

DÉLIVRANCE AUTOMATISÉE DES PRODUITS DE L'ANESTHÉSIE



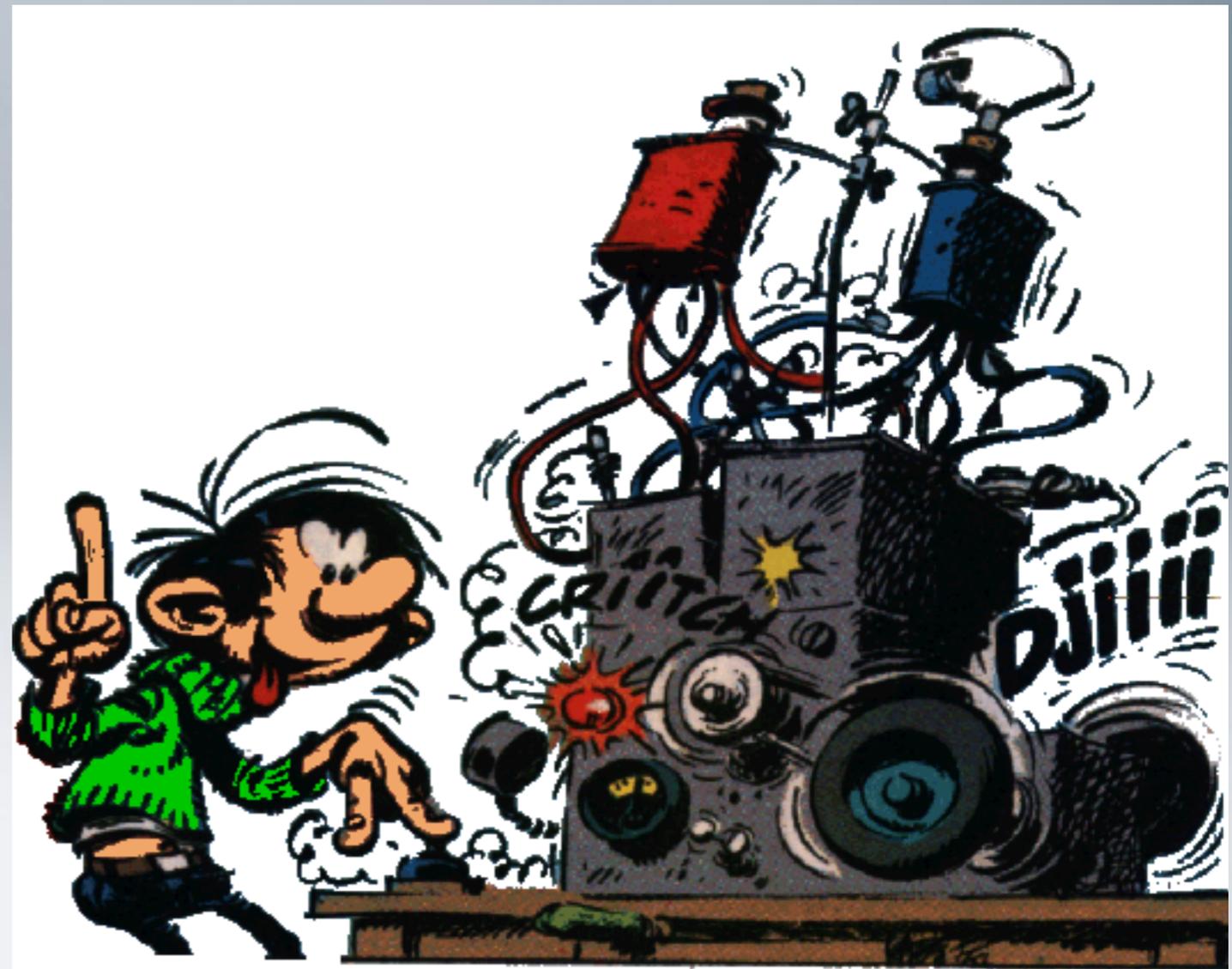
Médecin en Chef DONAT
Centre de traitement des Brûlés, HIA Percy
ICAR 2019

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

Pas de conflit d'intérêt

DÉFINITIONS

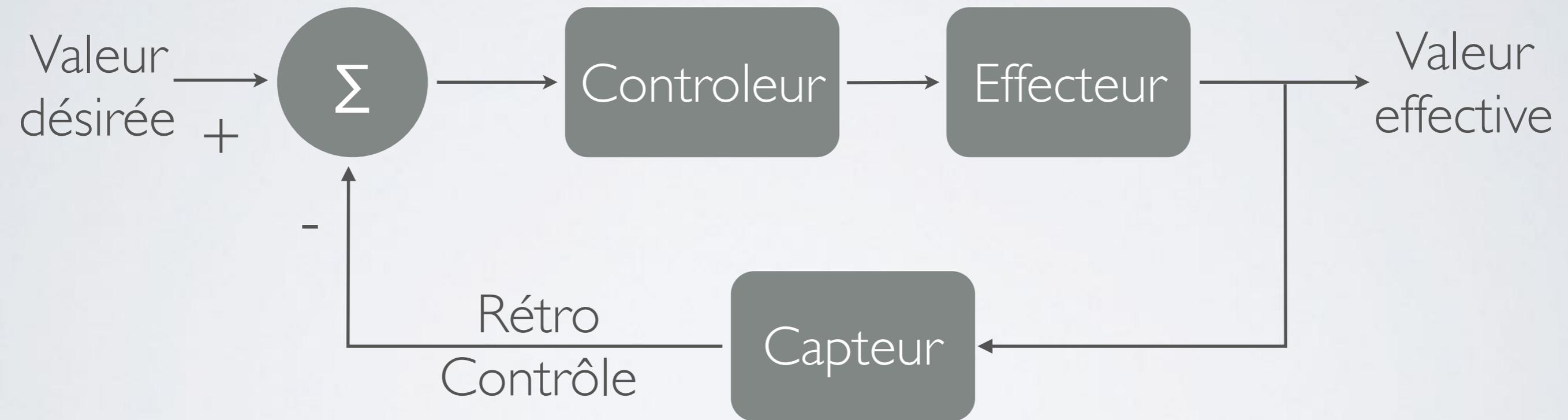
- Dispositif automatisé : se comporte de manière automatique, pas d'intervention humaine
- Comportement figé ou adapté à son environnement = rétro contrôle

