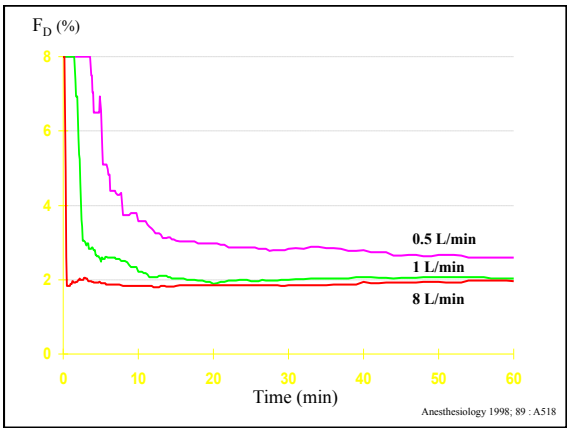
Vaporizer setting (= F_D)

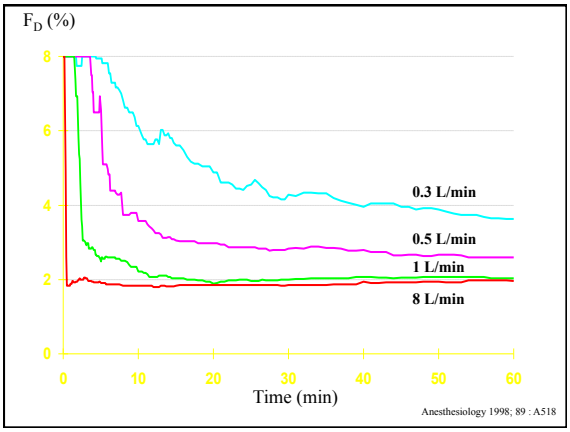


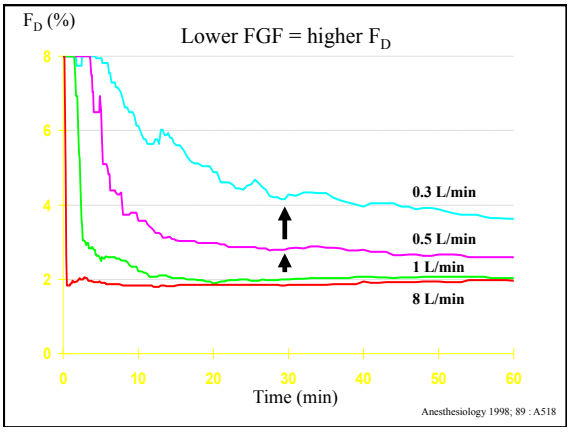
Anesthesiology 1998; 89 : A518



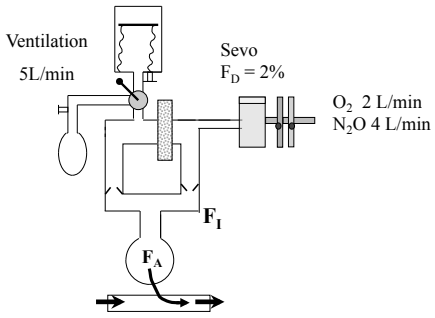
Anesthesiology 1998; 89 : A518

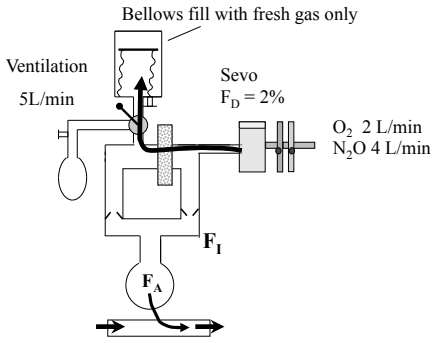

F_D (%)
8
6
4
2
0
0.5 L/min
1 L/min
8 L/min
0
10
20
30
40
50
60
Time (min)
Anesthesiology 1998; 89 : A518

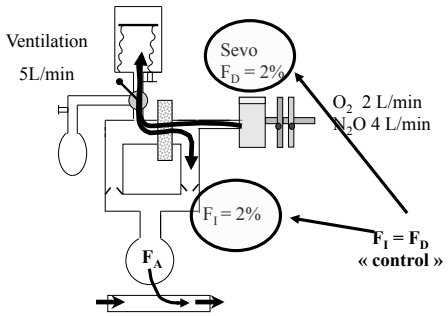

F_D (%)
8
6
4
2
0
0.3 L/min
0.5 L/min
1 L/min
8 L/min
0
10
20
30
40
50
60
Time (min)
Anesthesiology 1998; 89 : A518


F_D (%)
Lower FGF = higher F_D
8
6
4
2
0
0.3 L/min
0.5 L/min
1 L/min
8 L/min
0
10
20
30
40
50
60
Time (min)
Anesthesiology 1998; 89 : A518

