

# DÉLIVRANCE AUTOMATISÉE DES PRODUITS DE L'ANESTHÉSIE



Médecin en Chef DONAT  
Centre de traitement des Brûlés, HIA Percy  
ICAR 2019

- Principes
- Historique
- Exemple d'utilisation
- Analyse de la littérature

Pas de conflit d'intérêt

# DÉFINITIONS

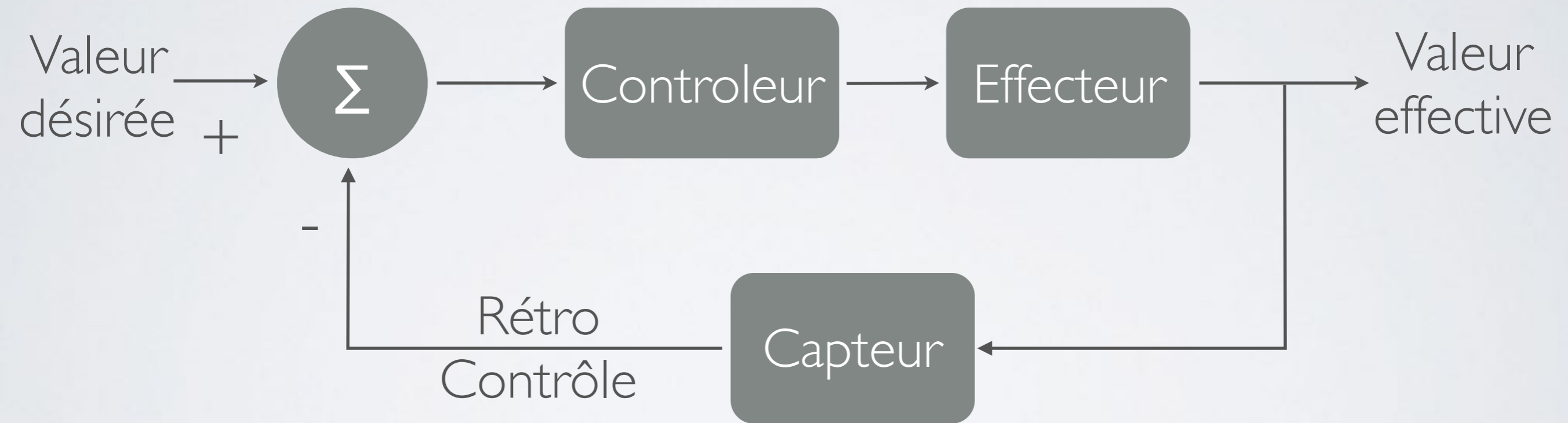
- Dispositif automatisé : se comporte de manière automatique, pas d'intervention humaine
- Comportement figé ou adapté à son environnement = rétro contrôle

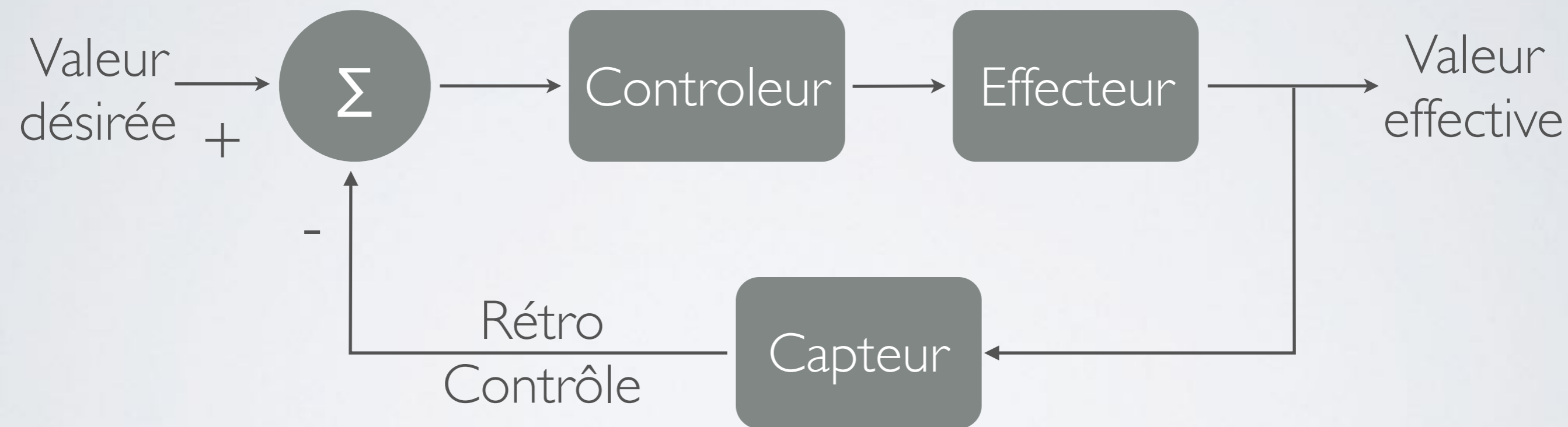


# LE RÉTRO- CONTRÔLE

- Boucle : application d'un protocole avec décision humaine ou non, ex : protocole insuline, protocole loxen...
- Boucle automatisée: gestion par un algorithme informatique