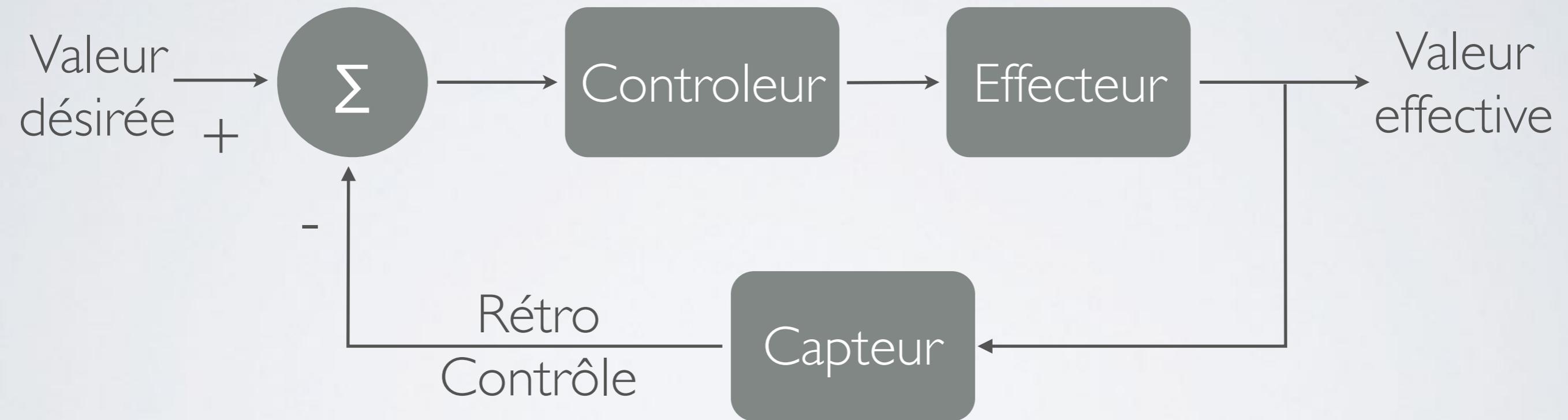


LE RÉTRO- CONTRÔLE

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

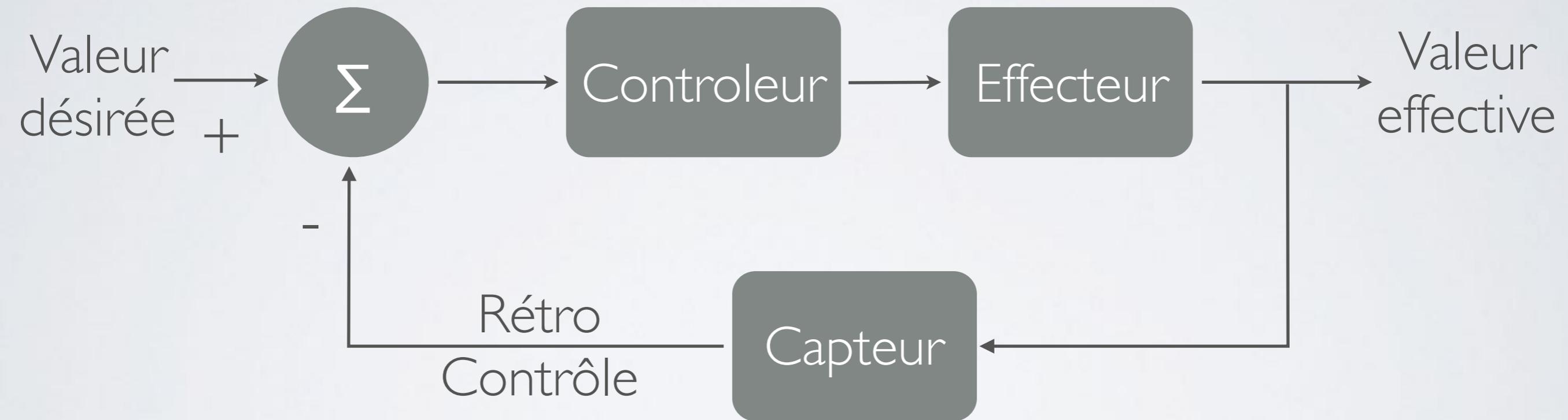






Exemple de la régulation de la température

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