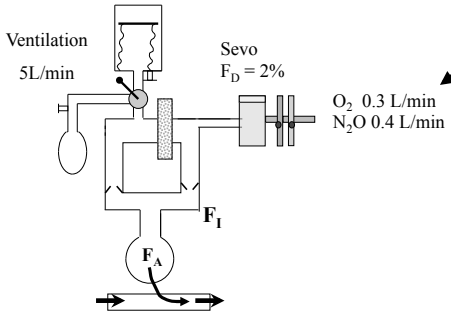
"High" FGF: FGF > MV

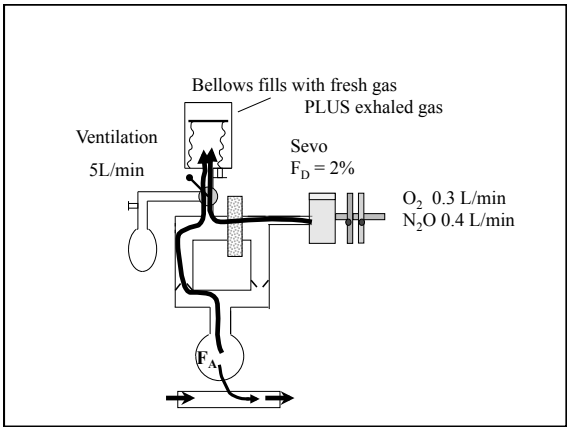


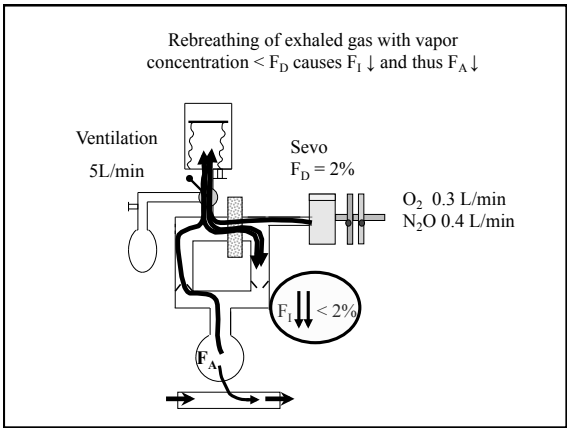


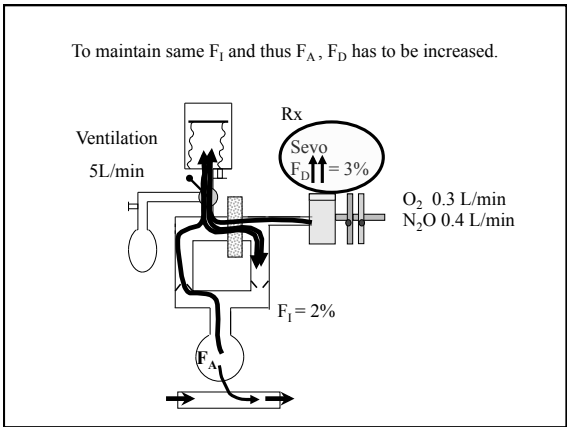


"Low" FGF: FGF < MV

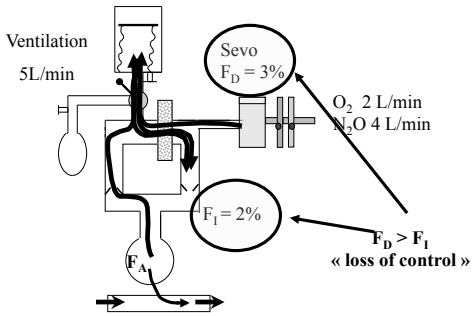



Bellows fills with fresh gas
PLUS exhaled gas
Ventilation
5L/min
Sevo
F_D = 2%
O_2 0.3 L/min
N_2O 0.4 L/min
F_A


Rebreathing of exhaled gas with vapor concentration < F_D causes $F_I \downarrow$ and thus $F_A \downarrow$
Ventilation
5L/min
Sevo
F_D = 2%
O_2 0.3 L/min
N_2O 0.4 L/min
F_I < 2%
F_A


To maintain same F_I and thus F_A, F_D has to be increased.
Rx
Ventilation
5L/min
Sevo
F_D = 3%
O_2 0.3 L/min
N_2O 0.4 L/min
F_I = 2%
F_A

A difference has developed between F_I and F_D.