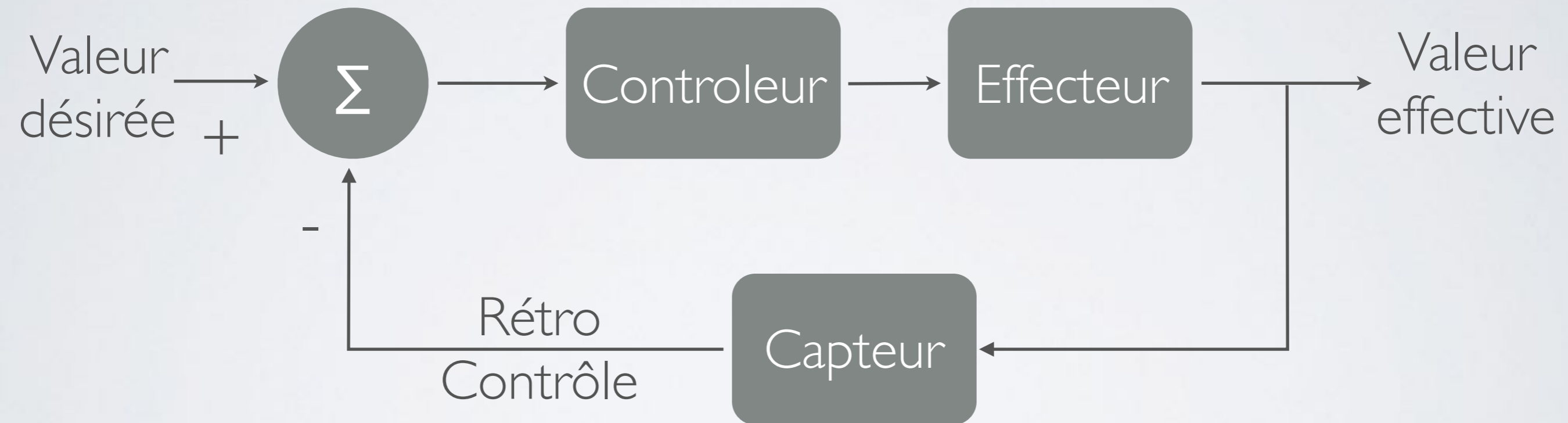






Exemple de la régulation de la température

$T^{\circ} = 25^{\circ}\text{C}$

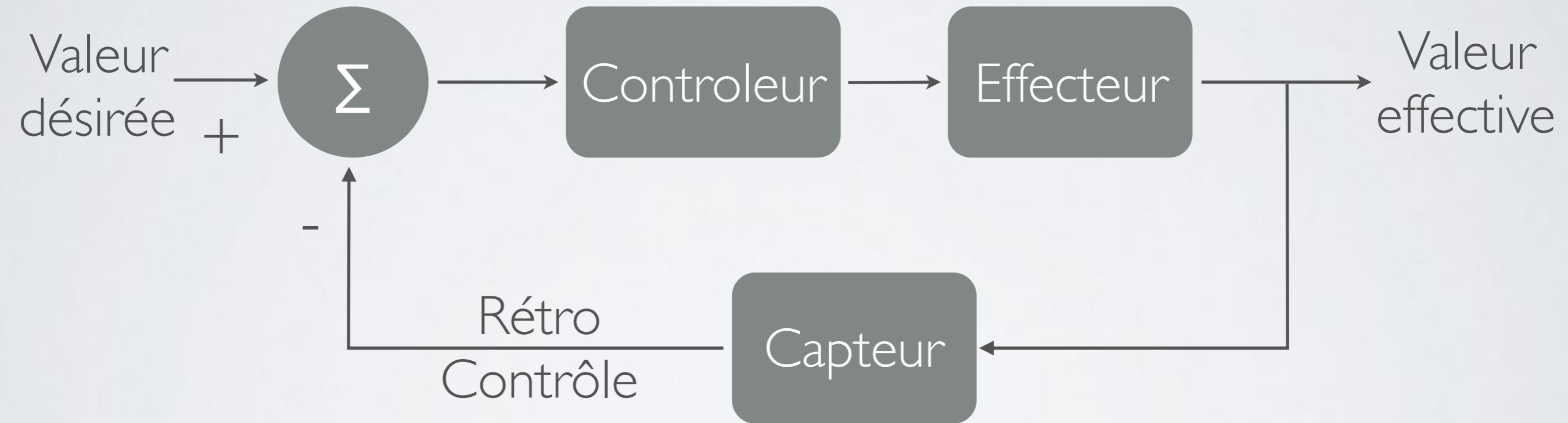


Exemple de la régulation de la température

$T^{\circ} = 25^{\circ}\text{C}$

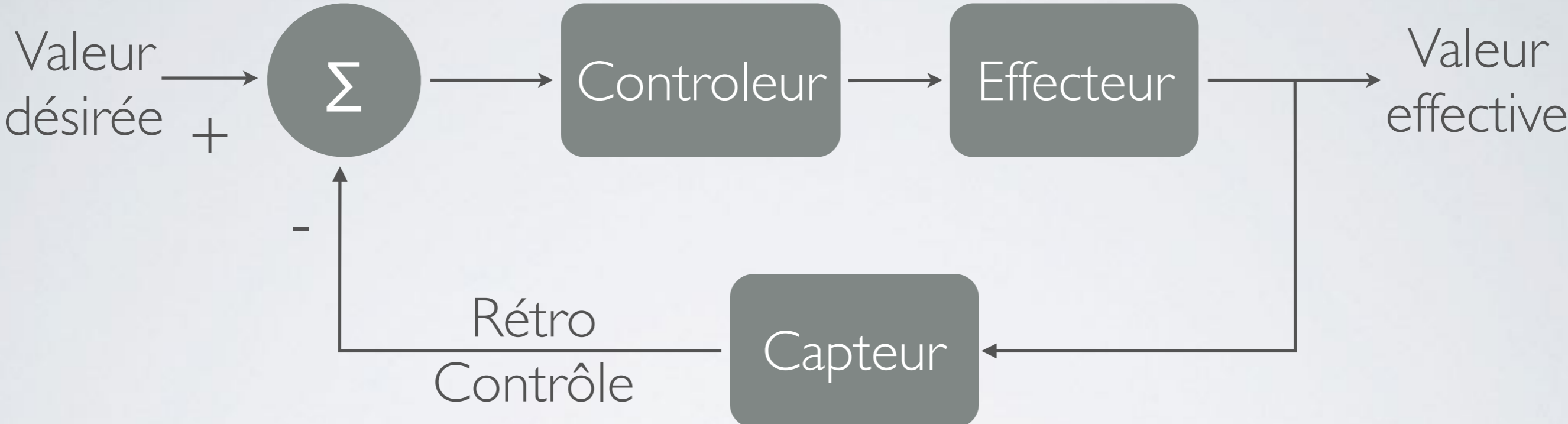


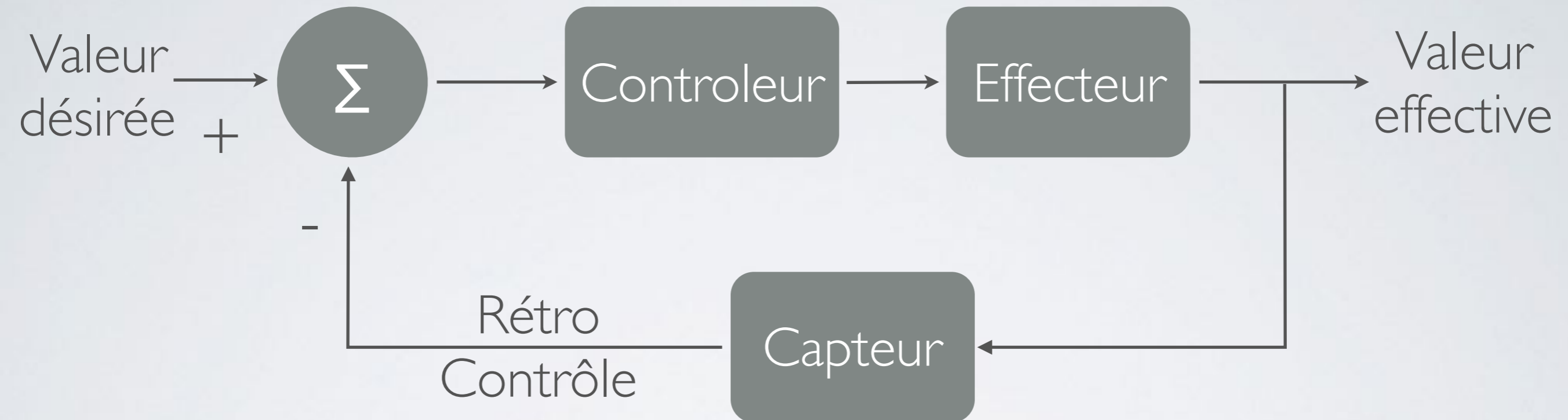
Radiateur



Exemple de la régulation de la température

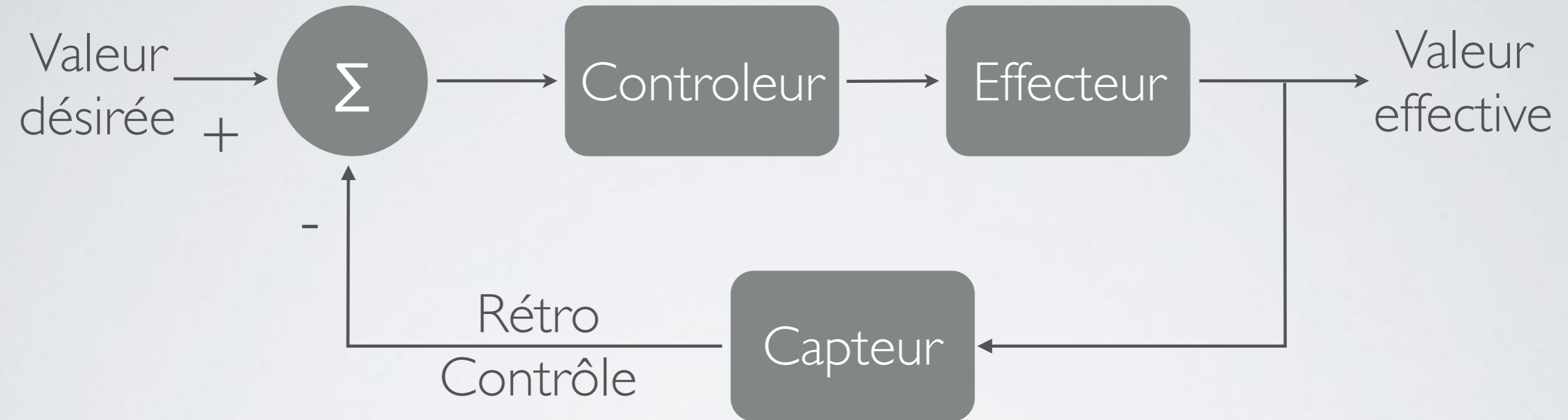






Exemple de l'adaptation de l'insuline

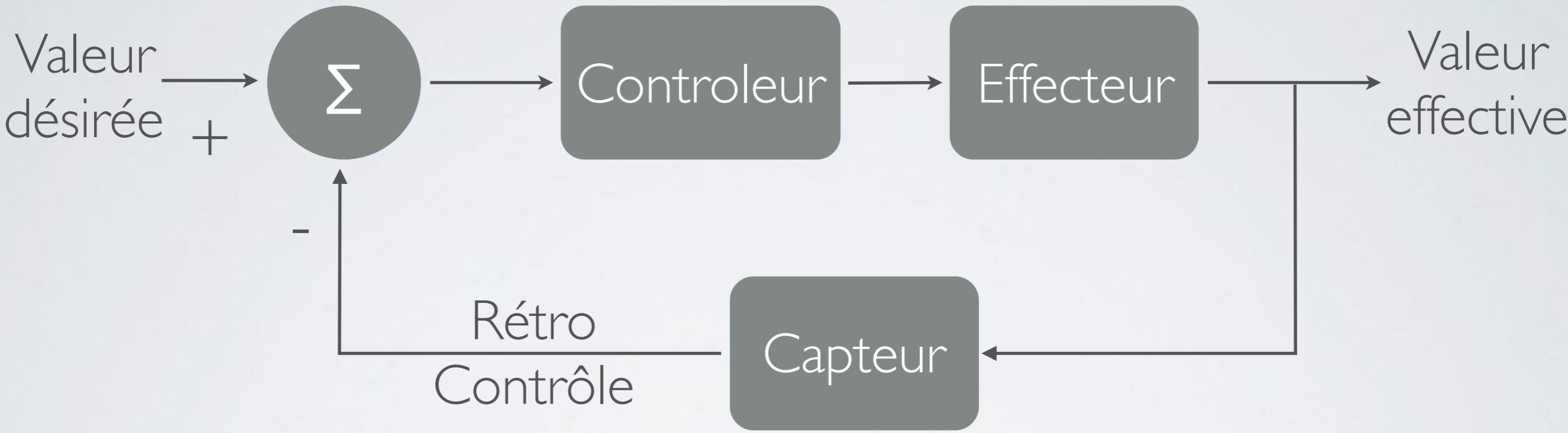
$5 < \text{gly} < 7 \text{ mmol/L}$



Exemple de l'adaptation de l'insuline

$5 < \text{gly} < 7 \text{ mmol/L}$

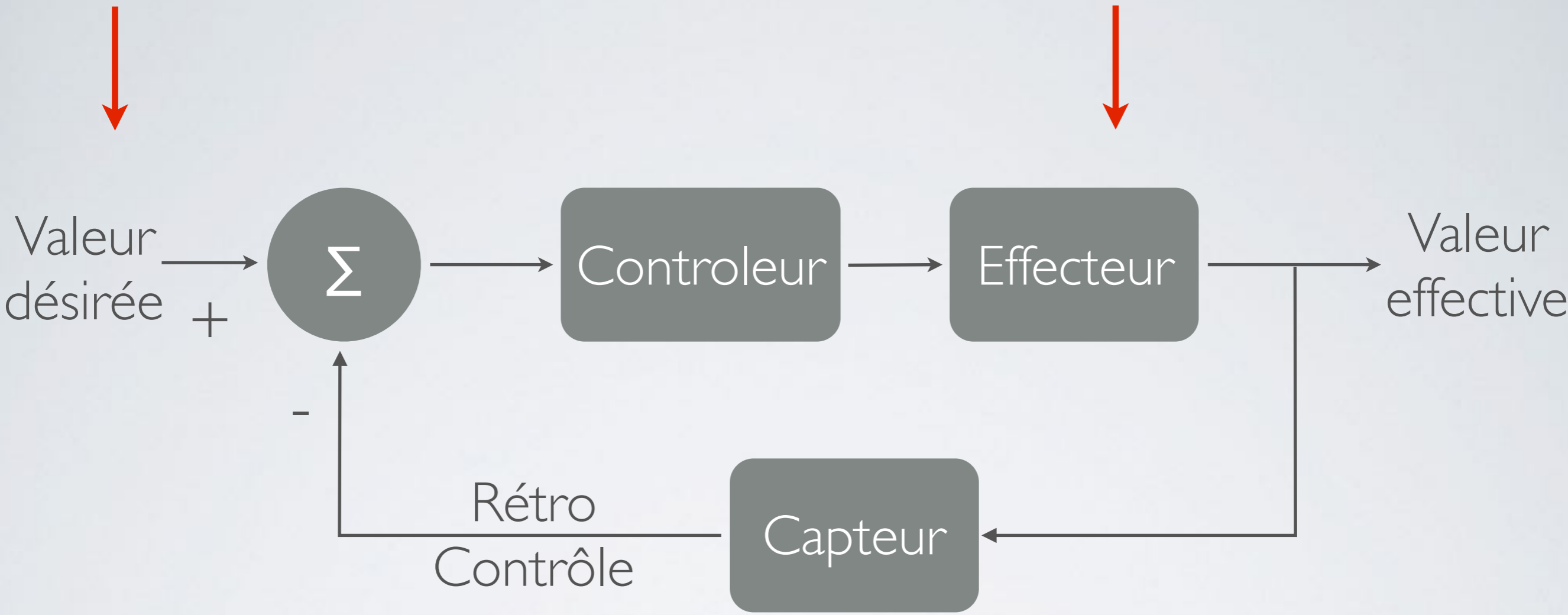
PSE Insuline



Exemple de l'adaptation de l'insuline

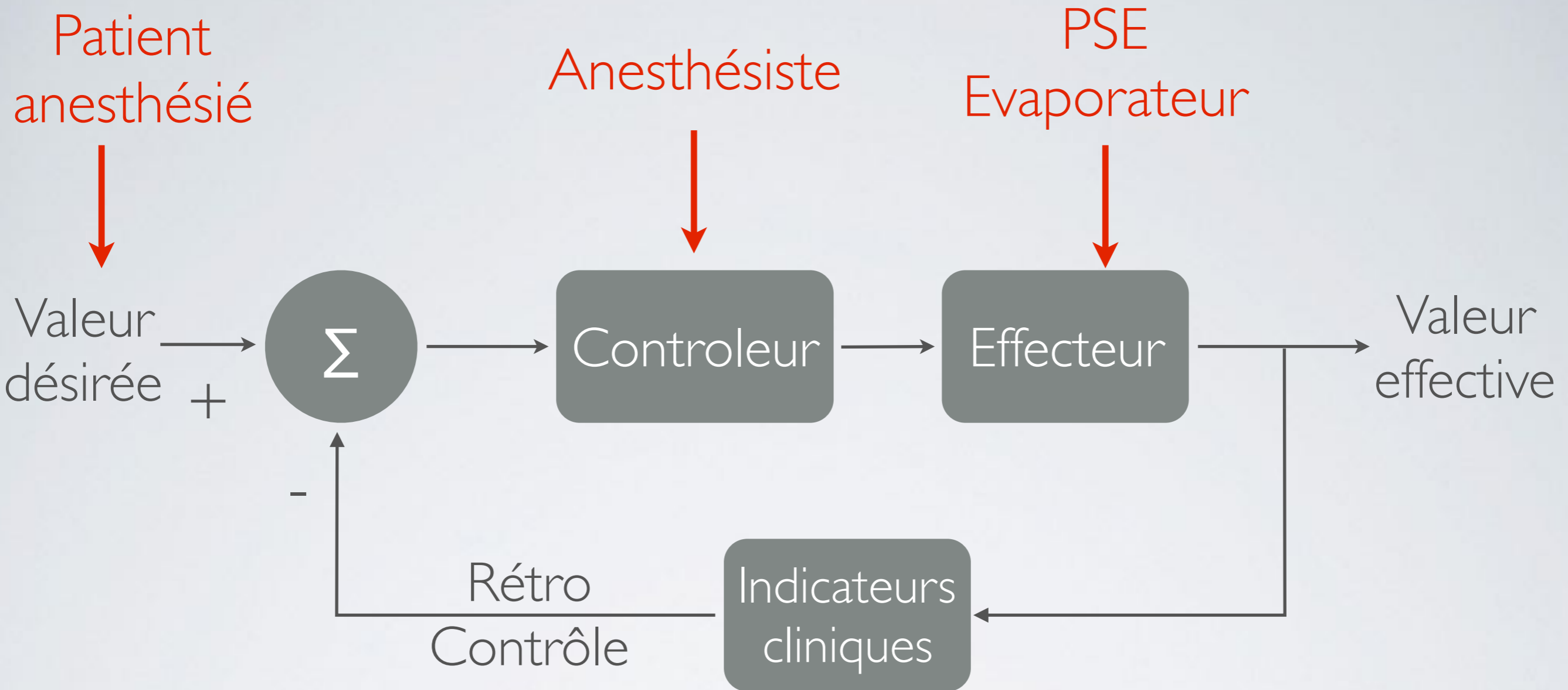
$5 < \text{gly} < 7 \text{ mmol/L}$

PSE Insuline



Glycémie capillaire

Exemple de l'adaptation de l'insuline

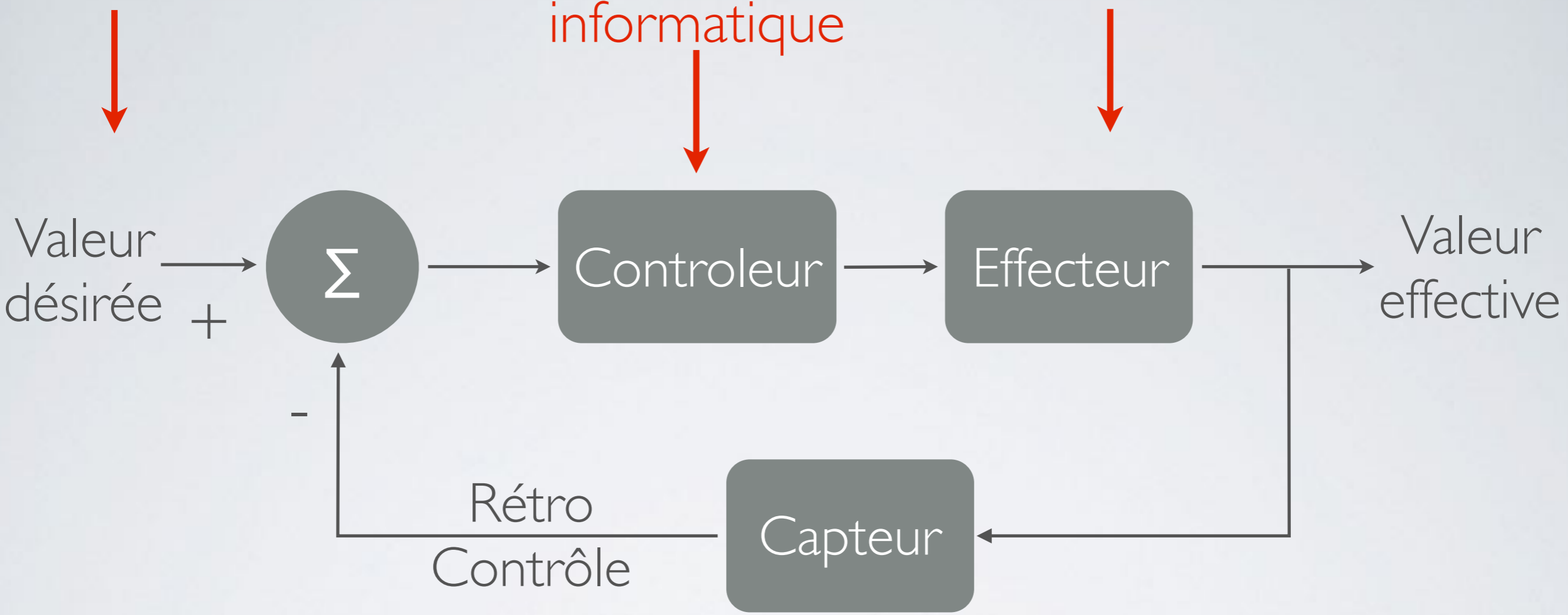


## Exemple de l'anesthésie

45 < BIS < 60

Programme informatique

PSE



## Exemple de l'anesthésie

Le contrôleur est l'anesthésiste, mais peut aussi être un programme informatique

Kuck K, Johnson KB. The Three Laws of Autonomous and Closed-Loop Systems in Anesthesia. Anesth Analg. 2017;124(2):377-80.

HISTORIQUE



# ELECTROENCEPHALOGRAPHICALLY CONTROLLED ANESTHESIA IN ABDOMINAL SURGERY

*JAMA* 1950, 144 (13)

CHARLES W. MAYO, M.D.  
REGINALD G. BICKFORD, M.B.,  
and  
ALBERT FAULCONER Jr., M.D.  
Rochester, Minn.

50 patients, ETHER  
“Major Surgical procedures  
varying age, both sexes  
Without untoward effect “

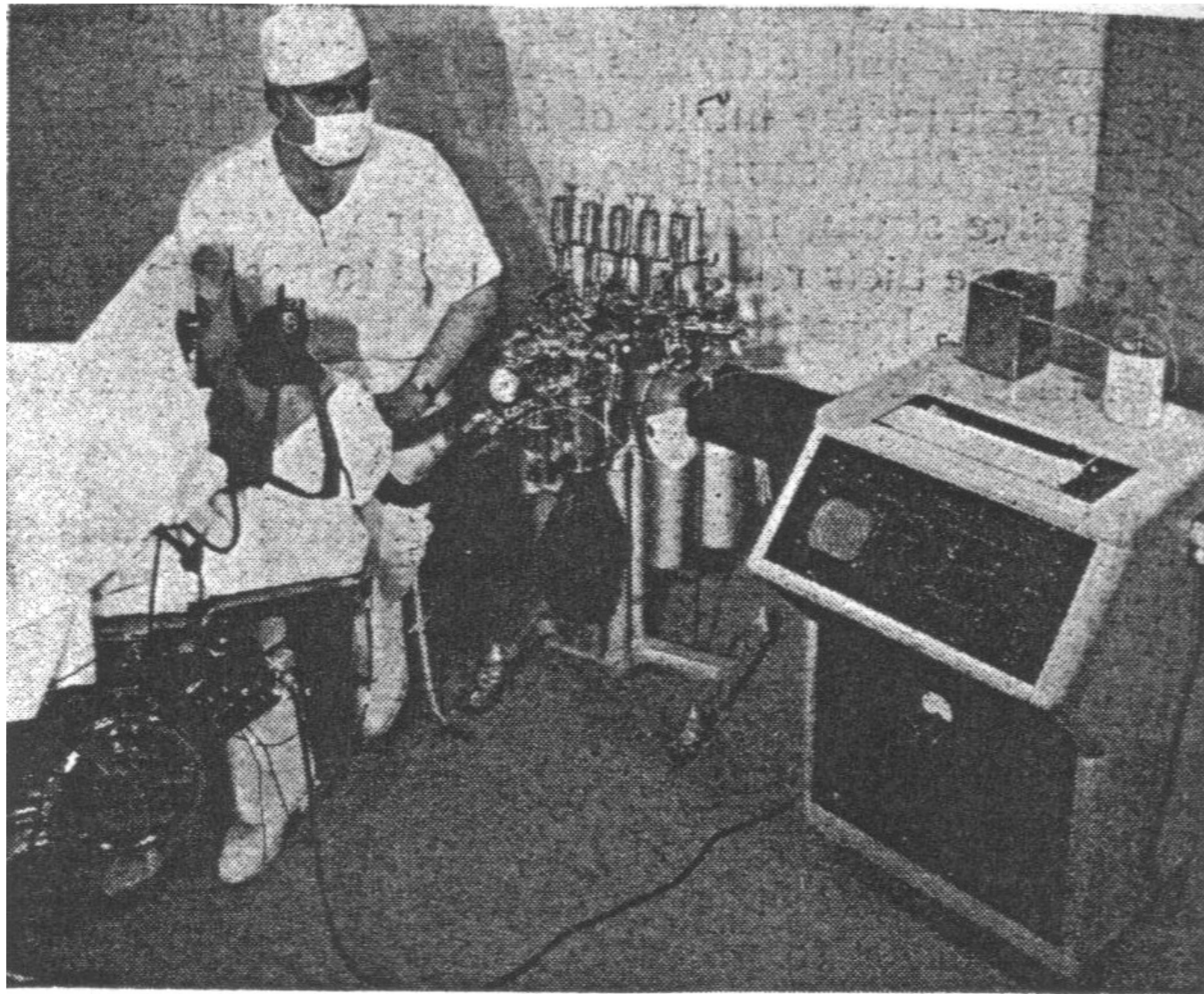
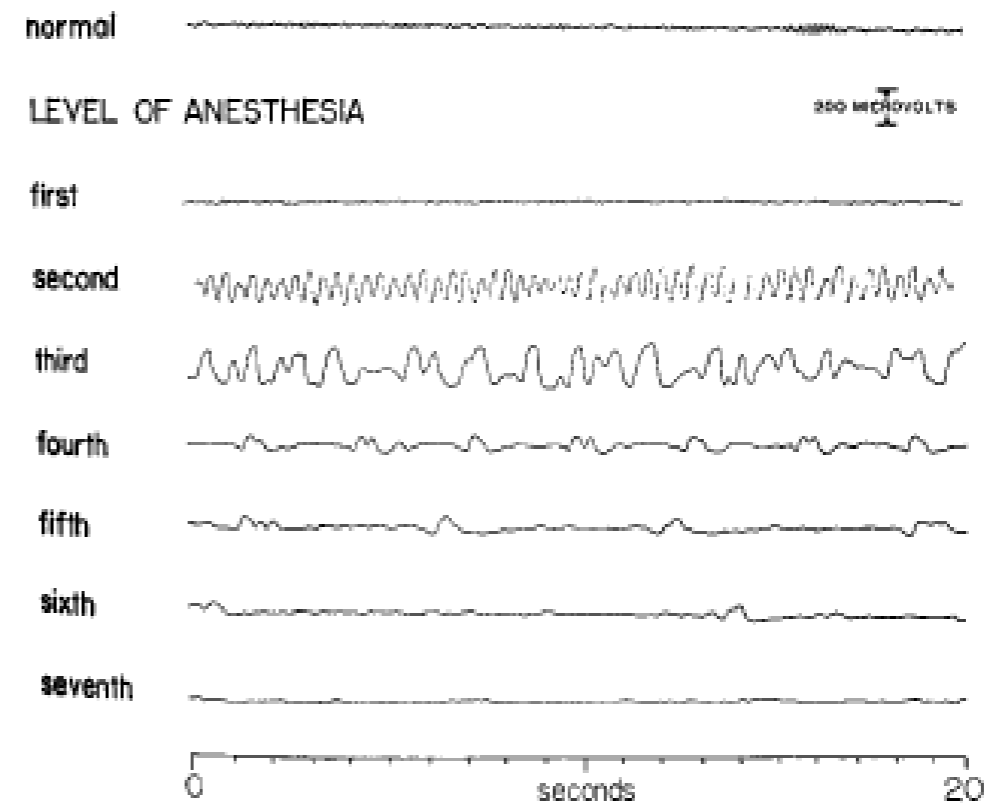


Fig. 2.—Automatic administration of ether.