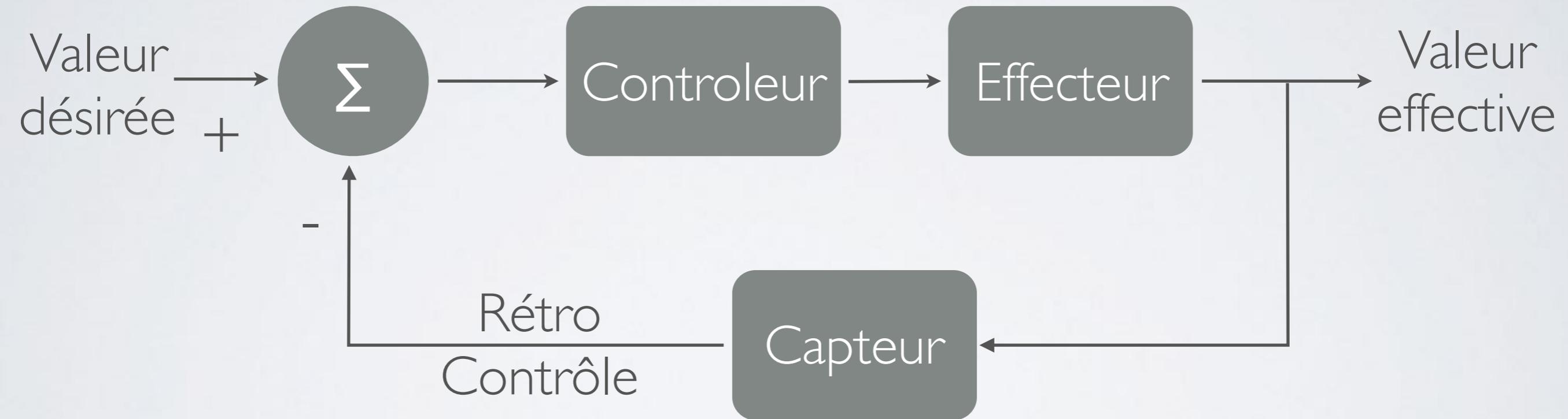


Exemple de la régulation de la température

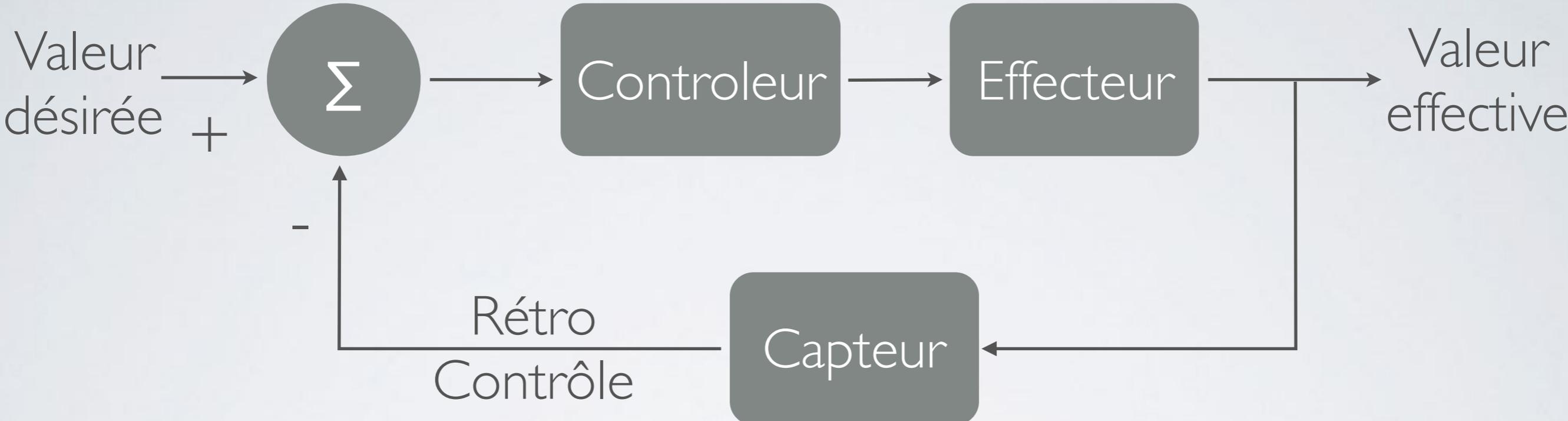
$T^{\circ} = 25^{\circ}\text{C}$

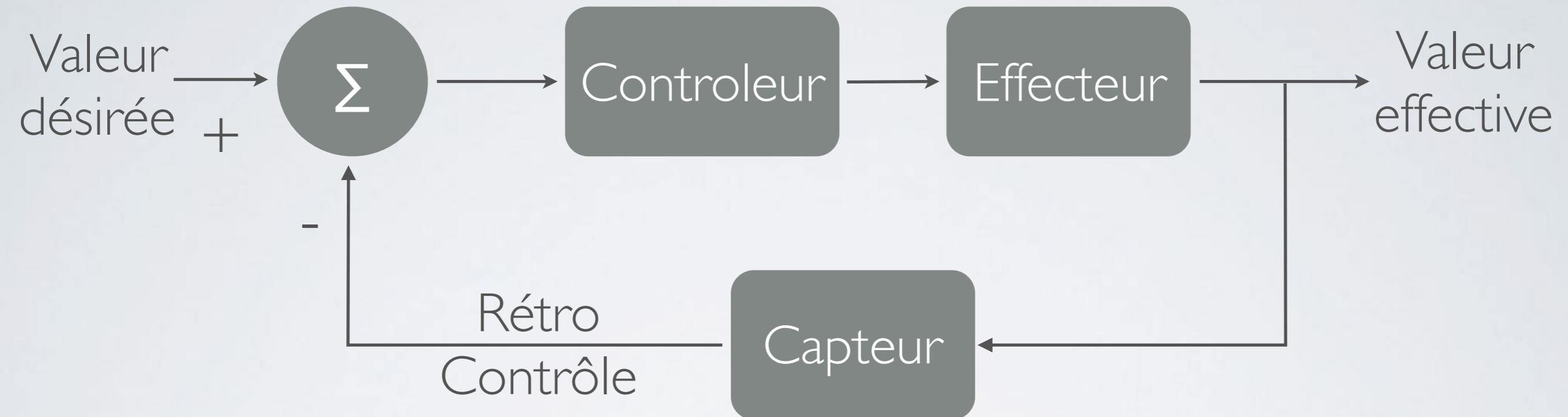


Radiateur



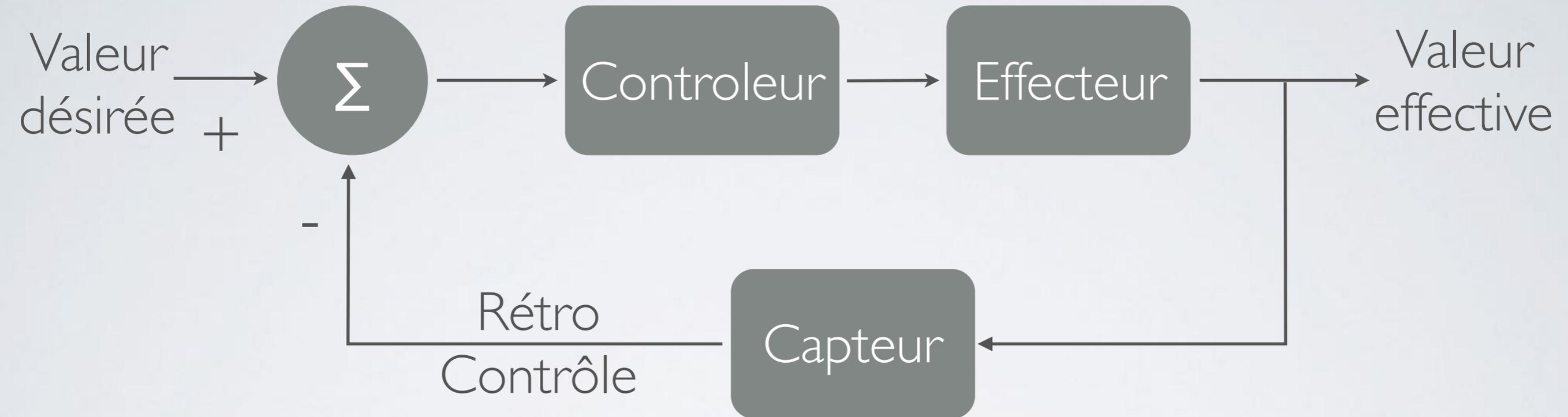
Exemple de la régulation de la température