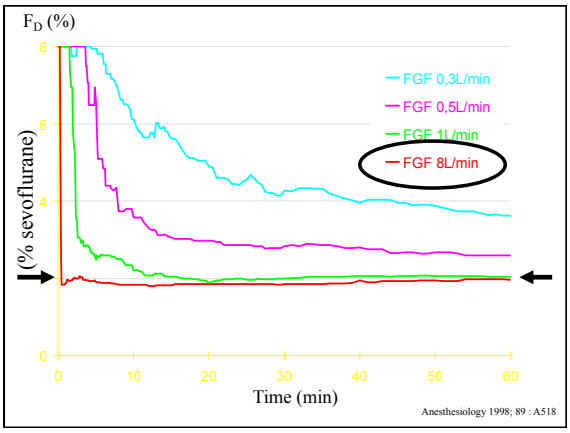
This "dilutional" effect becomes more prominent with FGF < 1.5-2 L/min

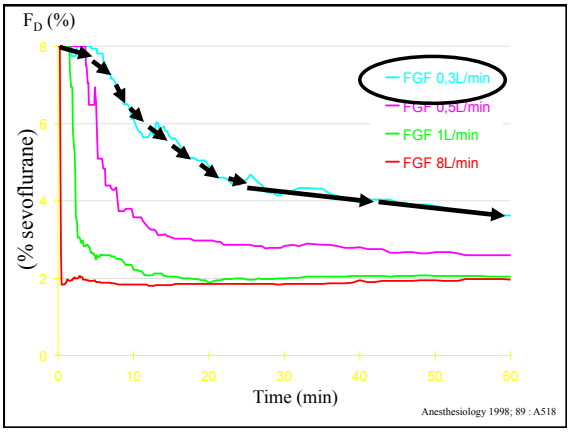
With lower FGF, we have the impression to "lose control"

This is why we intuitively use FGF = 1.5 - 2 L/min: F_D still matches F_I

FGF << 1 L/min not frequently used because

- more vaporizer adjustments needed



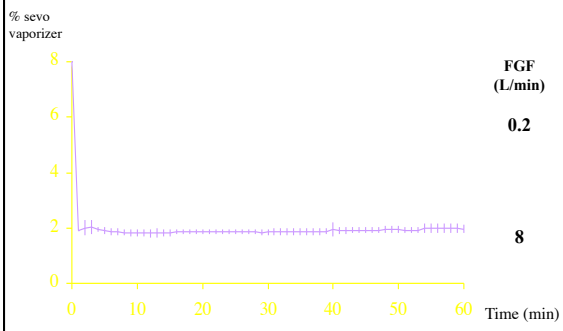


FGF << 1 L/min not frequently used because

- more vaporizer adjustments needed

- it becomes harder to predict F_D in the individual patient

... F_D variability increases with lower FGF



A&A1999; 88:S344;Anesthesiology 1998; 3A, A518, 1998

FGF << 1 L/min not frequently used because

- more vaporizer adjustments needed
- it becomes harder to predict F_D in the individual patient
- choice of carrier gas effect F_D more pronounced

Hendrickx et al. Anesthesiology 2002;97:400-4

Clinical implication: more attention needed

potentially more distractive
especially right after induction

→ over- and under- dosing

Even with high flows we under-dose many of our patients...

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 18, 2011 VOL. 365 NO. 7

Prevention of Intraoperative Awareness in a High-Risk Surgical Population

Michael S. Avidan, M.B., B.Ch., Eric Jacobsohn, M.B., Ch.B., David Glick, M.D., M.B.A., Beth A. Burnside, B.A., Lini Zhang, M.D., Alex Villafranca, M.S., Leah Karl, B.A., Saima Kamal, M.D., Brian Torres, B.S.N., Michael O'Connor, M.D., Alex S. Evers, M.D., Stephen Gradwohl, B.S., Nan Lin, Ph.D., Ben J. Palanca, M.D., Ph.D., and George A. Mashour, M.D., Ph.D., for the BAG-RECALL Research Group.*

- Prospective study
- Target: ≥ 0.7 MAC

Overall, during the maintenance of anesthesia, the ETAC was greater than 0.7 age-adjusted MAC a median of 84.8% of the time (interquartile range, 67.2 to 95.3).