The Pioneers : control anesthesia depth by EEG

# BISPECTRAL INDEX

1980's : BIS

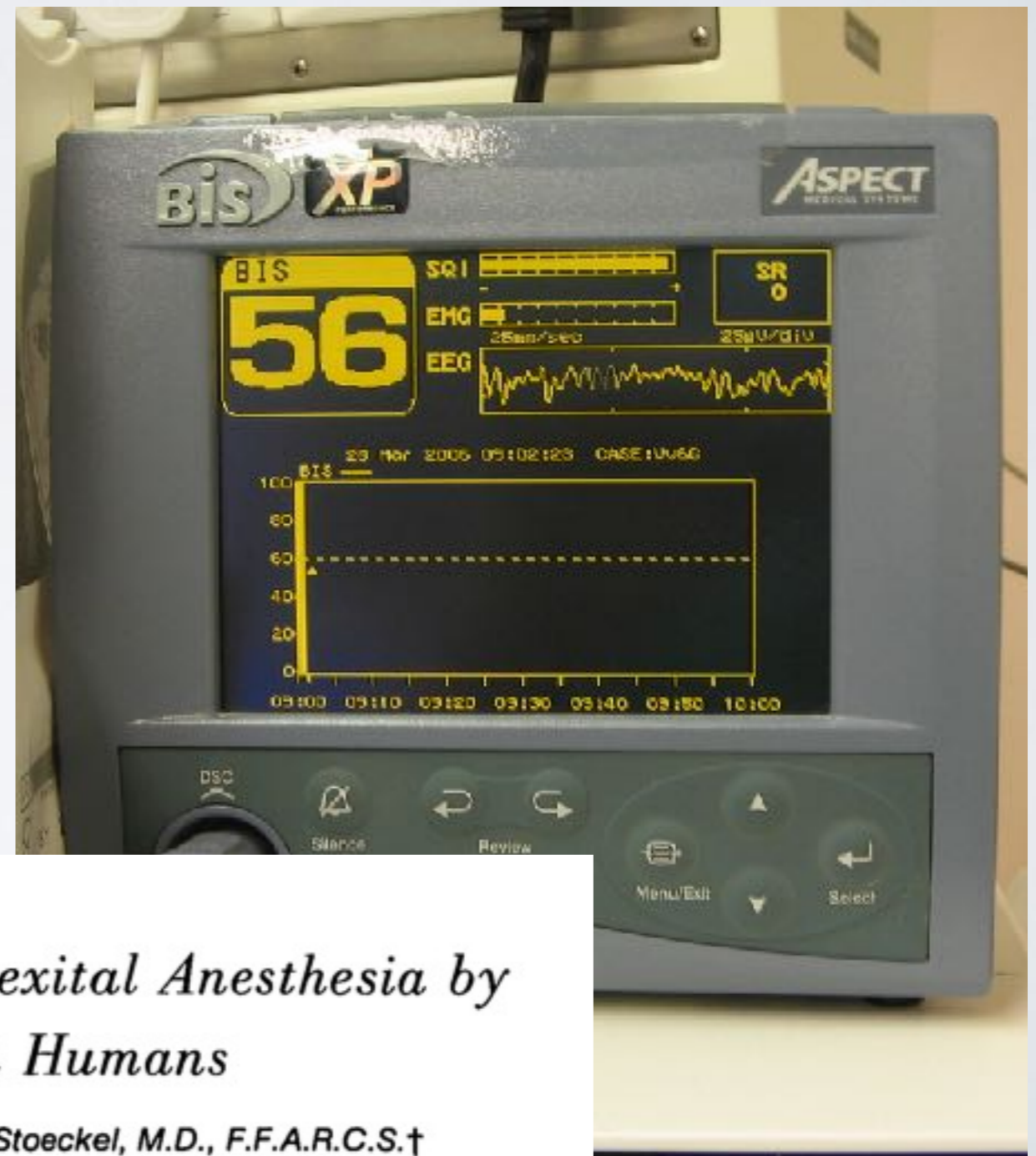
Derived index of the EEG, developed as a continuous measure of sedation and loss of consciousness (adequate anesthesia range 45-60)



# BISPECTRAL INDEX

1980's : BIS

Derived index of the EEG, developed as a continuous measure of sedation and loss of consciousness (adequate anesthesia range 45-60)



Anesthesiology  
67:341-347, 1987

*Closed-loop Feedback Control of Methohexital Anesthesia by  
Quantitative EEG Analysis in Humans*

Helmut Schwilden, M.D., Ph.D.,\* Jürgen Schüttler, M.D.,\* Horst Stoeckel, M.D., F.F.A.R.C.S.†

# HISTORIQUE

- AIVOC (TCI) et ses limites
- 1996 : commercialisation Diprifusor® (Marsch 1991)
- Variabilité intra et inter individuelle
- Limites : effectif ! Schnider (24 malades) Minto (65 sains)

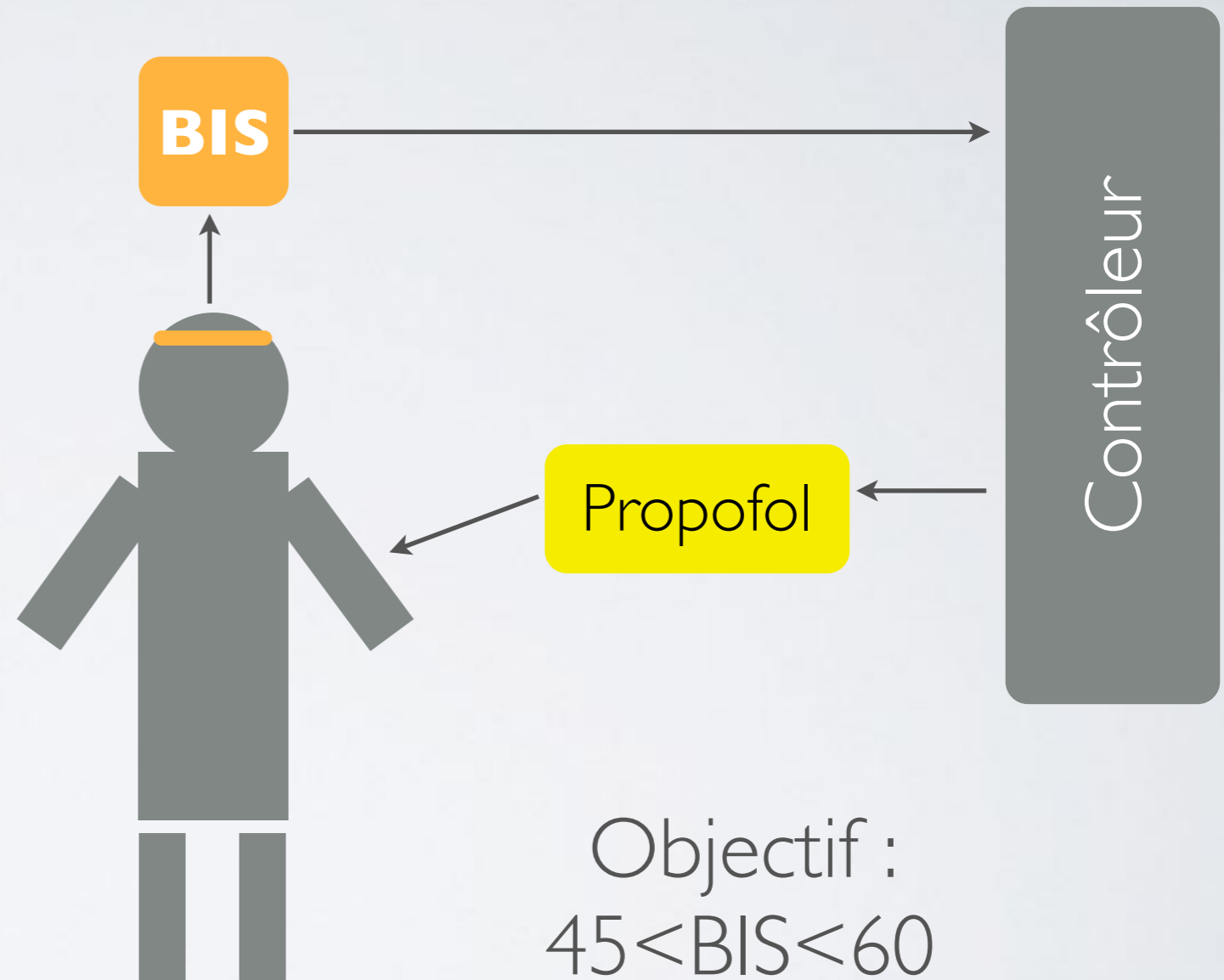


Schnider TW, Minto CF, Gambus PL, Andresen C, Goodale DB, Shafer SL, et al. The influence of method of administration and covariates on the pharmacokinetics of propofol in adult volunteers. *Anesthesiology*. 1998;88(5):1170-82.

Minto CF, Schnider TW, Egan TD, Youngs E, Lemmens HJ, Gambus PL, et al. Influence of age and gender on the pharmacokinetics and pharmacodynamics of remifentanyl. I. Model development. *Anesthesiology*. 1997;86(1):10-23.

# HISTORIQUE

- Simple boucle propofol
- Simple ? uniquement hypnotique
- Valeur Rétrocontrôle pour évaluation profondeur anesthésie ?
  - BIS
  - Entropy
  - Neurosense



# HISTORIQUE

Mortier, Anaesthesia 1998	Propofol	BIS	entretien
Kenny, BJA 1999	Propofol	BIS	entretien
Morley, Anaesthesia 2000	Propofol	BIS	entretien
Struys, Anesthesiology 2001	Propofol	BIS	entretien
Absalom, Anesthesiology 2002	Propofol	BIS	entretien
Absalom, BJA 2003	Propofol	BIS	entretien
Liu, Eur J Anesthesiol 2006	Propofol	BIS	induction/entretien
West, Paediatr Anaesth 2013	Propofol	BIS	induction/entretien
Moore, Anesth Analg 2011	Propofol	BIS	induction/entretien

# HISTORIQUE

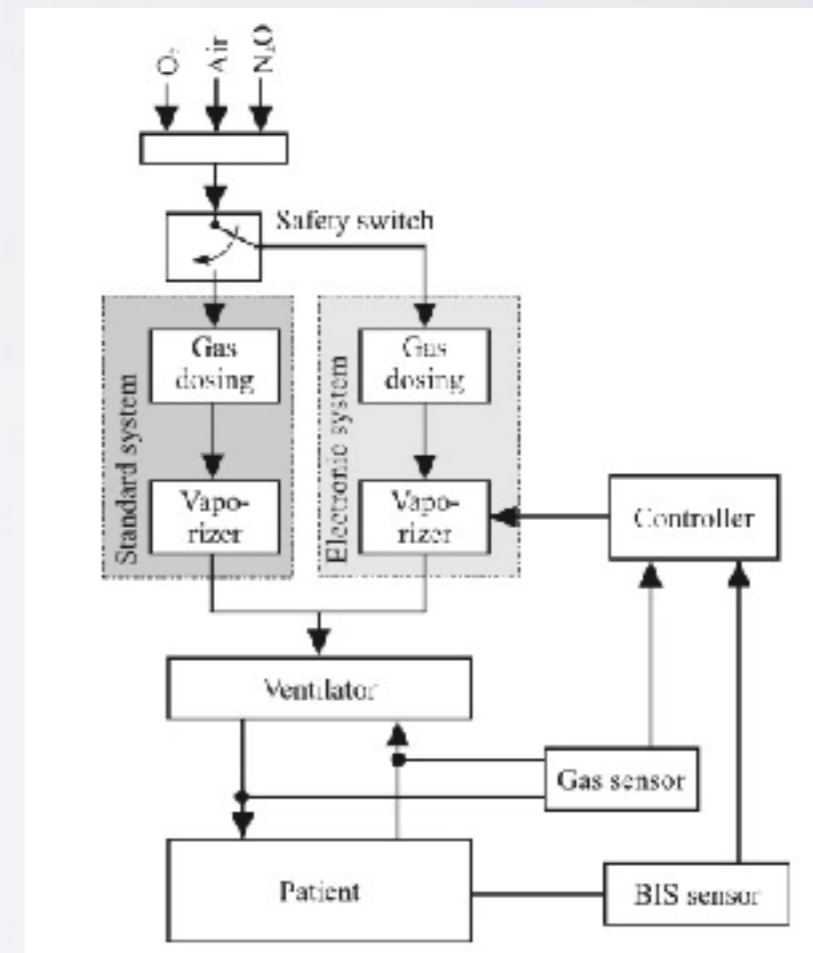
Anesthesiology 2004; 101:591-602

© 2004 American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

## ***A New Closed-Loop Control System for Isoflurane Using Bispectral Index Outperforms Manual Control***

Stephan Locher, M.D.,\* Konrad S. Stadler, M.Sc., Ph.D.,§ Thomas Boehlen, M.D.,\* Thomas Bouillon, M.D.,\*  
Daniel Leibundgut, M.Eng.,† Peter M. Schumacher, M.Sc., Ph.D.,† Rolf Wymann, M.D.,\* Alex M. Zbinden, M.D., Ph.D.‡

- Closed loop BIS / AVH
- Cible  $40 < \text{BIS} < 60$ , Closed loop pour entretien



# HISTORIQUE

- Etape suivante : double boucle : hypnotiques + morphiniques
- Difficulté : évaluer niveau analgésie/anti-analgésie ?
- Différentes solutions...



# EVALUATION ANTINOCICEPTION

Nombreux index, validation ?

- Analyse variabilité RR (ANI®)
- Différentiel RE/SE (Entropy®)
- Pupillométrie
- Variations BIS
- Analyse RC et PA (Cardean®)
- Analyse signal Plethysmographie (SPI)
- Conductance cutanée
- Variations Neurosens
- Combinaisons : Nociception level, AnalgoScore,....