Exemple de l'adaptation de l'insuline

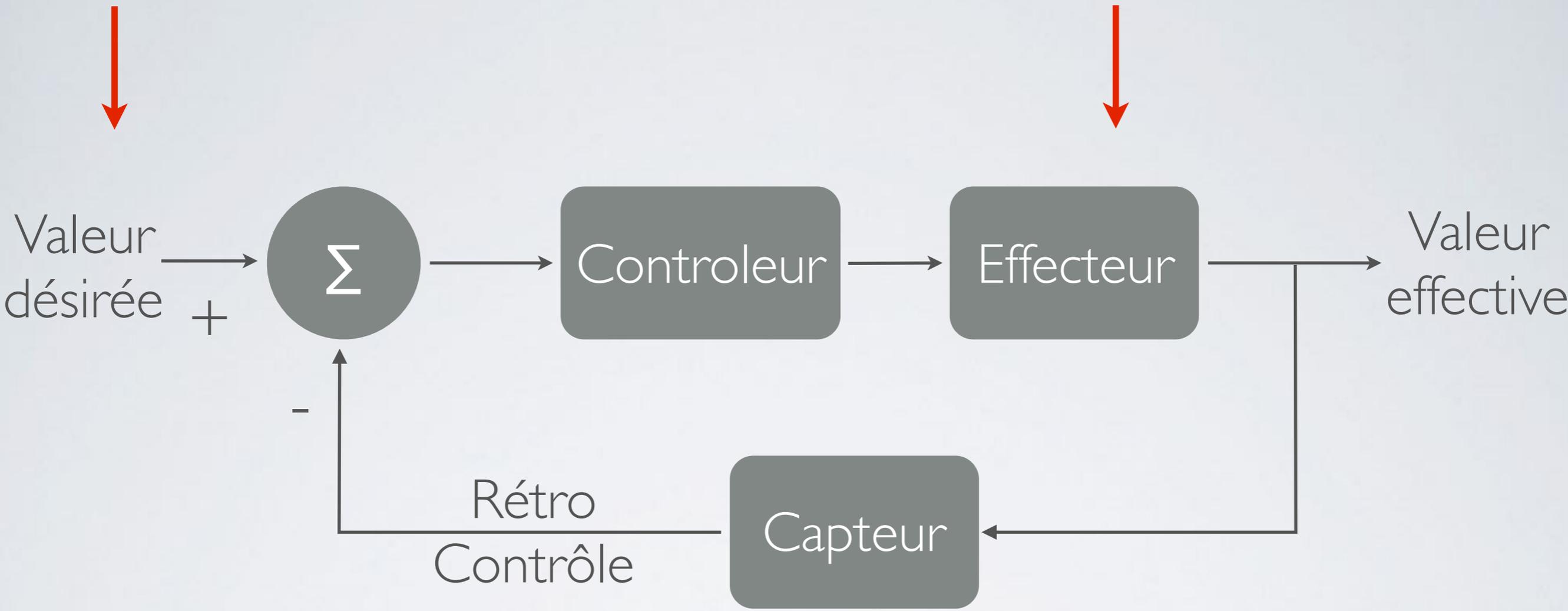
$5 < \text{gly} < 7 \text{ mmol/L}$



Exemple de l'adaptation de l'insuline