15.2% was underdosed

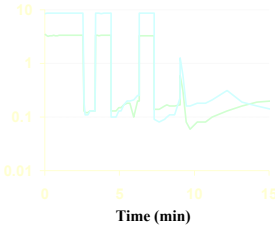
Obvious solution: target F_A

Let machine manage FGF and F_D to get target F_A

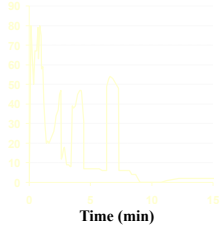
Target control makes the use of low flow very simple, so we now use it routinely

Zeus

FGF

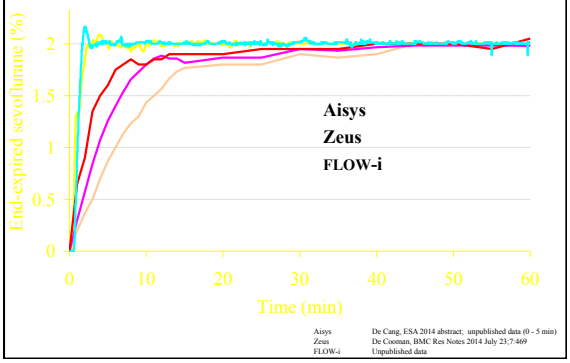


Liquid injection rate



Personal observations

Rate of rise of end-expired % (F_A)



Aisys	De Cang, ESA 2014 abstract; unpublished data (0 - 5 min)
Zeus	De Cooman, BMC Res Notes 2014 July 23;7:469
FLOW-i	Unpublished data

How Technology Will Secure the Future of Inhalation Anesthesia

1. Why low flow (LFA)

2. Why target control
   - teaching alone insufficient
   - more convenient, less distraction → consistent use
   - safety agent (over and under dosing)
     O_2

3. Why prediction displays (drug interactions, times)

4. The smartest pilot and the really smartest pilot

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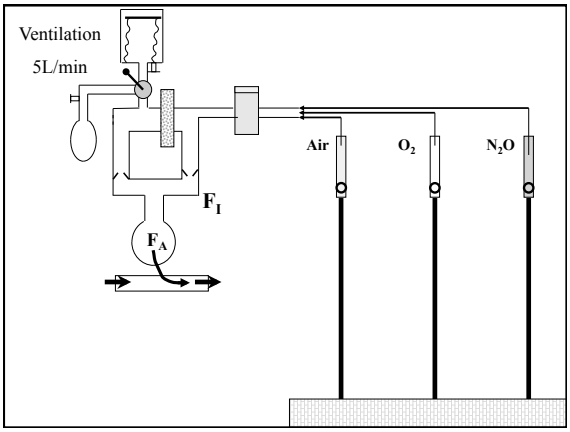
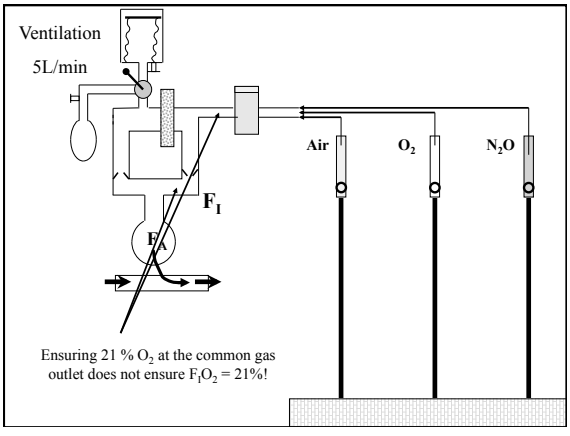
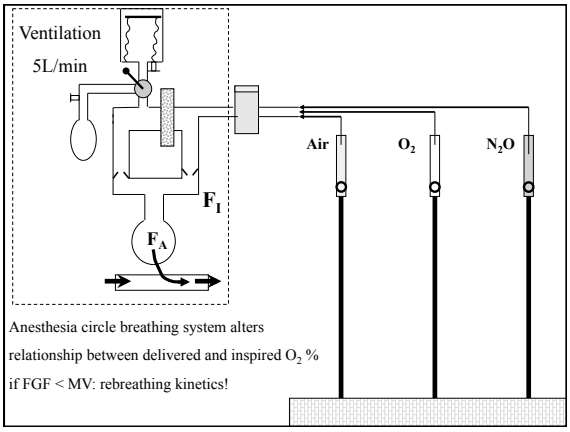
Movie


Ventilation
5L/min
Air
O_2
N_2O
F_I
F_A


Ventilation
5L/min
Air
O_2
N_2O
F_I
F_A
Ensuring 21 % O_2 at the common gas outlet does not ensure F_IO_2 = 21%!



Anesthesia circle breathing system alters relationship between delivered and inspired O_2 %

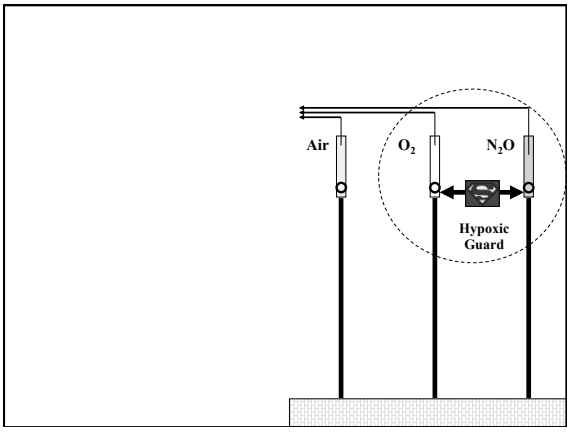
if FGF < MV: rebreathing kinetics!