# HISTORIQUE

Liu, Anesth Analg 2011	Propofol/Remifentanil	BIS	Induction/entretien
Besch, BJA 2011	Propofol/Remifentanil	BIS	entretien
Liu, Anesthesiology 2012	Propofol/Remifentanil	Entropy	Induction/entretien
Hemmerling, BJA 2013	Propofol/Remifentanil	BIS/AnalgoScore	Induction/entretien
Puri, Anesth Analg 2016	Propofol/Remifentanil	BIS	Induction/entretien
West, Anesth Analg 2018	Propofol/Remifentanil	Neurosens	Induction/entretien

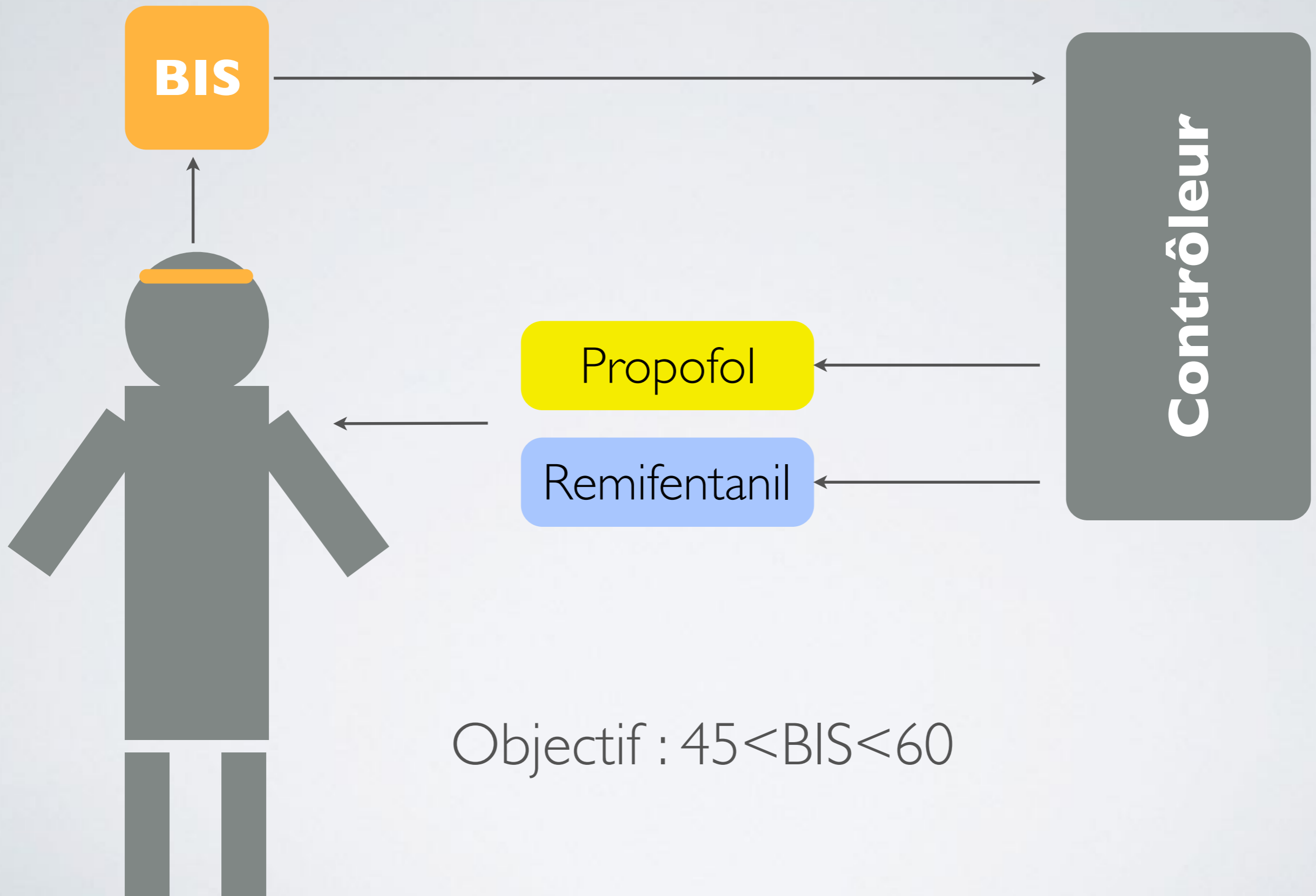
# Boucles complexes : Hypnotique / Morphinique / Curare

MacSleepy



# UN EXEMPLE : CLOSED-LOOP «FOCH»

- 2006 : Hôpital Foch, Dr Liu & Dr Chazot
- Système de délivrance automatisée des produits de l'anesthésie.
- Gère l'administration d'hypnotique et de morphinique de l'induction jusqu'au réveil.



Objectif :  $45 < \text{BIS} < 60$

# EN PRATIQUE

- Hypnotiques et Morphiniques a très courte durée d'action : Propofol 10 mg/ml et Ultiva 20 mcg/ml
- Algorithme basé sur l'analyse du signal de BIS, interprétation séquentielle (30-90 sec), objectif :  $45 < \text{BIS} < 60$
- Curarisation manuelle
- Enregistrement des événements marquants de l'intervention sur le logiciel (intubation, incision, écarteurs, fin anesthésie,...), Feuille d'anesthésie informatisée





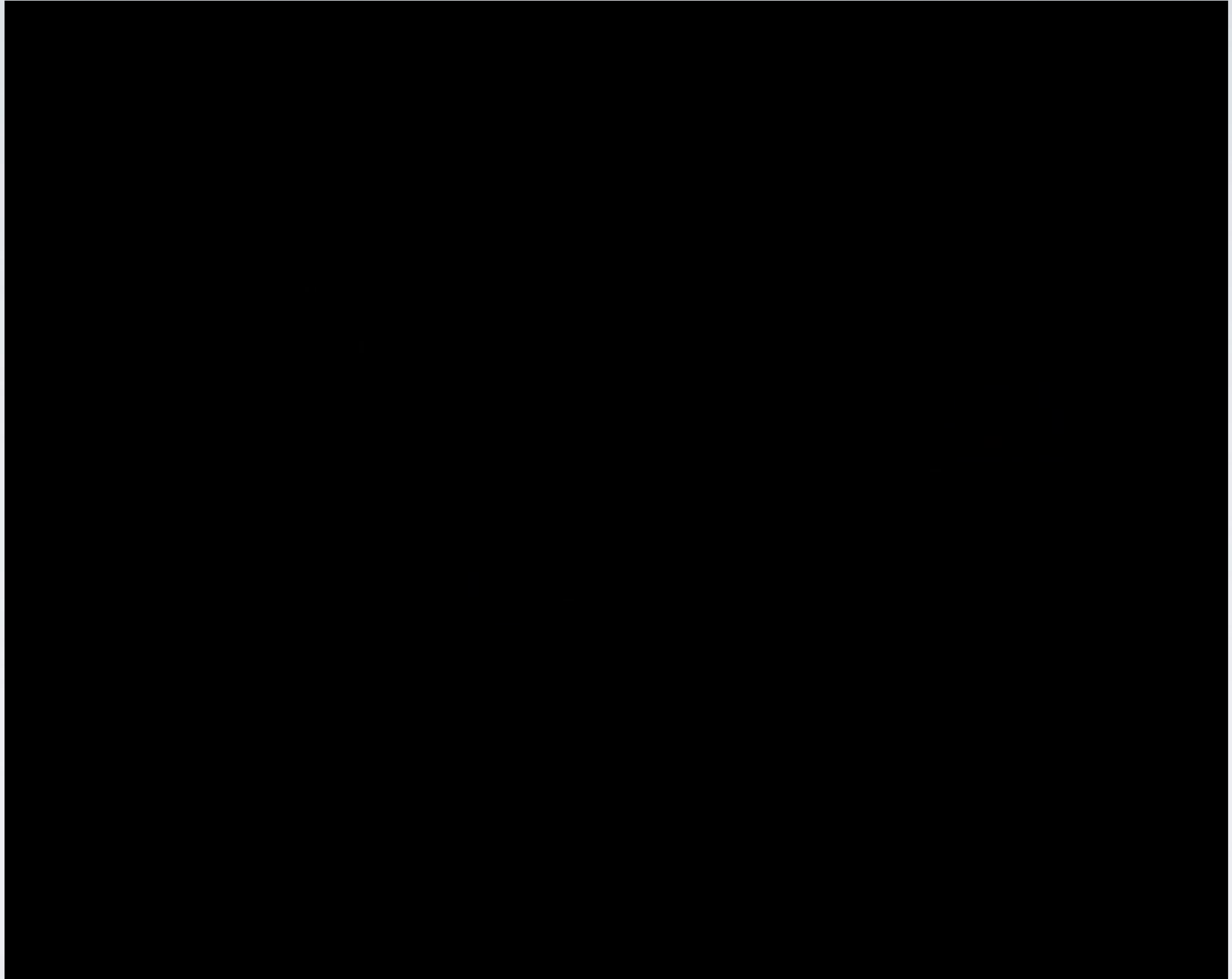
Computer monitor displaying medical software with multiple panels:

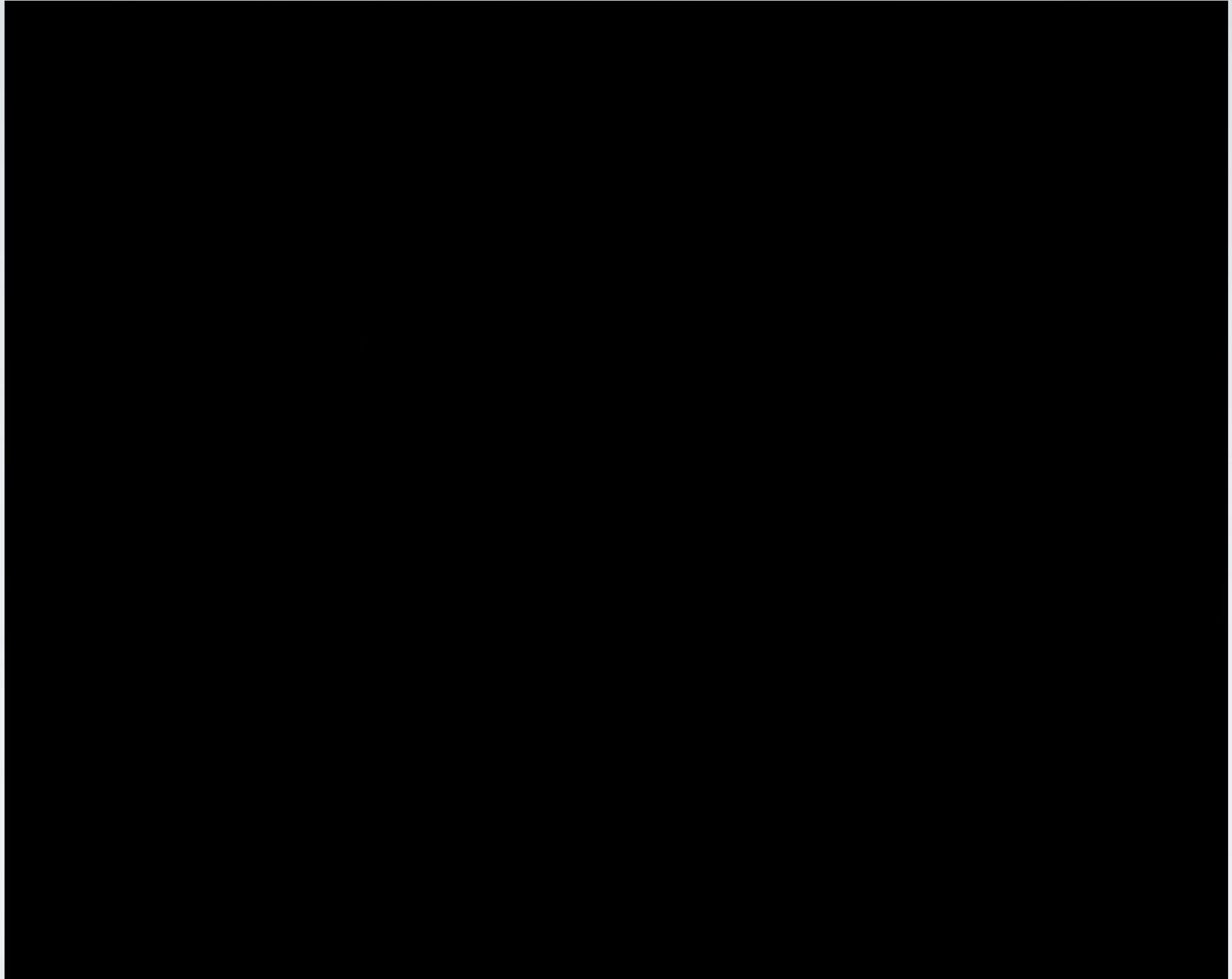
- Top Left Panel:** Shows numerical values and graphs. Includes fields for "Active Target" (2.2), "Plasma" (3.25), and "E-Net" (1.20).
- Top Middle Panel:** Shows numerical values and graphs. Includes fields for "Active Target" (8.6), "Plasma" (5.00), and "E-Net" (5.61).
- Top Right Panel:** Titled "Steps of Catheterization", listing various medical steps such as "Cannavag", "Prepatal Passage in Manual", "Postatal Passage in Manual", "Prepatal BladderPassat", "Postatal BladderPassat", "Ant", "Nuchocatheter", "Retract catheter", "Prepatal Lincite Int", "Postatal Lincite Int", "Prepatal Lincite Sup", "Postatal Lincite Sup", and "Prepatal Lincite Sup".
- Bottom Left Panel:** Shows a graph with a blue line and numerical values.
- Bottom Middle Panel:** A large blue area with the word "Aspect" visible.
- Bottom Right Panel:** Titled "Masks", listing various medical masks and procedures such as "Aut H1A", "Catheter", "Cannex Inlet", "E-cath", "E-phibite", "E-catheter", "E-catheter Paul", "Inchite", "Inchite", "Laryngoscope", "Masque larynx", "Masque", "Mouvement", "Neurophysiologie / Catheterisation", "Pente du reflex ciliale", "Prepatalion", and "Prepatal. Ouvre les yeux".

Medical equipment including a monitor with the brand name "ANEBBOX" and a control panel with various buttons and dials.

Operating room environment showing a surgeon in yellow scrubs and a green cap performing an operation on a patient lying on a table. The patient is covered with blue drapes and has various monitoring wires attached. The room is filled with medical equipment, including monitors and a large overhead light fixture illuminating the surgical site.







# ANESTHÉSIE DU BRÛLÉ

<b>Nombre de patients</b>	<b>100</b>
<b>Sexe (M/F) (nombre)</b>	<b>59/41</b>
<b>Age (années)</b>	<b>50±20 ; 47 (35-67)</b>
<b>Taille (Cm)</b>	<b>168,9±11,6 ; 170 (160-176)</b>
<b>Poids (kg)</b>	<b>72±18 ; 71 (60-82)</b>
<b>IMC</b>	<b>25±5,5 ; 24,2(21,9-26,8)</b>
<b>Score ASA (nombre)</b>	
1	22
2	57
3	19
4	1
<b>Score ABSI</b>	<b>6,9±3,7 ; 6 (5-7)</b>
<b>Surface cutanée brûlée (%)</b>	<b>18±19 ; 12 (4-25)</b>
<b>Inhalation de fumée (nombre)</b>	<b>13</b>
<b>BIS&lt;40</b>	<b>18 (11-28)</b>
<b>BIS&gt;60</b>	<b>6 (4-10)</b>
<b>BIS 40-60</b>	<b>74 (63-83)</b>
<b>Global Score</b>	<b>31 (23-47)</b>
<b>Consommation Propofol (mg/kg/h)</b>	<b>5,0 (4-8)</b>
<b>Consommation rémifentanil (µg/kg/h)</b>	<b>0,19 (0,14-0,28)</b>

AVANTAGES

# DIMINUTION DES DOSES



**Table 2. Clinical Data and Performance of Induction Phase**

	Manual TCI (n = 81)	Closed-loop (n = 83)	P Value
Premedication, none/hydroxyzine/diazepam	9/50/22	10/54/19	NS
Duration of induction, s	271 ± 120	320 ± 125	0.0002
Propofol induction dose, mg/kg	1.8 ± 0.6	1.4 ± 0.5	< 0.0001
Propofol target, µg/ml	3.8 ± 1.2	3.2 ± 1.0	< 0.0001
Remifentanyl induction dose, µg/kg	2.5 ± 1.2	2.7 ± 1.1	NS
Remifentanyl target, µg · kg <sup>-1</sup> · min <sup>-1</sup>	6.0 ± 2.2	6.1 ± 2.2	NS
Use of neuromuscular blocker, %	91	90	NS
Ephedrine bolus, %	16	12	NS
Antihypertensive therapy, %	0	1	NS
Overshoot BIS < 40, s	29 ± 50	12 ± 26	0.005
Undershoot BIS > 70, s	7 ± 18	10 ± 24	NS

Data are presented as mean ± SD, number, or % of total patients in each group.

Closed-loop = closed-loop group; duration of induction = time elapsed from the start of propofol administration to the moment when the Bispectral Index (BIS) value fell to and remained under 60 for 30 s; manual TCI = manual target-controlled infusion group guided by BIS; NS = not significant; overshoot BIS < 40: duration of BIS under 40 in a period of 3 min after the BIS value fell and remained under 60; undershoot BIS > 70: duration of BIS greater than 70 in a period of 3 min after the BIS value fell and remained under 60.