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

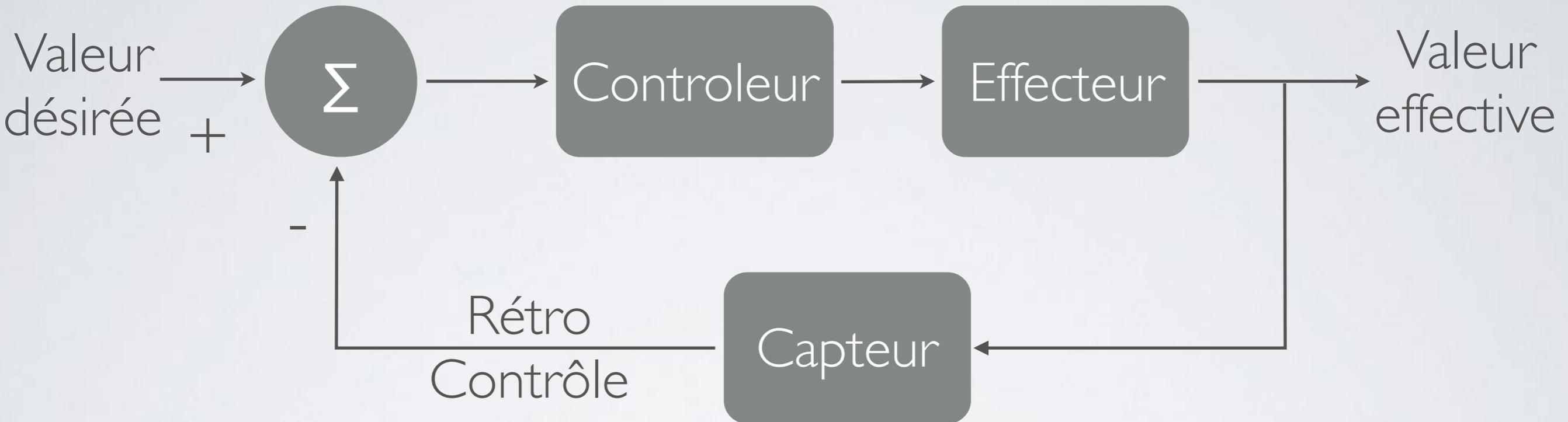
PSE Insuline



Exemple de l'adaptation de l'insuline

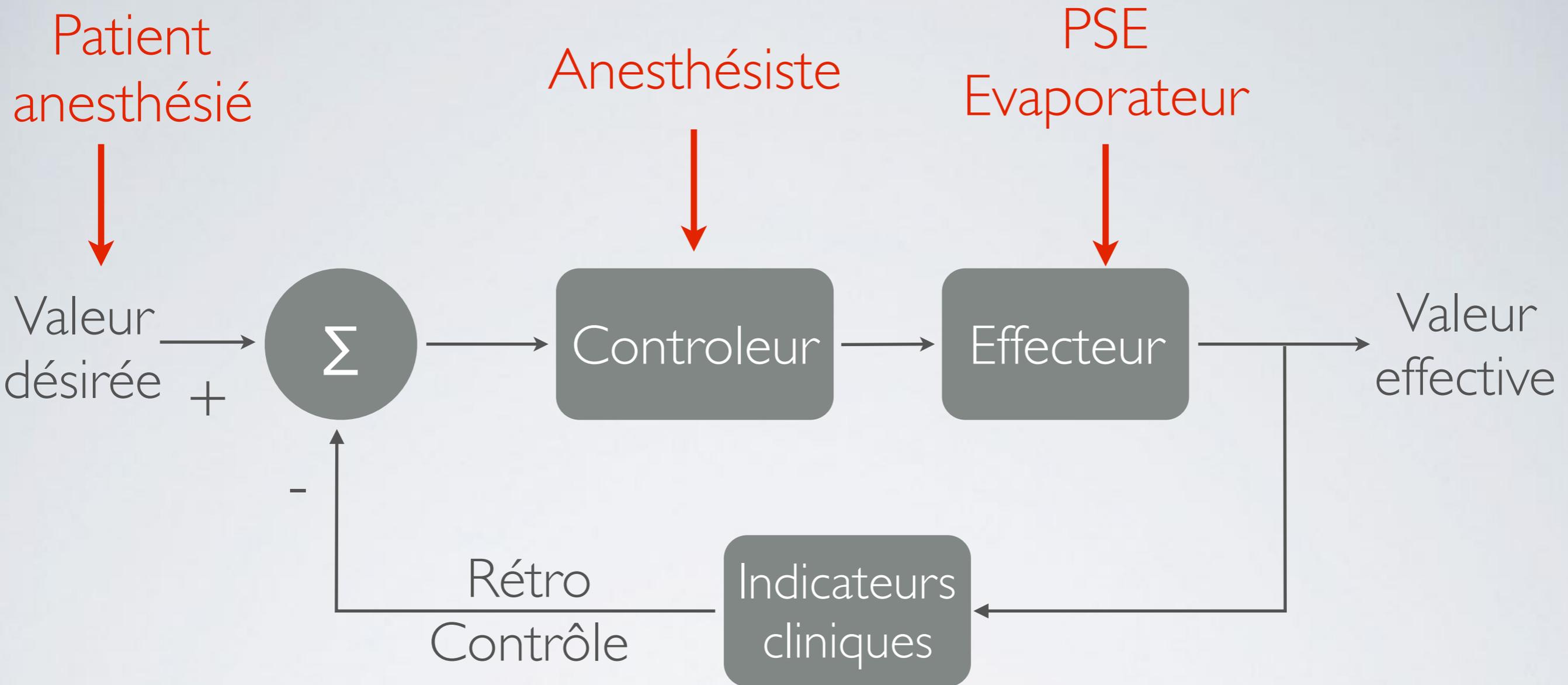