Protection Against Accidental Delivery of Hypoxic Gas Mixtures

ANSI Standard 51.13.1

The anesthesia workstation shall be provided with

- a device to protect against an operator selected delivery
- of a O_2/N_2O mixture
- having < 21 % O_2 in the fresh gas **or** in the inspired gas

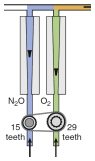


Examples of hypoxic guard systems

Ohmeda Link 25

a chain that links N_2O and O_2

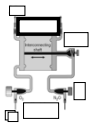
mechanical



Dräger S-ORC

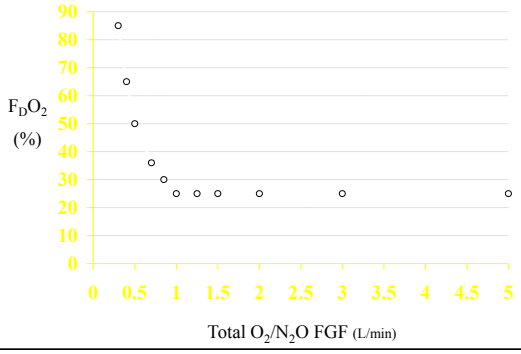
Sensitive Oxygen Ratio Controller

pneumatical - mechanical



www.navat.org

S-ORC limits = lowest possible F_DO_2 % the S-ORC allows us to use with a certain FGF



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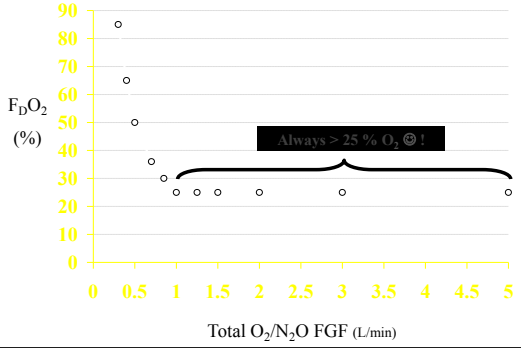

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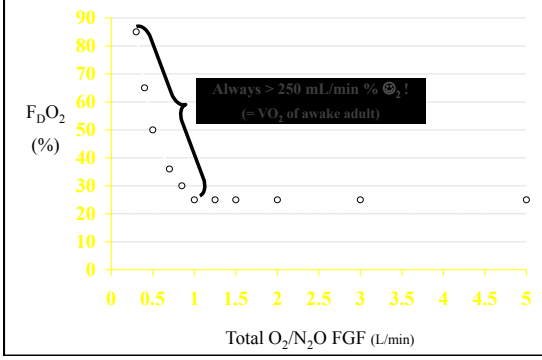
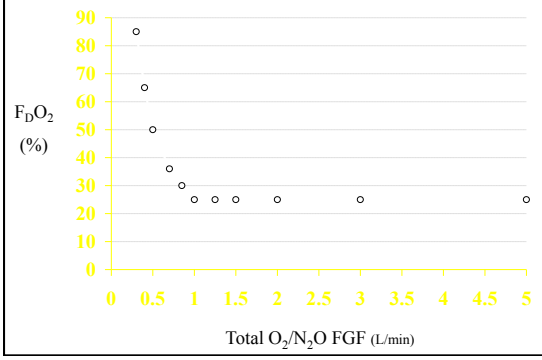
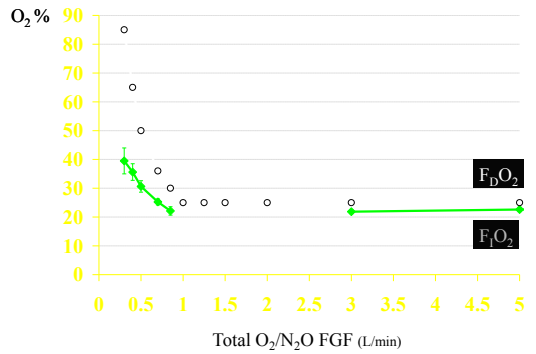


But do these F_DO_2 limits ensure $F_IO_2 \geq 21$ % ?