Liu N, Chazot T, Trillat B, Pirracchio R, Law-Koune JD, Barvais L, et al. Feasibility of closed-loop titration of propofol guided by the Bispectral Index for general anaesthesia induction: a prospective randomized study. *Eur J Anaesthesiol.* 2006 Jun;23(6):465-9.

# DIMINUTION DES DOSES



**Table 2. Clinical Data and Performance of Induction Phase**

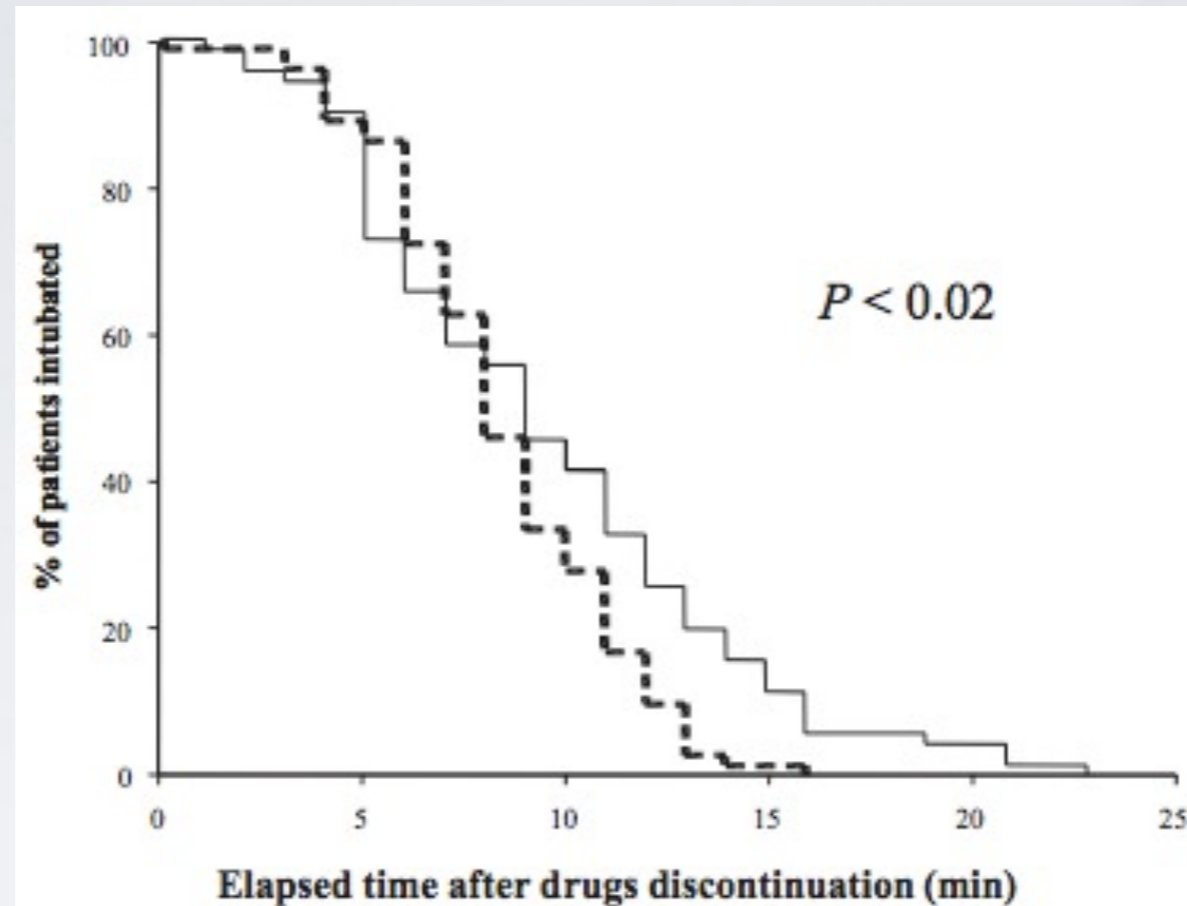
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# RÉVEIL PLUS RAPIDE



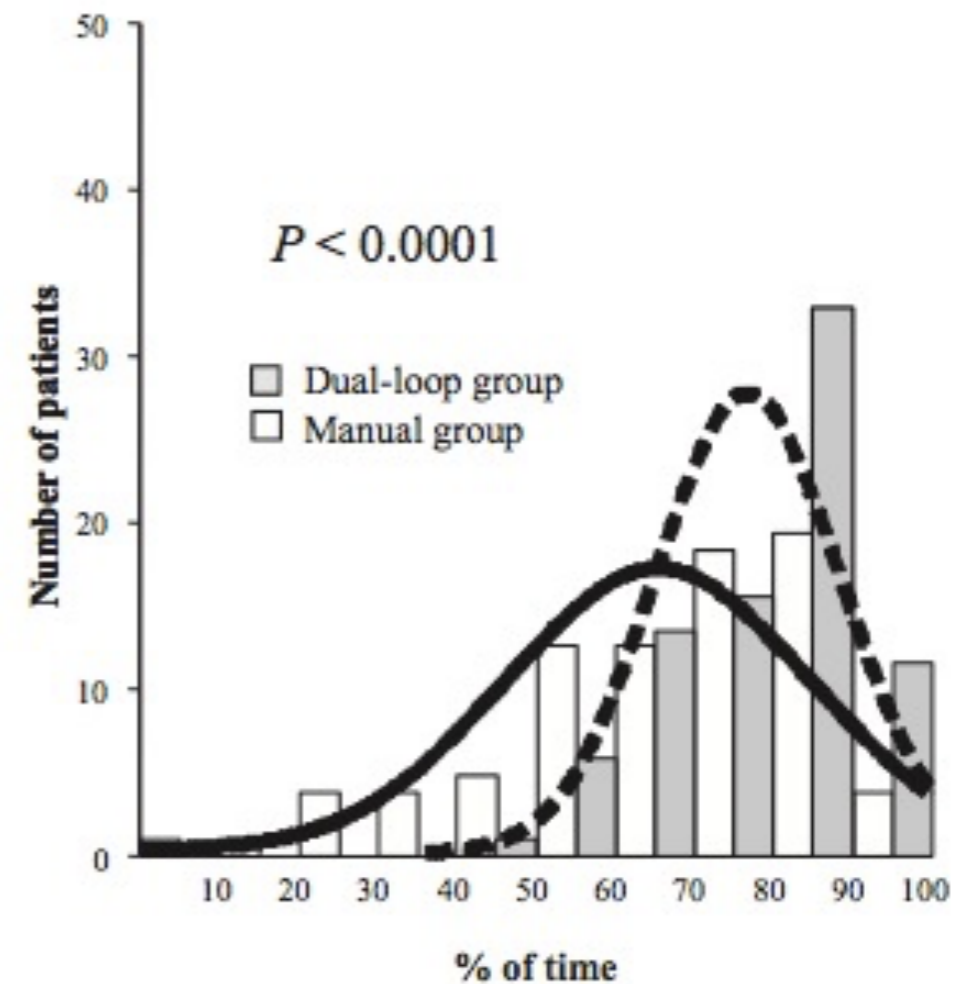
**Figure 7.** Kaplan-Meier analysis of remaining intubated patients after the discontinuation of propofol and remifentanyl in dual-loop (dashed line) and manual (solid line) groups.

**ANESTHESIOLOGY**   
The Journal of the American Society of Anesthesiologists, Inc.

Liu N, Chazot T, Genty A, Landais A, Restoux A, McGee K, et al. Titration of propofol for anesthetic induction and maintenance guided by the bispectral index: closed-loop versus manual control: a prospective, randomized, multicenter study. *Anesthesiology*. 2006 Apr;104(4):686-95.

# PERFORMANCE

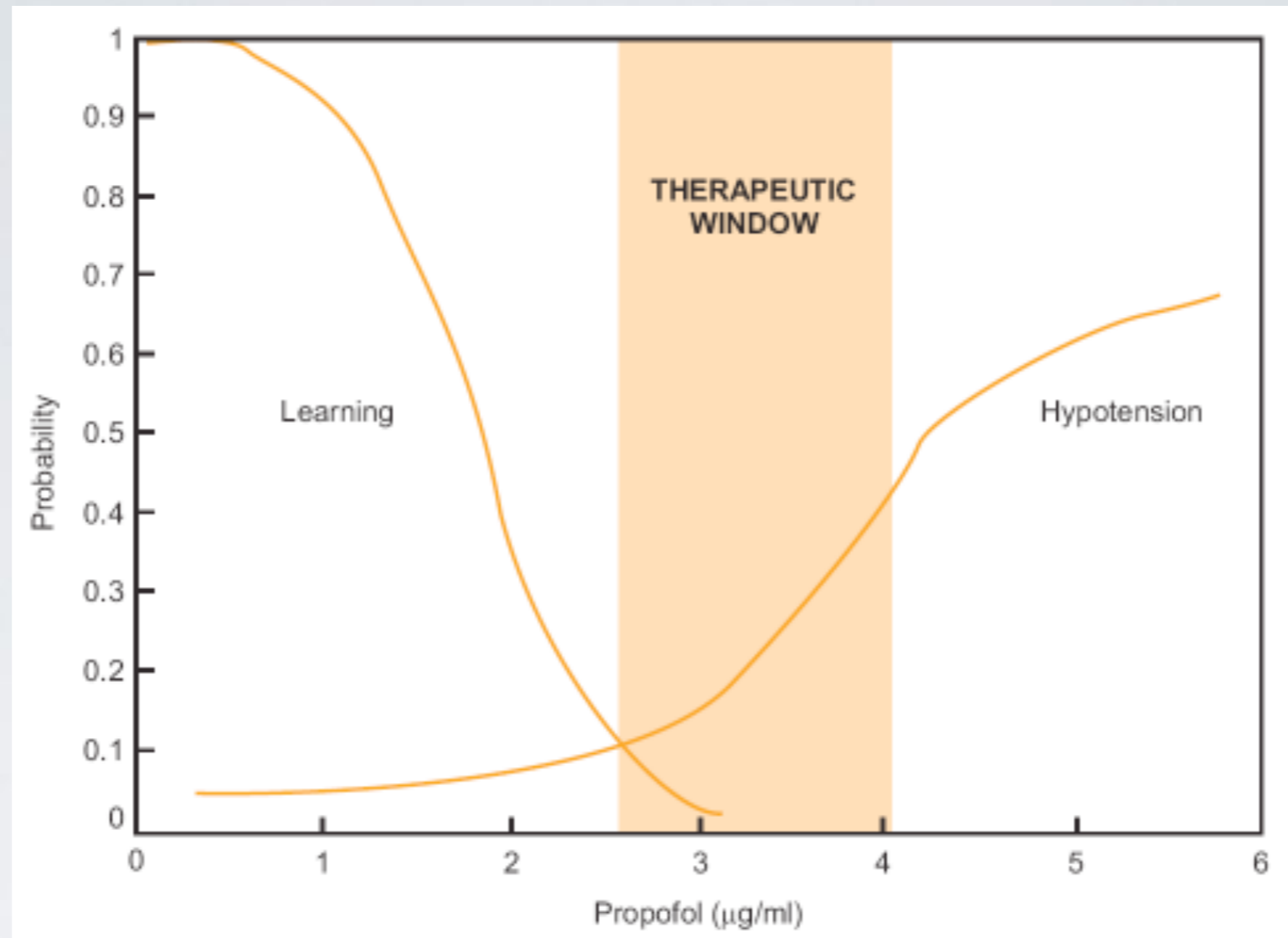
- Maintain BIS in the target area better than manual



**Figure 5.** Histogram of percentage of time that the Bispectral Index value was between 40 and 60, which is defined as adequate maintenance control. Normal distribution curve for dual-loop (dashed line) and manual (solid line) groups.

**ANESTHESIA & ANALGESIA**  
*The Gold Standard in Anesthesiology*





- Eviter les épisodes de surdosage : effets hémodynamiques, burst suppression (EEG)
- Eviter les épisodes de sous dosage : mémorisation

Argenteuil, Dreux, Tenon, HEGP, Necker, Bicêtre, HIA  
Percy, Pitié, Bécclere

**10 ans**  
**15000 anesthésies**  
**>5000 inclusions**

**27 centers**  
**+ 120 users**  
**50 prototypes**

Tours  
Rennes  
Angers  
Bordeaux

Nouméa



Strasbourg

Besançon

Dijon

Lyon

Bruxelles Berlin Tchad Burundi

Award of Best Clinical application of Technology  
ASA 2010 / Society for technology in Anaesthesia

# CHARGE DE TRAVAIL

Libère du temps médical et paramédical : permet de compléter la mise en condition du patient, transfusion...



# SÉCURITÉ

Diminue le risque d'erreur d'injection :

- pas de manipulation de seringue,
- si erreur de dilution : effet masqué par l'adaptabilité du système de rétrocontrôle



# REPRODUCTIBILITÉ

- Uniformisation et reproductibilité de la conduite de l'anesthésie.
- Traitement reproductible de situations cliniques identiques
- Evaluation continue et non itérative

# ADAPTABILITÉ

Adaptation aux situations complexes :

- obèse, gigantisme, brûlés...

Adapté aux chirurgies hémorragiques :

- utilisé en chirurgie cardiaque et vasculaire, chirurgie de la greffe...

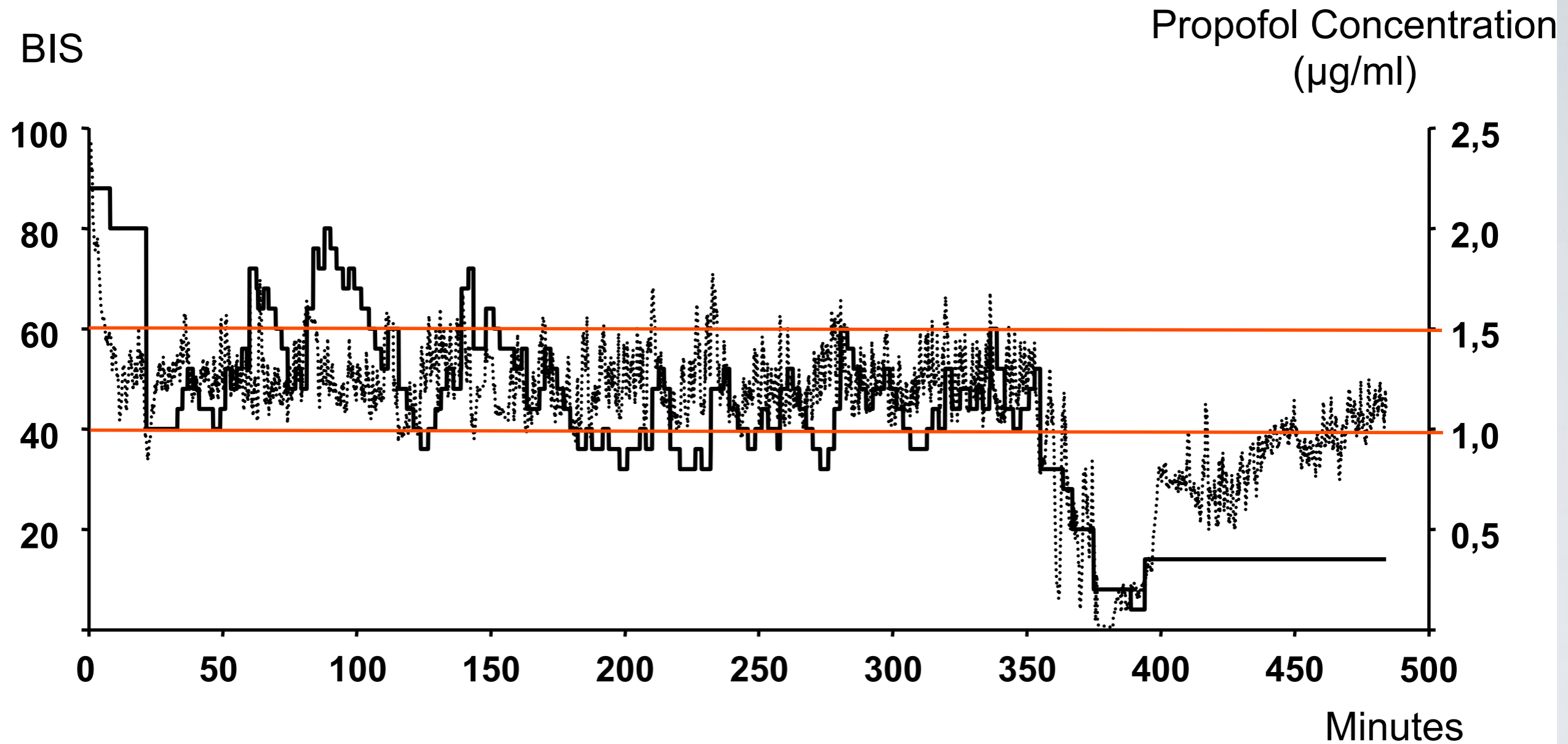
➔ Adaptation fine des doses grâce au rétrocontrôle

Liu N, Chazot T, Trillat B, Michel-Cherqui M, Marandon JY, Law-Koune JD, et al. Closed-loop control of consciousness during lung transplantation: an observational study. *J Cardiothorac Vasc Anesth.* 2008 Aug;22(4):611-5.