$5 < gly < 7 \text{ mmol/L}$

PSE Insuline



Glycémie capillaire

Exemple de l'adaptation de l'insuline

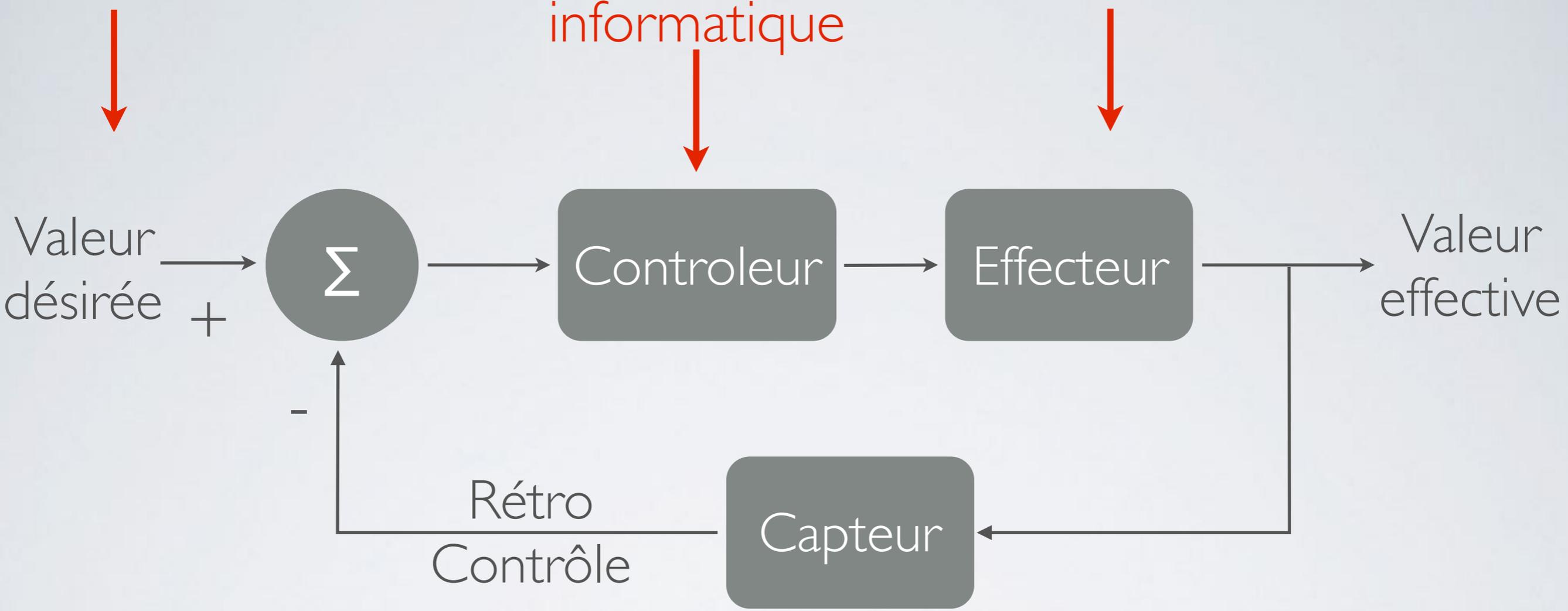