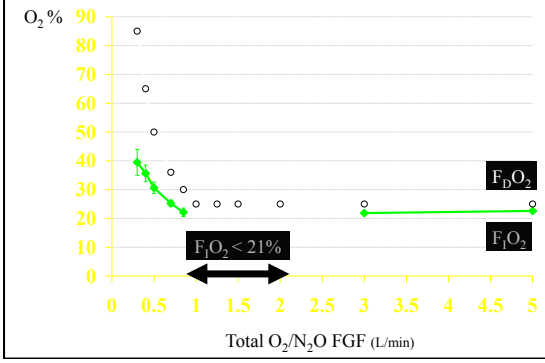
De Cooman S, Schollaert C, Hendrickx JF, et al. J Clin Mon Comput, 2014, Oct 1



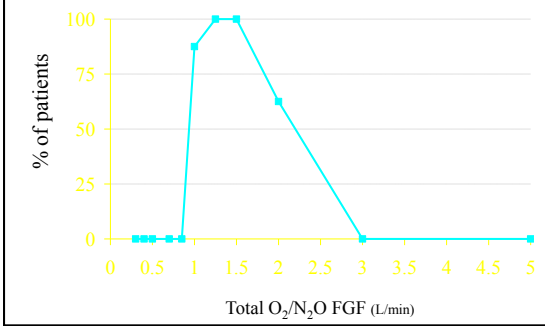
These hypoxic guard limits did ensure $F_IO_2 \geq 21$ % ...



... but these did NOT: this is NOT a safe zone!

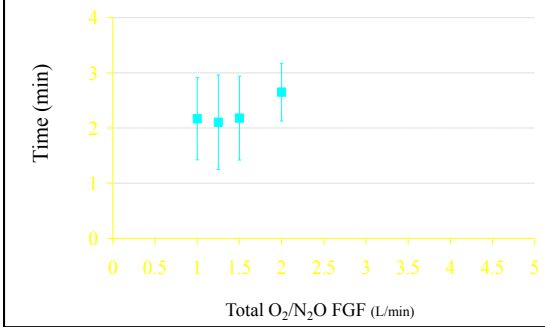


% of patients with F_IO_2 < 21 %

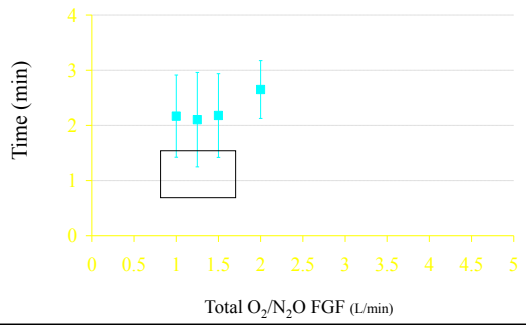


Time after which F_IO_2 < 21 %

(baseline = 25%)



In some patients < 60 seconds!



Machine standards are outdated:

- effect of rebreathing not taken into account

- no requirements for O_2/air mixtures

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- effect of rebreathing not taken into account

- no requirements for O_2/air mixtures

Worse still: hypoxic guards perform worst with FGF
many of us are comfortable working with:1-2 L/min!

Solution?

EJA

Eur J Anaesthesiol 2015; **32**:371–373

EDITORIAL

O_2, anybody?

Jan F.A. Hendrickx, Andre M. De Wolf and Stefan De Hert

Where do we go from here?

Where do we go from here? Do we require even more stringent conventional hypoxic guard criteria? This is likely not a very good option, because mass balances predict that even more stringent criteria may not prevent a hypoxic F_IO_2 when, for example, patient oxygen consumption is higher than normal. Also, the configuration of the anaesthesia circle system may influence the effects of rebreathing. Therefore, we propose that all manufacturers develop 'smart' hypoxic guard systems on the basis of software and measured F_IO_2 (or possibly the end-expired O_2 concentration). With current anaesthesia machines, there are four different circumstances to be considered. First, the modern anaesthesia workstation with an electronic gas mixer and in automatic (target control) mode allows us to set a target F_IO_2 (or end-expired O_2 concentration), and its algorithms will set the required individual fresh gas flows using feedback control from measured F_IO_2. This is the ultimate solution because in this mode, there is no need for a conventional hypoxic guard system. Currently, only three such workstations are available: the Aisys, the Zeus and the FLOW-i. Second, such a workstation, when used in a manual (nontarget-controlled/conventional) mode, should have an electronic ('smart') hypoxic guard system that will, when necessary, adjust fresh gas flows of the individual carrier gases based on measured F_IO_2 or end-expired O_2 concentration, thereby overruling the anaesthesia provider. Currently, only one such workstation is available, the FLOW-i. If F_IO_2 decreases below 21%, within 20 s, the system will increase the fresh gas flows and the O_2 concentration delivered at the common gas outlet, restoring F_IO_2 to at least 25% within 73 s after its activation.[3]