Liu N, Lory C, Assenzo V, Cocard V, Chazot T, Le Guen M, et al. Feasibility of closed-loop co-administration of propofol and remifentanyl guided by the bispectral index in obese patients: a prospective cohort comparison. *Br J Anaesth.* 2015;114(4):605-14.

Declerck A, Liu N, Gaillard S, Chazot T, Laloe PA, Fischler M, et al. Closed-loop titration of propofol and remifentanyl guided by Bispectral Index in a patient with extreme gigantism. *J Clin Anesth.* 2009;21(7):542-4.

# ACR per opérateur



# EN OPEX

Tchad : 21 patients

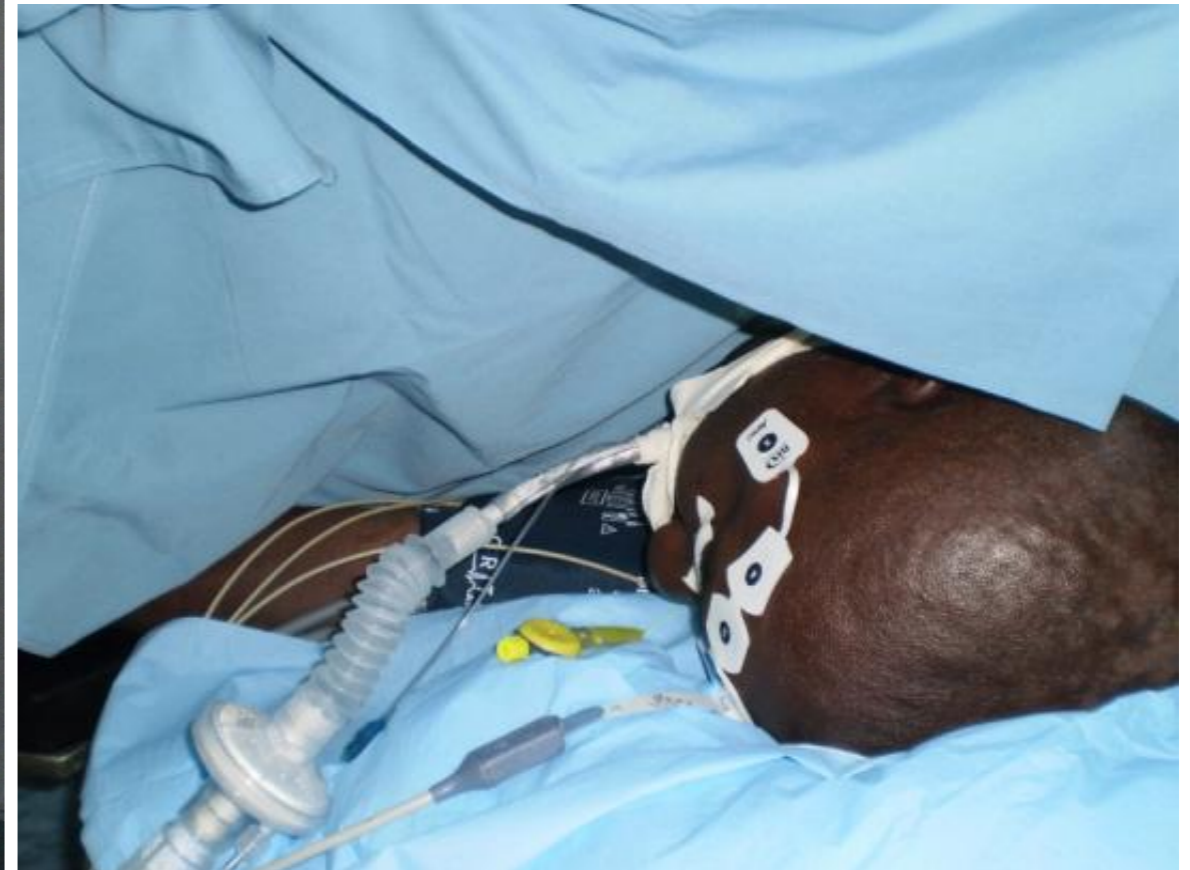
	<b>Durée (min)</b>	<b>40&lt;BIS&lt;60 (%)</b>	<b>BIS&lt;40 (%)</b>	<b>BIS&gt;60 (%)</b>
<b>Moyenne (écart type)</b>	<b>124,1 (42,1)</b>	<b>82 (11,1)</b>	<b>14,1 (9,3)</b>	<b>3,8 (2,8)</b>

données personnelles MC BATJOM





# Closed-loop Anesthesia in Kamenge, BURUNDI July 2010



# ANALYSE DE LA LITTÉRATURE

■ SYSTEMATIC REVIEW ARTICLE

## **Clinical Performance and Safety of Closed-Loop Systems: A Systematic Review and Meta-analysis of Randomized Controlled Trials**

Brogi E, Cyr S, Kazan R, Giunta F, Hemmerling TM. Clinical Performance and Safety of Closed-Loop Systems: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Anesth Analg*. 2017;124(2):446-55.

ANALYSIS

LITERATURE

SYSTEMATIC REVIEW ARTICLE

**Clinical Performance and Safety of Closed-Loop Systems: A Systematic Review and Meta-analysis of Randomized Controlled Trials**

Authors	Year of publication	Type of closed loop	No. of treatment/control	Controlled variable
Agarwal et al <sup>20</sup>	2009	CLADS	22/18	BIS
Biswas et al <sup>21</sup>	2013	CLADS	20/20	BIS
Breton et al <sup>22</sup>	2012	Glucose control (sCTR)	26/26	BG
		Glucose control (eCTR)	12/12	
Cavalcanti et al <sup>23</sup>	2009	CAIP	56/58	BG
Claire et al <sup>24</sup>	2001	cFiO <sub>2</sub> system	14/14	SpO <sub>2</sub>
Claire et al <sup>25</sup>	2011	cFiO <sub>2</sub> system	32/32	SpO <sub>2</sub>
Dauber et al <sup>26</sup>	2013	Insulin therapy	10/10	BG
De Smet et al <sup>27</sup>	2008	Propofol administration	20/20	BIS
Dojat et al <sup>28</sup>	2000	PSV control	10/10	RR, Vt, EtCO <sub>2</sub>
Dussaussoy et al <sup>10</sup>	2014	Dual loop	18/18	BIS
Elleri et al <sup>29</sup>	2013	Insulin delivery	12/12	BG
Hallenberg et al <sup>30</sup>	2014	CLAC	34/34	SpO <sub>2</sub>
Hemmerling et al <sup>31</sup>	2010	Propofol administration	20/20	BIS
Hemmerling et al <sup>8</sup>	2013	McSleepy	93/93	BIS Analgoscore TOF
Hovorka et al <sup>32</sup>	2010	Insulin delivery	12/12	BG
Johannigman et al <sup>33</sup>	2009	FiO <sub>2</sub> control	15/15	SpO <sub>2</sub>
Kee et al <sup>34</sup>	2012	AP control	108/103	AP
Le Guen et al <sup>35</sup>	2013	Dual loop	15/14	BIS
Leelarathna et al <sup>36</sup>	2013	Glucose control	12/12	BG
Lellouche et al <sup>37</sup>	2013	Intelli-Vent system	30/30	EtCO <sub>2</sub> , SpO <sub>2</sub>
Liu et al <sup>38</sup>	2006	Propofol administration	83/81	BIS
Liu et al <sup>39</sup>	2011	Dual loop	83/84	BIS
Liu et al <sup>40</sup>	2012	Dual loop	30/31	SE, RE
Locher et al <sup>41</sup>	2004	Isoflurane	10/10	BIS
Ly et al <sup>42</sup>	2014	USS	20/29	BG
Nimri et al <sup>43</sup>	2013	MDLAP	12/12	BG
Nimri et al <sup>44</sup>	2014	MDLAP	19/19	BG
Plank et al <sup>45</sup>	2006	MPC control	30/30	BG
Puri et al <sup>9</sup>	2007	CLADS	20/20	BIS
Renard et al <sup>46</sup>	2010	Intraperitoneal pump	8/8	BG
Schädler et al <sup>47</sup>	2012	SmartCare/PS	150/150	RR Vt EtCO <sub>2</sub>
Madhavan et al <sup>48</sup>	2011	IAADS	20/20	BIS
Sng et al <sup>49</sup>	2014	Dual loop	106/107	AP
Solanki et al <sup>50</sup>	2010	CLADS	20/20	BIS
Struys et al <sup>51</sup>	2001	Propofol administration	10/10	BIS
Urschitz et al <sup>52</sup>	2004	FiO <sub>2</sub> control	12/12	SpO <sub>2</sub>

Brogi E, Cyr S, Kazan R, Giunta F, Hemmerling TM. Clinical Performance and Safety of Closed-Loop Systems: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Anesth Analg.* 2017;124(2):446-55.

# ANALYSIS

# TEMPERATURE

SYSTEMATIC REVIEW ARTICLE

Clinical  
System  
Random

Authors	Year of publication	Type of closed loop	No. of treatment/control	Controlled variable
Agarwal et al <sup>20</sup>	2009	CLADS	22/18	BIS
Biswas et al <sup>21</sup>	2013	CLADS	20/20	BIS
Breton et al <sup>22</sup>	2012	Glucose control (sCTR)	26/26	BG
		Glucose control (eCTR)	12/12	
Cavalcanti et al <sup>23</sup>	2009	CAIP	56/58	BG
Claire et al <sup>24</sup>	2001	cFiO <sub>2</sub> system	14/14	SpO <sub>2</sub>
Claire et al <sup>25</sup>	2011	cFiO <sub>2</sub> system	32/32	SpO <sub>2</sub>
Dauber et al <sup>26</sup>	2013	Insulin therapy	10/10	BG
De Smet et al <sup>27</sup>	2008	Propofol administration	20/20	BIS
Dojat et al <sup>28</sup>	2000	PSV control	10/10	RR, Vt, EtCO <sub>2</sub>

Study	Automated Control		Manual Control	
	Total	Mean	Total	Mean
Agarwal 2009	19	80.40	18	69.6
Biswas 2013	20	77.40	20	75.0
De Smet 2008	20	75.00	20	43.0
Dussaussoy 2014	18	94.00	18	74.0
Hemmerling 2010	20	84.00	20	66.0
Hemmerling 2013	93	81.40	93	69.6
Le Guen 2013	15	73.75	14	37.5
Liu 2006	83	89.00	81	70.0
Liu 2011	83	82.00	84	71.0
Liu 2012	30	80.00	31	60.0
Locher 2004	10	99.50	10	89.7
Madhavan 2011	20	84.60	20	75.9
Puri 2007	20	87.32	20	77.3
Solanki 2010	20	68.70	20	45.4
Struys 2001	10	89.00	10	49.0

Random effects model 481 479  
Heterogeneity: I-squared=85.8%, tau-squared=68.86, p<0.0001

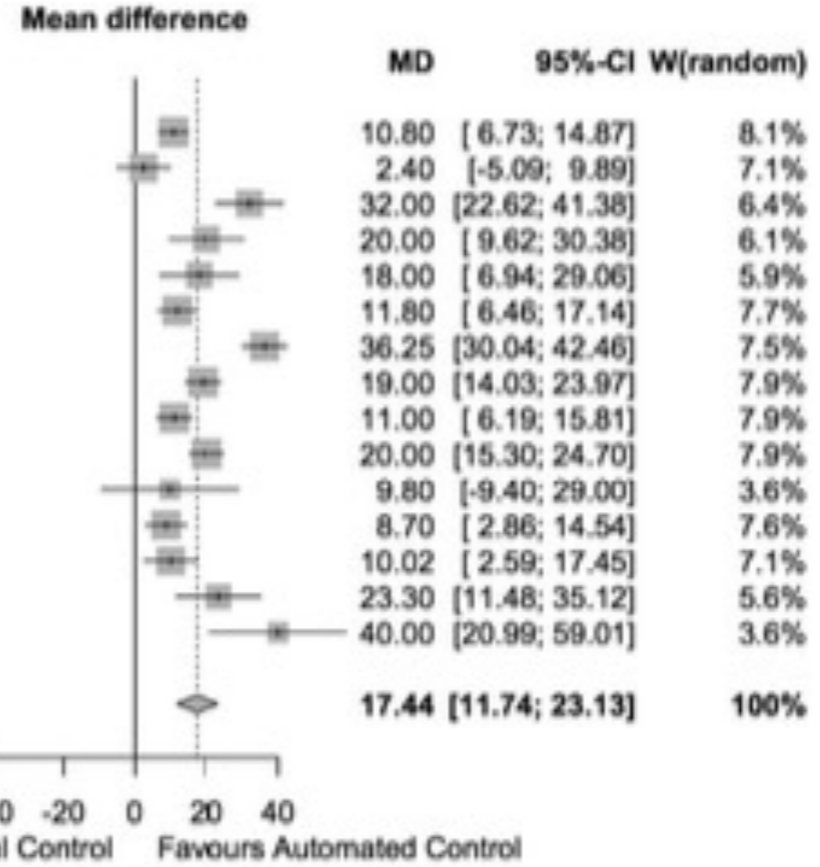


Figure 2. Forest plot presenting the percentage of time a given target (bispectral index or SE) was maintained within the desired range in closed-loop delivery systems (automated control) in comparison with manual control. The diamond represents the pooled results while the horizontal line represents the 95% confidence interval (CI).

Solanki et al <sup>29</sup>	2010	CLADS	20/20	BIS
Struys et al <sup>31</sup>	2001	Propofol administration	10/10	BIS
Urschitz et al <sup>32</sup>	2004	FiO <sub>2</sub> control	12/12	SpO <sub>2</sub>

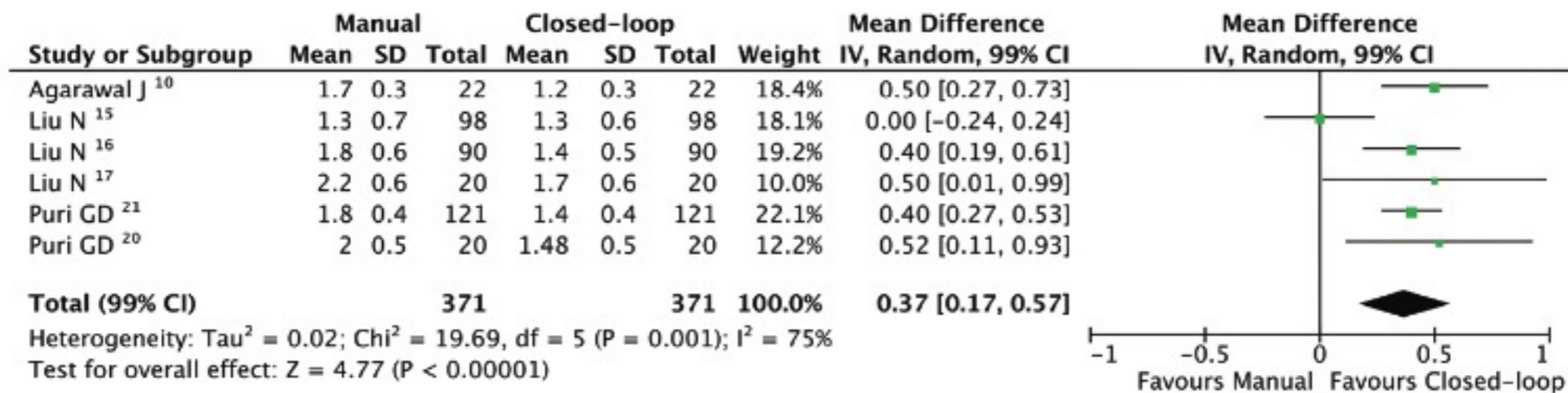
Brogi E, Cyr S, Kazan R, Giunta F, Hemmerling TM. Clinical Performance and Safety of Closed-Loop Systems: A Systematic Review and Meta-analysis of Randomized Controlled Trials. Anesth Analg. 2017;124(2):446-55.