Exemple de l'anesthésie

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 “

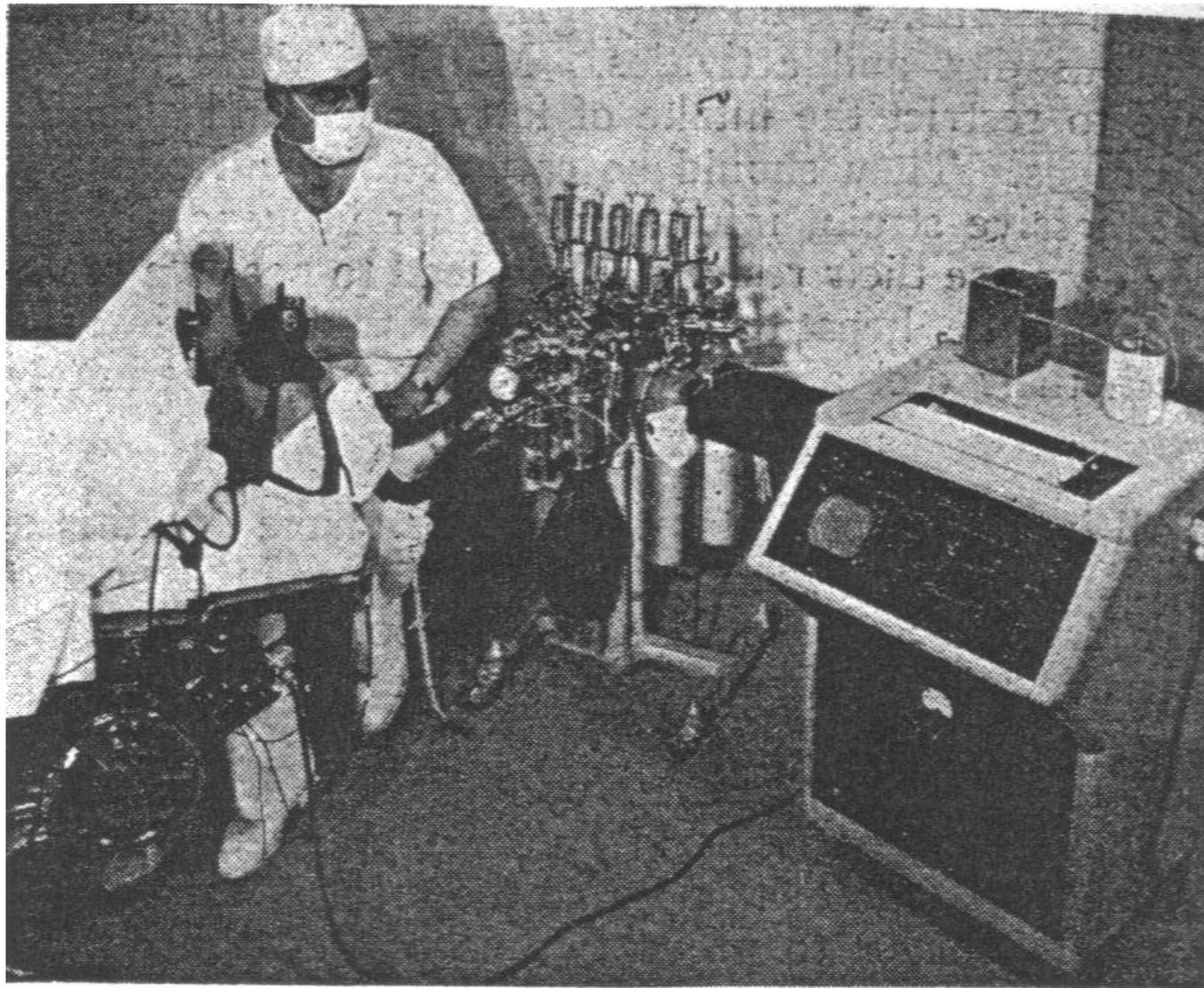
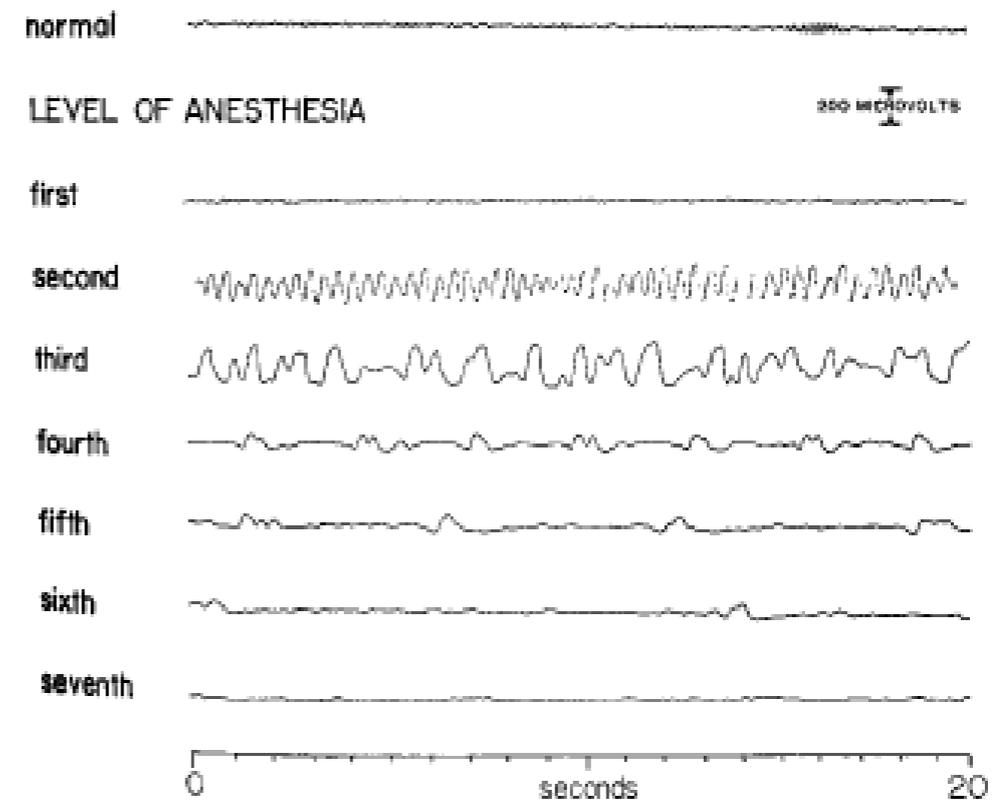