Solution = target F_IO_2 or F_AO_2 directly

Aisys **Zeus** **FLOW-i**

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→ need back-up
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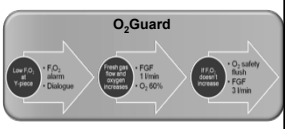

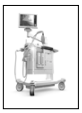

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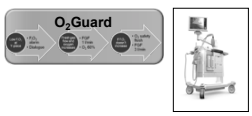

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How Technology Will Secure the Future of Inhalation Anesthesia

1. Why low flow (LFA)

2. Why target co
   - LFA more convenient, less distraction
   - conventional LFA teaching = inconsistent use
   - safety agent
     O_2

Solved. We use it in every OR

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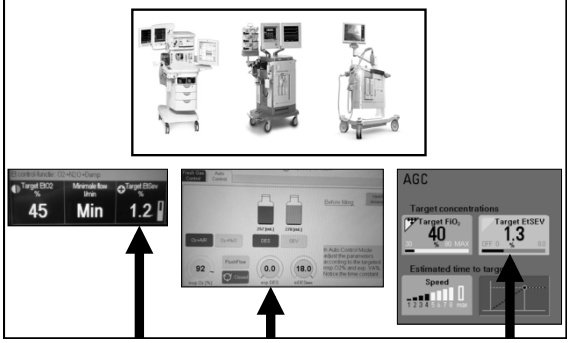
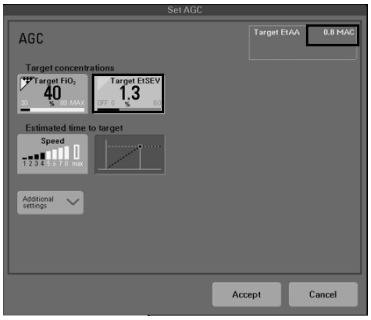
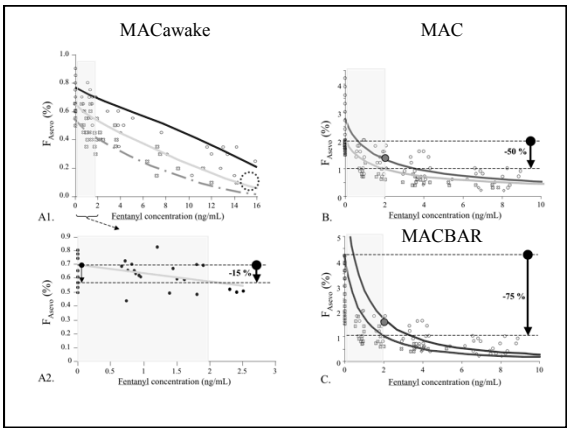
We use it every day in 1 OR.
Work in progress. This is the future.

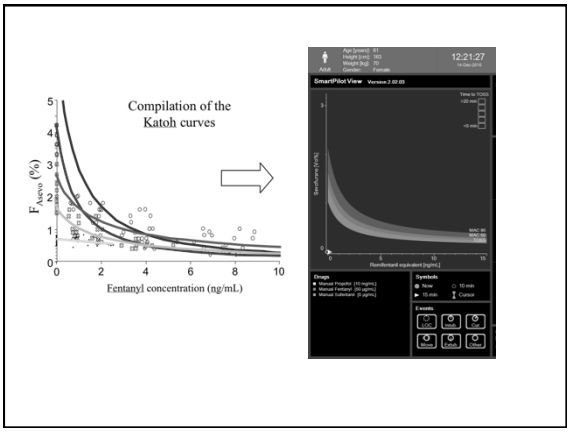
Target controlled low flow: what target sevo to select?

You *have* to pick a number

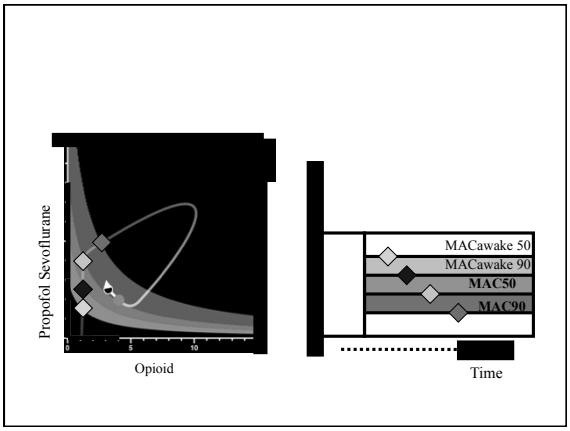





MACawake
MAC
A1.
A2.
B.
C.
MACBAR
-50 %
-15 %
-75 %
Fentanyl concentration (ng/mL)


Compilation of the
Katoh curves
Fentanyl concentration (ng/mL)