# ANALYSIS OF THE LITERATURE

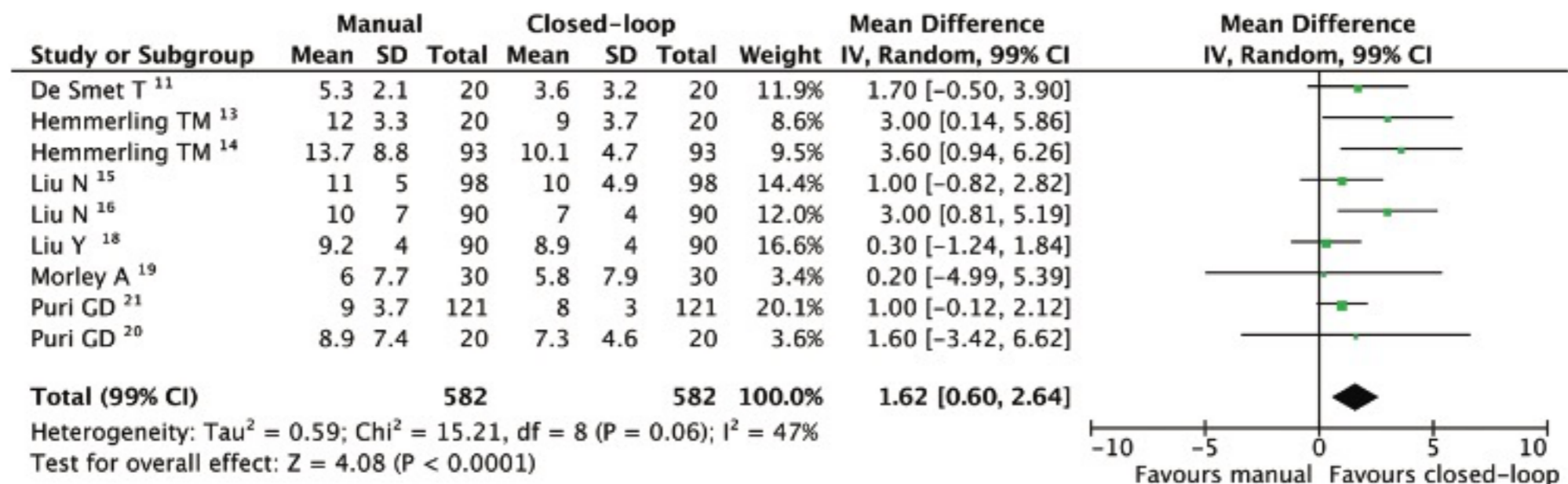
**Table 1. Description of the 12 Trials Included in the Meta-analysis**

First Author	Year	Journal	Setting	No. of Centers	Device
Agarwal <sup>10</sup>	2009	Acta Anaesthesiol Scand	Elective cardiac surgery requiring cardiopulmonary bypass	1	CLADS™
De Smet <sup>11</sup>	2008	Anesth Analg	Ambulatory ovocytes retrieval	1	RUGLOOP II™
Dussaussy <sup>12</sup>	2014	J Clin Monit Comput	Elective surgery including lung resections, carotid surgery, major vascular surgery, peripheral vascular surgery, and minor procedures	1	Infusion Toolbox 95™
Hemmerling <sup>13</sup>	2010	Can J Anaesth	Elective abdominal, thoracic, urologic, and spine or upper extremity orthopedic surgery	1	Self-designed interface
Hemmerling <sup>14</sup>	2013	Br J Anesth	Elective surgery requiring general anesthesia with an expected duration of ≥60 min, including abdominal, thoracic, urologic, and orthopedic procedures	1	McSleepy™
Liu <sup>15</sup>	2011	Anesth Analg	Elective surgery requiring general anesthesia or combined regional/general anesthesia expected to last >30 min and requiring tracheal intubation	4	Infusion Toolbox 95™
Liu <sup>16</sup>	2006	Anesthesiology	Elective surgical procedures requiring general anesthesia of at least 30 min	3	Infusion Toolbox 95™
Liu <sup>17</sup>	2006	Eur J Anesthesiol	Elective general, gynecologic, urologic, orthopedic, or lung surgery	1	Infusion Toolbox 95™
Liu <sup>18</sup>	2015	Plos One	General anesthesia expected to last >120 min, including head and neck surgery, chest wall and breast surgery, thoracic surgery, hepatobiliary and gastrointestinal surgery, and urologic and gynecologic surgery	3	CONCERT-CL™
Morley <sup>19</sup>	2000	Anesthesia	Gynecologic or general surgery	1	Monitor™
Puri <sup>20</sup>	2007	Anesth Intensive Care	Elective cholecystectomy, upper and lower abdominal surgery, hernia surgery under general anesthesia	1	CLADS™
Puri <sup>21</sup>	2015	Anest Analg	Elective nonthoracic, nonvascular, nonneurosurgic procedure of expected duration of 1–3 h under general anesthesia without combined regional anesthesia	6	CLADS™

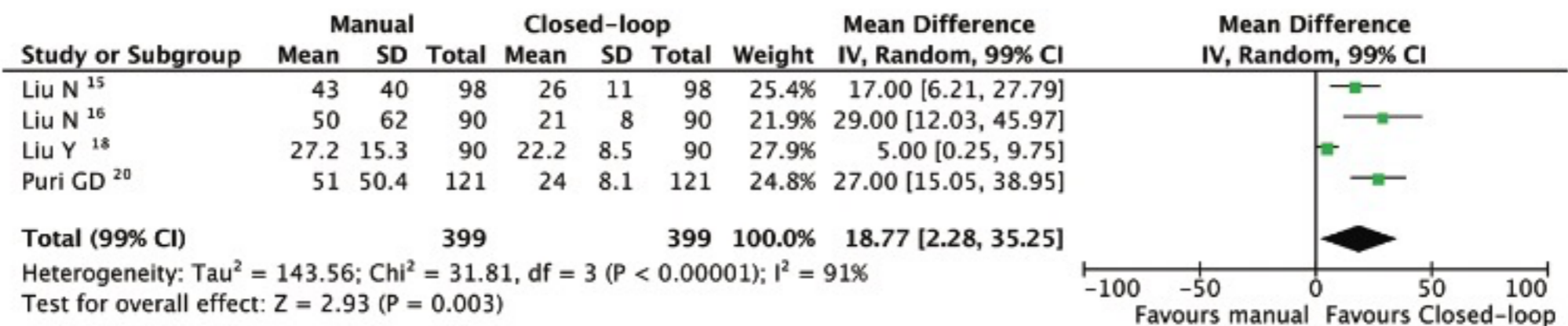
Pasin L, Nardelli P, Pintaudi M, Greco M, Zambon M, Cabrini L, et al. Closed-Loop Delivery Systems Versus Manually Controlled Administration of Total IV Anesthesia: A Meta-analysis of Randomized Clinical Trials. *Anesth Analg*. 2017;124(2):456-64.



**Figure 3.** Forest plot of dose of propofol for anesthesia induction (milligram per kilogram). CI indicates confidence interval.



**Figure 2.** Forest plot of recovery times (minutes). CI indicates confidence interval.



**Figure 5.** Forest plot of the Global Scores. CI indicates confidence interval.

# CRITÈRES DE RÉUSSITE

- Choix de la valeur à contrôler et du moniteur
- Robustesse du moniteur
- Système réactif : agent(s) délai et durée action courte
- Type de contrôleur : choix de l'algorithme
  - PID (proportionnal/integral/derivative)
  - Autoapprentissage (AI)
  - Modélisation Bayésienne
  - Régulation par script

# LES PROBLÈMES

- Absence d'anticipation du contrôleur
- Fiabilité matériel et capteur
- Choix de la valeur antinociception
- Outcome ?



# COMMERCIALISATION...

- Actuellement, pratique reste cantonné à la sphère de l'essai clinique ...contraintes
- Pour transformer ces résultats encourageant en utilisation courante, il faudra :
  - sécurité
  - transparence du contrôleur
  - facilité d'utilisation
- Quel bénéfice clinique ? Si meilleure conduite anesth, meilleur Outcome ?

# ANESTHESIOLOGY

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## **Anesthetic Management Using Multiple Closed- loop Systems and Delayed Neurocognitive Recovery**

A Randomized Controlled Trial

Alexandre Joosten, M.D., Ph.D., Joseph Rinehart, M.D.,  
Aurélie Bardaji, M.D., Philippe Van der Linden, M.D., Ph.D.,  
Vincent Jame, M.D., Luc Van Obbergh, M.D., Ph.D.,  
Brenton Alexander, M.D., Maxime Cannesson, M.D., Ph.D.,  
Susana Vacas, M.D., Ph.D., Ngai Liu, M.D., Ph.D.,  
Hichem Slama, Ph.D., Luc Barvais, M.D., Ph.D.

*ANESTHESIOLOGY* 2019; XXX:00–00

# CRUEL

Délivrance automatisé anesthésie  
Gestes endoscopiques  
Seul dispositif commercialisé USA, CEE  
Objectif : remplacer anesthésiste...

...

Echec commercial, arrêt de production  
mars 2016



# CONCLUSION

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- La délivrance automatisée des produits de l'anesthésie est une réalité
- Avantages reconnus et recul satisfaisant

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# CONCLUSION

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- Hétérogénéité des systèmes
- Commercialisation ?





popul@Aroma gh No. 1 | remédicol@Aroma gh No. 2

Drug	History	Comment	Overview
TARGET	Active Target	1.8	1.8
GO	1.8	Plasma	1.81
STOP	1.80	1 Rect	
On target			
Boucle ON			
on Target: 1			00 04 05

01:24 01:25 01:26 01:27 01:28 01:29

01:35:33 35.0 ml/h ml 82.5 mg 825.0

Drug	History	Comment	Overview
TARGET	Active Target	6.0	6.0
GO	6.0	Plasma	6.00
STOP	6.00	1 Rect	
On target			
Boucle ON			
on Target: 1			00 14 54

01:24 01:25 01:26 01:27 01:28 01:29

01:35:33 57.2 ml/h ml 88.0 mg 1.8

Stages of C:14b99@boucle use

- Undo last
- Current: Remi Limite Inf
- \*\*\* Demarrage
- Propofol Passage en Manuel
- Remi Passage en Manuel
- Reprise BouclePropofol
- Reprise BoucleRemi
- \*\*\*
- R. Anesthésie
- detail: intubation
- Propofol Limite Inf
- \*\*\* Propofol Limite Sop
- \*\*\* Remi Limite Inf
- Remi Limite Sop
- weatherChange

Current Past

Windows

- Undo last
- \*\*\* Intubation
- \*\*\* Laryngoscopie
- Zuit V12
- Et intubation
- Et sans bulles
- Et afflux
- Et pleurésie
- Et intubation
- Et intubation Fluor
- Et intubation
- Et intubation
- Masque laryngé
- Morphine
- Mouvements
- Neurosympathique / Catécholamines
- Prote du reflex ciliaire
- Prechymose
- Fluxus: Ouvre les yeux

Current Past Other

Aspect a2000 No. 1-2000 | Aspect a2000 No. 1-2000

History	Comment
SFI	Period
0.0	STOP
01:35:29	STOP
Duration	
Signal N: 1	STOP

01:25:29 01:30:29 01:35:29

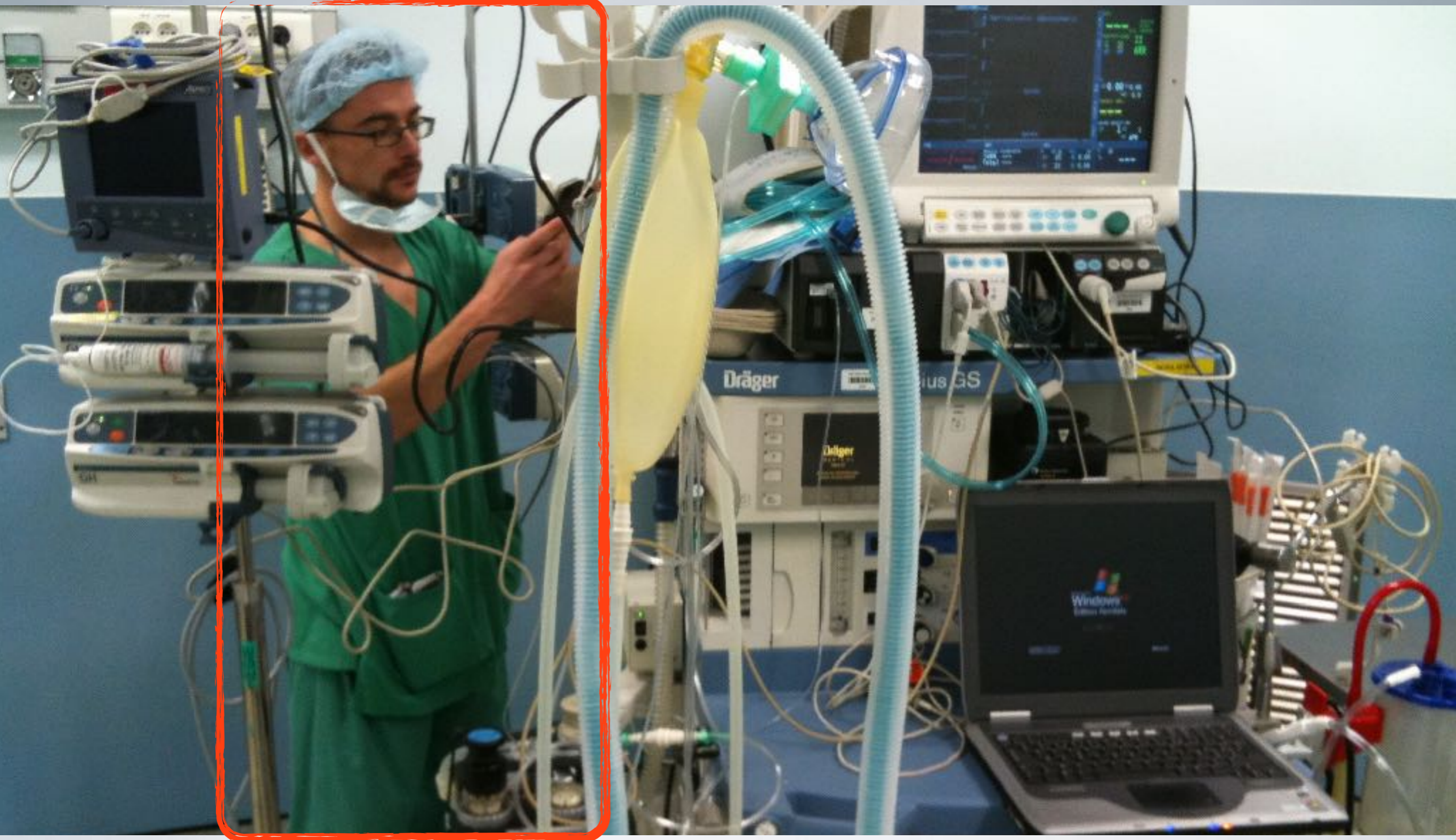
01:35:33 Running

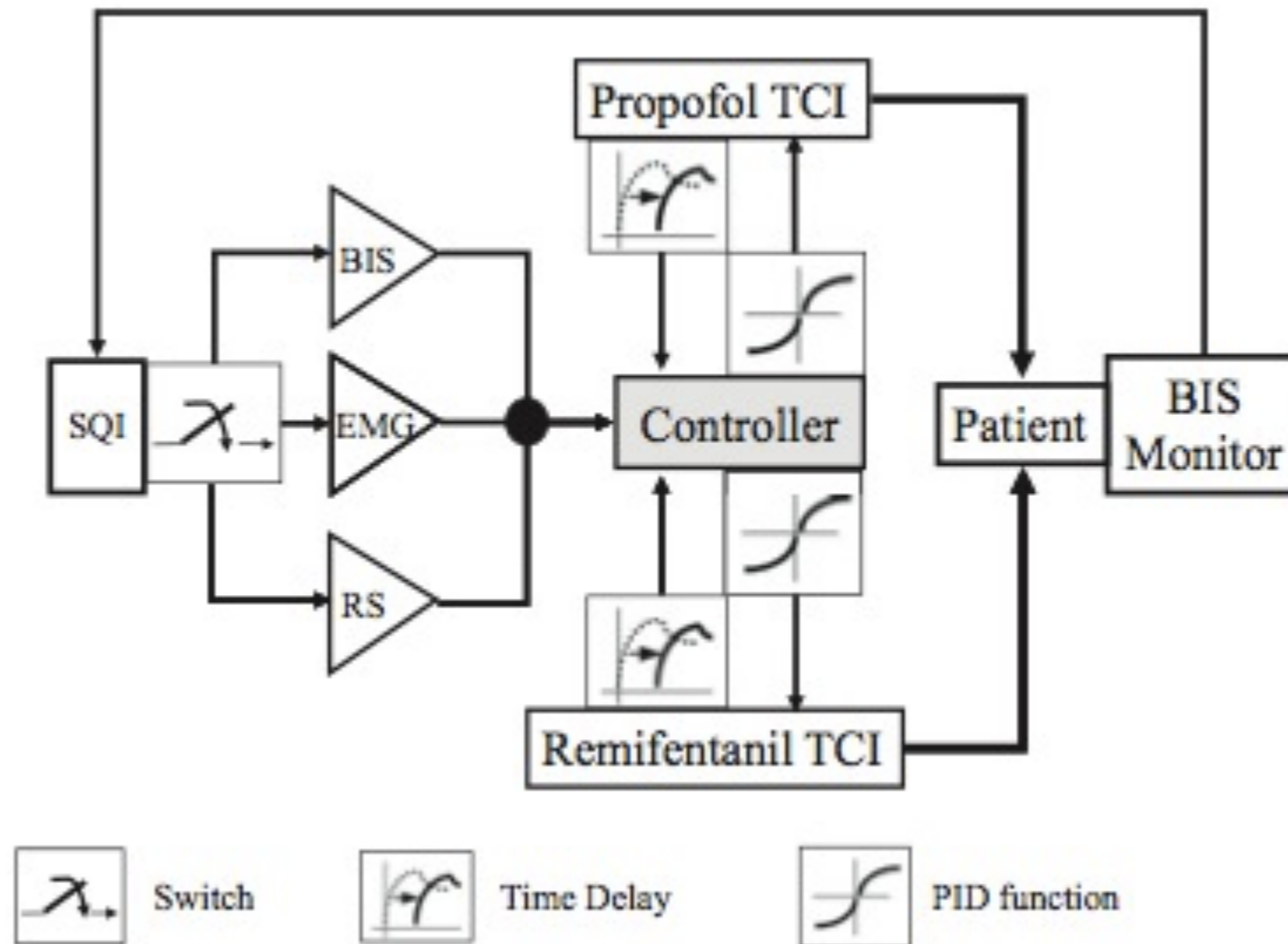
History	Comment
EC	Period
0.0	STOP
01:35:29	STOP
Duration	
Signal N: 1	STOP

01:25:29 01:30:29 01:35:29

01:35:33 Running

COMPAQ

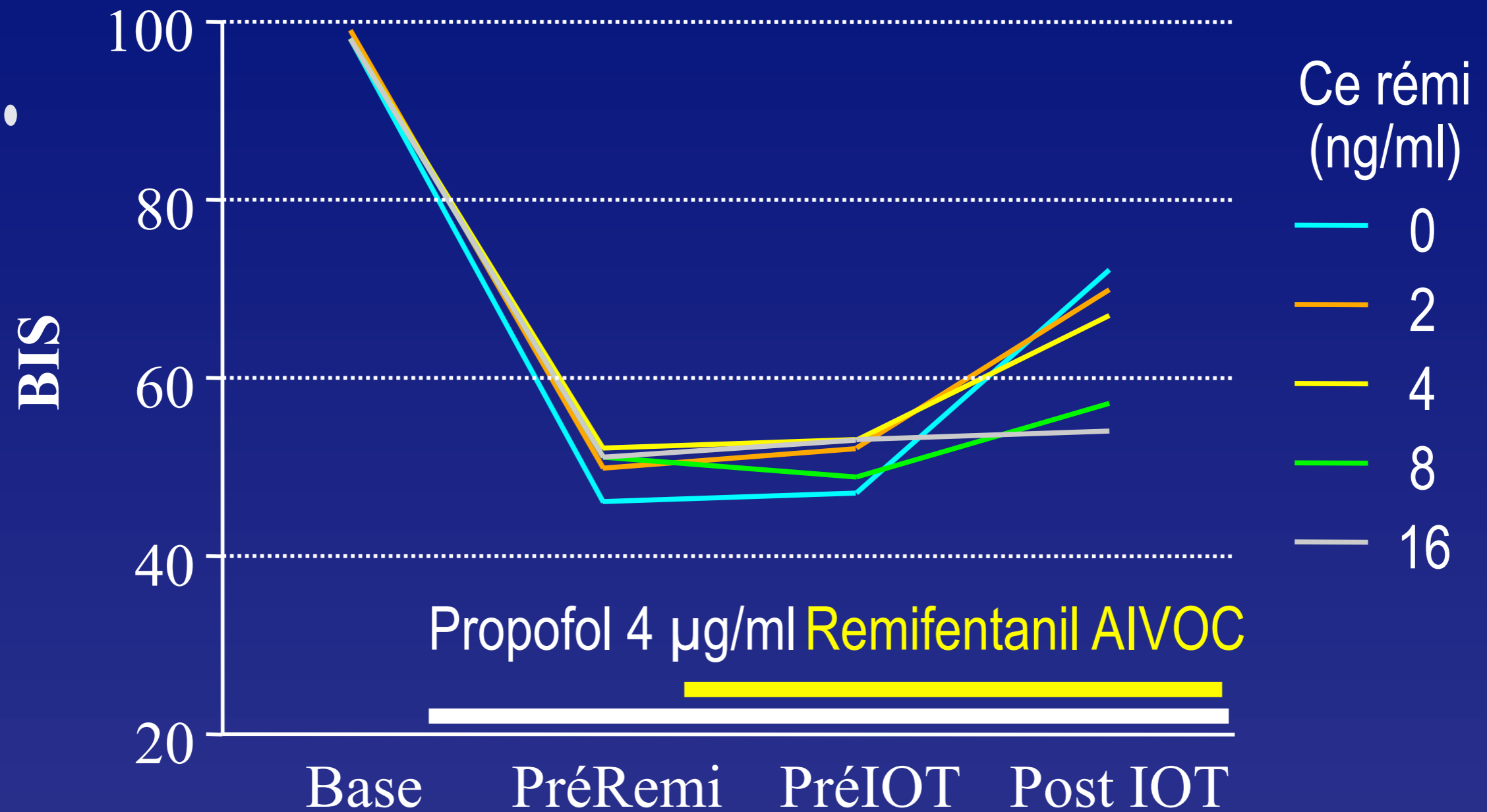




# ALGORITHME PID

- différence à la valeur cible,
- quantité déjà administrée,
- tendance de la valeur

# BIS et réaction à l'intubation en fonction de doses croissantes de rémifentanyl



# Independent Predictors of One-year Mortality

“Multivariate modeling identified three significant predictors of mortality: patient comorbidity, cumulative deep hypnotic time (Bispectral Index < 45) and intraoperative systolic hypotension.”

Predictor	Relative Risk [95% CI]	P Value
Charlson Comorbidity Score (3+ vs 0-2)	16.116 [10.110 – 33.717]	<0.0001
Cumulative Deep Hypnotic Time (BIS < 45) ( <i>per hour</i> )	1.244 [1.062-1.441]	0.0121
Hypotension SBP < 80 mm Hg ( <i>per minute</i> )	1.036 [1.006-1.066]	0.0125

c-statistic: 0.847, p < 0.001

Monk et al. Anesth Analg 2005

# Poor Outcome with “Deep Anesthesia”

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## Monk et al (Anesthesia & Analgesia 2005)

- “Anesthetic management and one-year mortality after noncardiac surgery” A&A 2005
- **Hazard ratio (HR) 1.24** for Year 1

## Lindholm et al (Anesthesia & Analgesia 2009)

- “Mortality within two years after surgery in relation to low intraoperative BIS values and pre-existing malignant disease” A&A 2009
- **Hazard ratio (HR) 1.13** (1.01-1.27) for Year 1 and 1.18 (1.08-1.29) for year 2

## Searleman et al (ASA Meeting 2008)

- “Deep Hypnotic Time and One-Year Mortality in Non-Cardiac and Cardiac Surgical Patients” 2008 ASA A-1
- **Hazard ratio (HR) 1.25** (1.13 to 1.37 ) for Year 1

## Watson et al (Critical Care Medicine 2009)

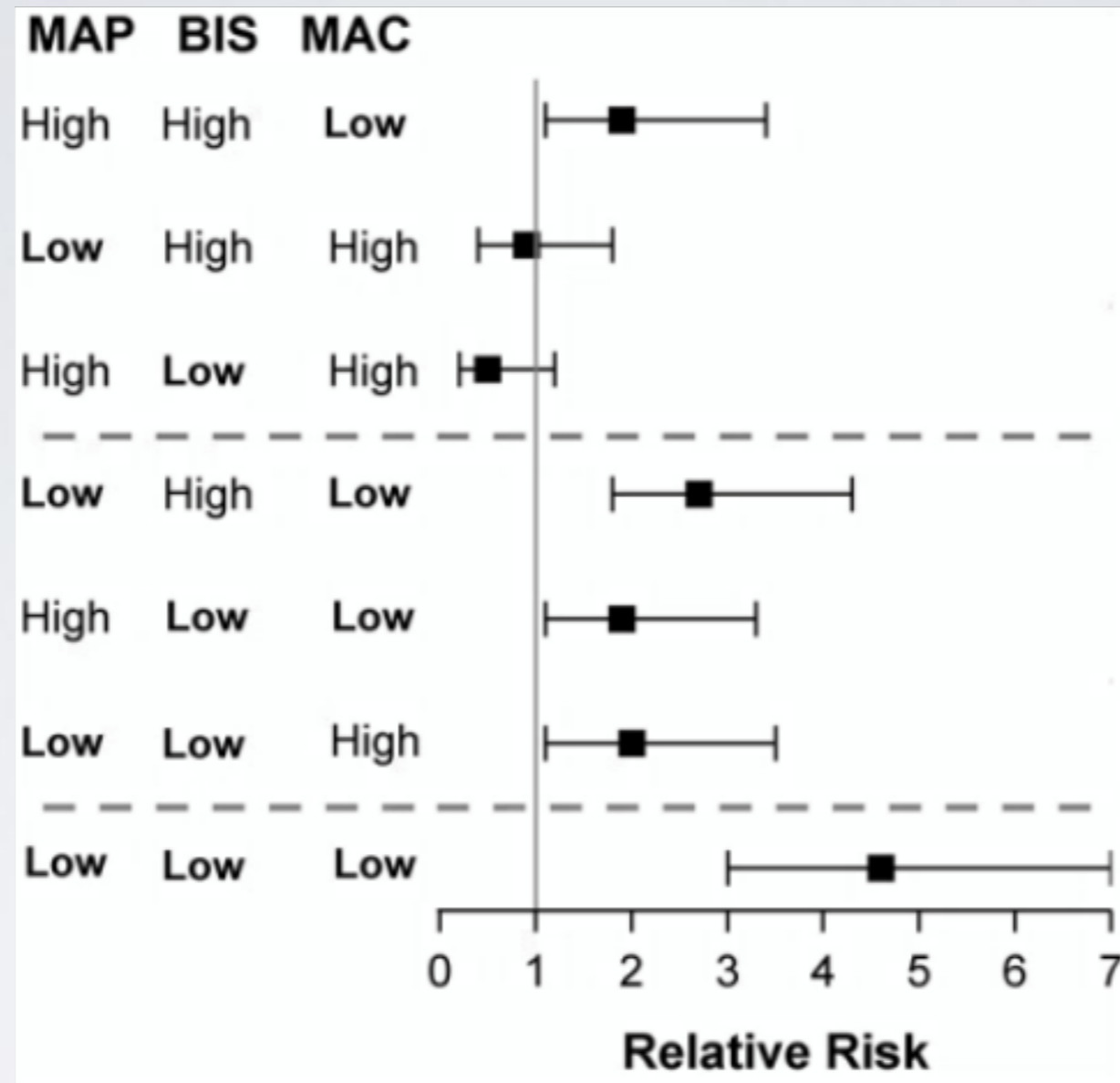
- “Presence of EEG suppression in critically ill patients is associated with increased mortality” CCM In Press
- **Hazard ratio (HR) 2.04** (1.12-3.70) for 6-month endpoint

## Karri S et al (Society of Cardiac Anesthesia 2009)

- Deeper Level Of Anesthesia Is Associated With Adverse Neurological Outcomes In Cardiac Surgical Patients; ANESTH ANALG 2009; 108(SCA Suppl);1-104
- **Hazard ratio (HR) 3.67** for neurological morbidity

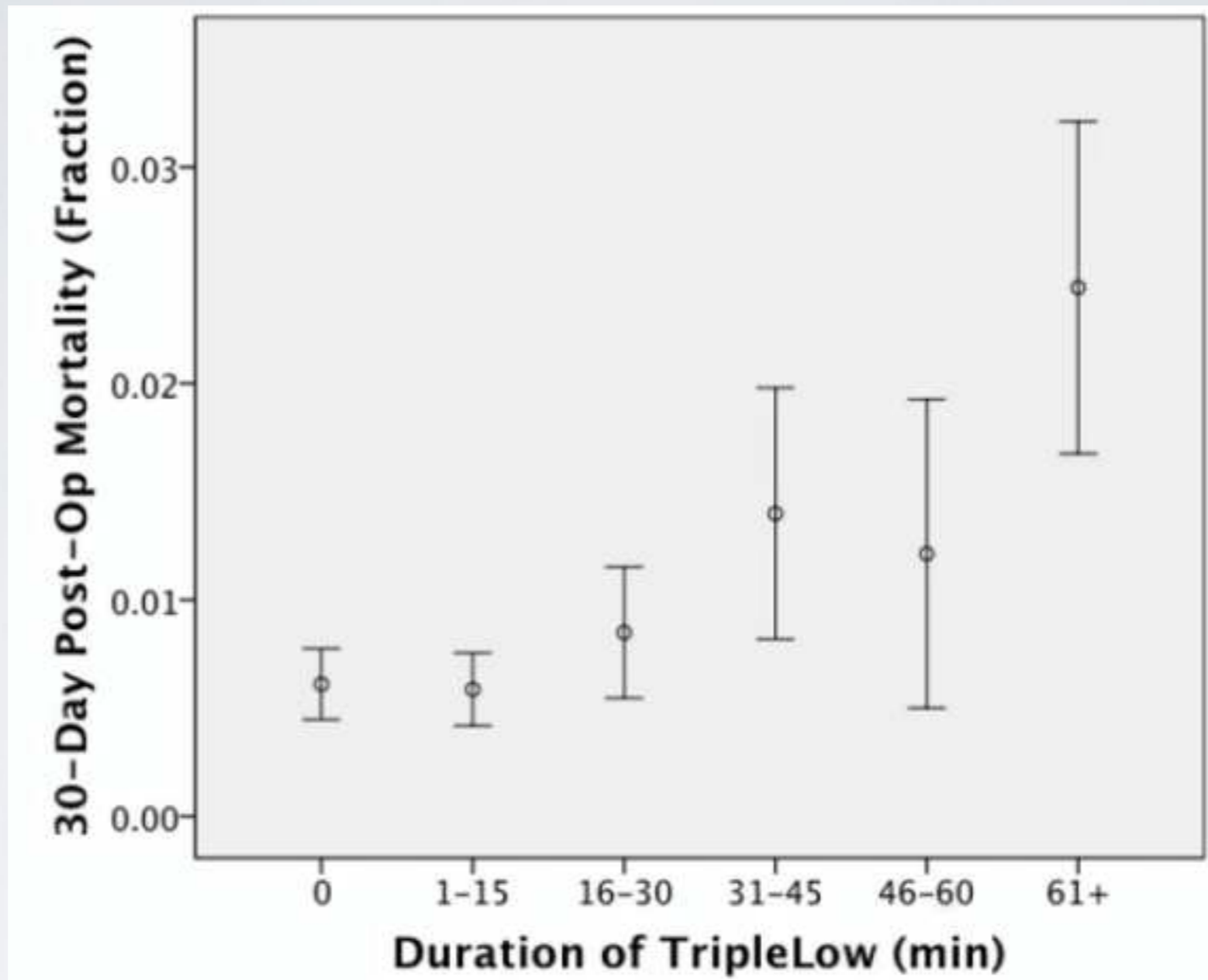
## Leslie et al (TIVA/TCI Congress 2009)

- Prospective/Randomized: *Avoidance of Deep Anesthesia* (BIS<45 for 5 min) results in lower mortality compared to standard practice.



Triple & double Low  
 MAC < 0.8 PAM < 75mmHg BIS < 45

Sessler DI, Sigl JC, Kelley SD, Chamoun NG, Manberg PJ, Saager L, Kurz A, Greenwald S: Hospital stay and mortality are increased in patients having a “triple low” of low blood pressure, low bispectral index, and low minimum alveolar concentration of volatile anesthesia. *ANestHeSIoLoGy* 2012; 116:1195–203



Sessler DI, Sigl JC, Kelley SD, Chamoun NG, Manberg PJ, Saager L, Kurz A, Greenwald S: Hospital stay and mortality are increased in patients having a “triple low” of low blood pressure, low bispectral index, and low minimum alveolar concentration of volatile anesthesia. *ANestHeSIoLoGy* 2012; 116:1195–203