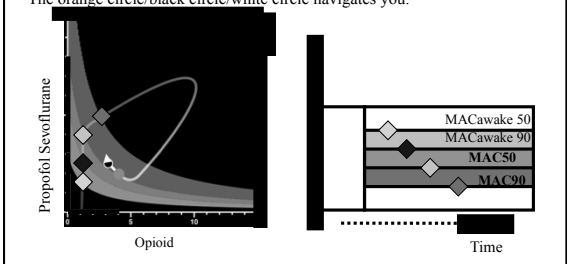

SmartPilotView
NSRI
100
Propofol
Fentanyl
0.0
Sufentanil
0.0



Depending on which drug is eliminated faster, you might want to choose more hypnotic or opioid to maintain a certain anesthetic depth - this will help ensure a fast emergence, as guided by the prediction.

Drug combinations possible.

The orange circle/black circle/white circle navigates you.



Abstract: **221**

ESA 2013

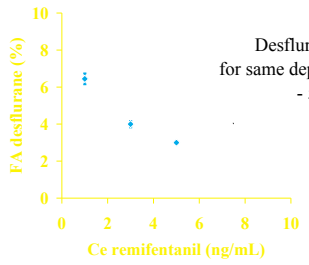
3 - Monitoring: Equipment and Computers

Drug interaction models are better predictors of tolerance/response to noxious stimuli compared to individual measured parameters

Hannivoort L.N., Proost J.H., Eleveld D.J., Struys M.M.R.F., Luginbühl M., Vereecke H.E.M.
University of Groningen, University Medical Center Groningen, Dept of Anaesthesiology, Groningen, Netherlands

	U	NSRI	Sevo	Remi	BIS
SAS	96%	96%	89% *	60% *	95%
TET	96%	94%	79% *	69% *	84% *
LMA	98%	95%	81% *	63% *	83% *
LAR	98%	95%	76% *	72% *	78% *

Optimizing desflurane in terms of drug interactions/context-sensitive $t_{1/2}$ guided by SmartPilot



Desflurane usage
for same depth (NSRI = 5)
- 53%

Carette R. Submitted, ESA 2016

Input info readily available:
- infusions: from injector, pump
- bolus: enter yourself or via bar codes in future
- "freebee": no need for electrodes

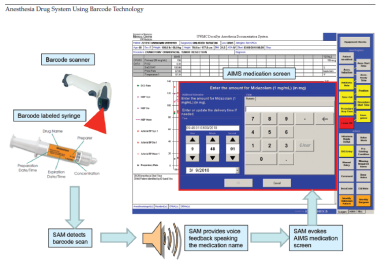
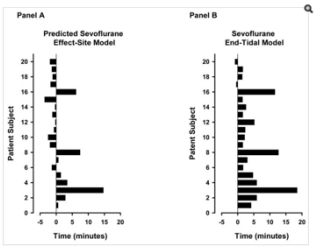


Figure 4. The workflow in Smart Anesthesia Manager (SAM) for barcode identification of a syringe with a Codonics Safe Label System (SLS) label. The dose of the drug is manually entered onto the touch screen of the Anesthesia Information Management System (AIMS) display. The time of scanning the drug appears in the medication administration time field by default; however, this time can be adjusted if necessary.

Jelacic S et al. Anesth Analg 2015;121:410-21

Road to more consistent and predictable wake-up

Vastly under-used and under-appreciated



Time from the 50% model prediction for unresponsiveness to the time of the observed return of responsiveness for the effect-site based (Panel A) and end-tidal based (Panel B) models. After termination of the anesthetic, the model predicted probability of unresponsiveness rapidly decreased over time. A negative, zero or positive number on the horizontal axis indicates that the observed return of responsiveness occurred prior to, exactly at, or after the 50% probability of unresponsiveness. The vertical axis represents each subject.

Johnson KB et al. Anesth Analg 2010:111:387-94

Smartest Pilot

Enter

- patient covariates
- surgeon's covariates (procedure, duration)
- costs of drugs, CO_2 absorbent, other
- adjust anticipated wake-up time

Machine will steer drug adminstration

Margin of error for inhaled agents: can be washed-out

Smartest Pilot

Enter

- patient covariates
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- costs of drugs, CO_2 absorbent, other
- adjust anticipated wake-up time

Machine will steer drug adminstration

Margin of error for inhaled agents: can be washed-out

Really Smartest Pilot

Us!

Biological variability
Equipment failure

Still:

"One of the most important reasons we need anesthesiologists (at least for now) is that only anesthesiologists can determine what drugs and especially what combination of drugs (and their proportioning) will be used in a specific patient. This is something that can (will) be taken over by smart equipment, but not quite yet..."

Andre De Wolf
Northwestern University
Chicago, IL, USA

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4. The smartest pilot and the really smartest pilot