Fig. 2.—Automatic administration of ether.



The Pioneers : control anesthesia depth by EEG

BISPECTRAL INDEX

1980's : BIS

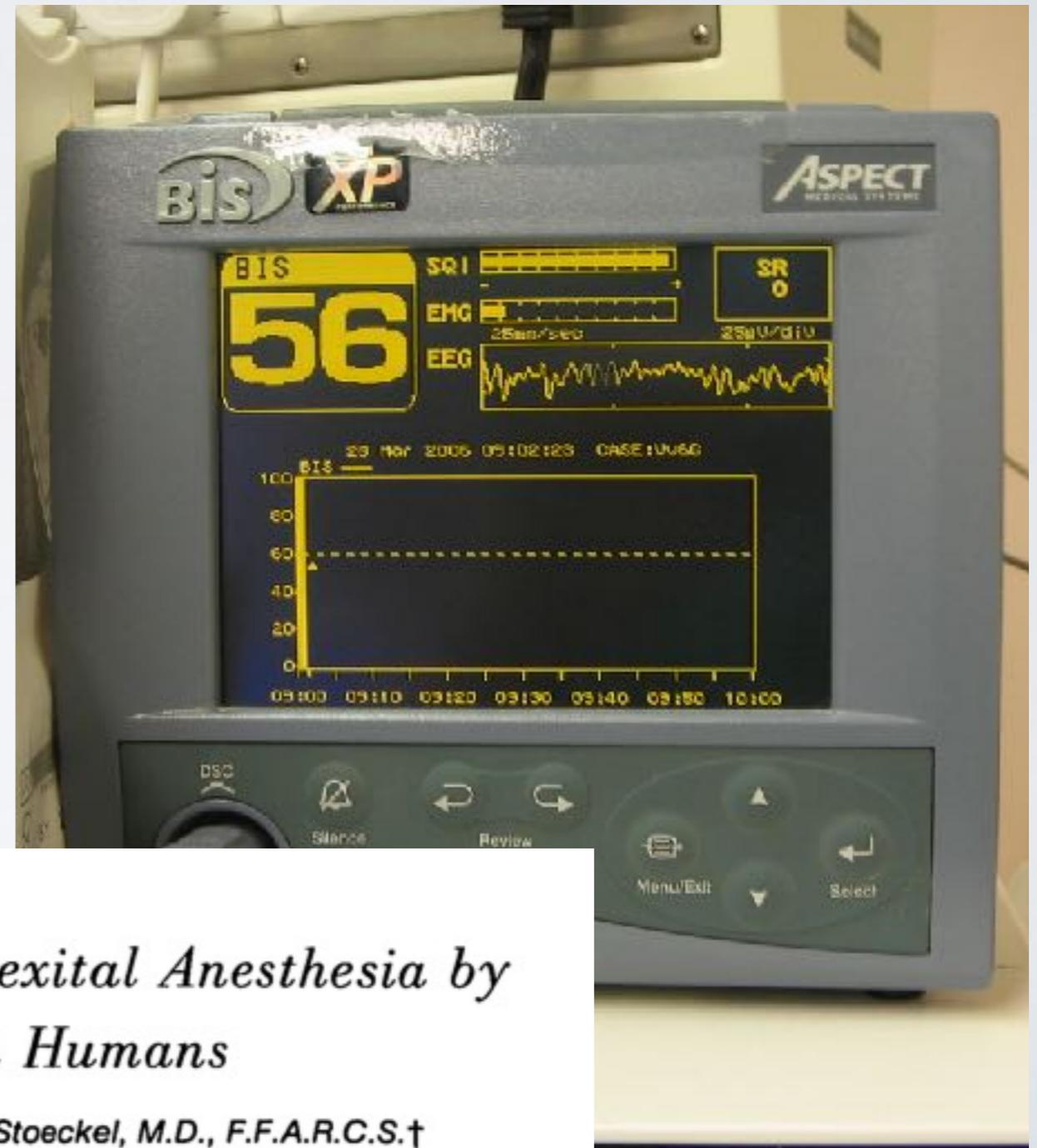
Derived index of the EEG, developed as a continuous measure of sedation and loss of consciousness (adequate anesthesia range 45-60)



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)

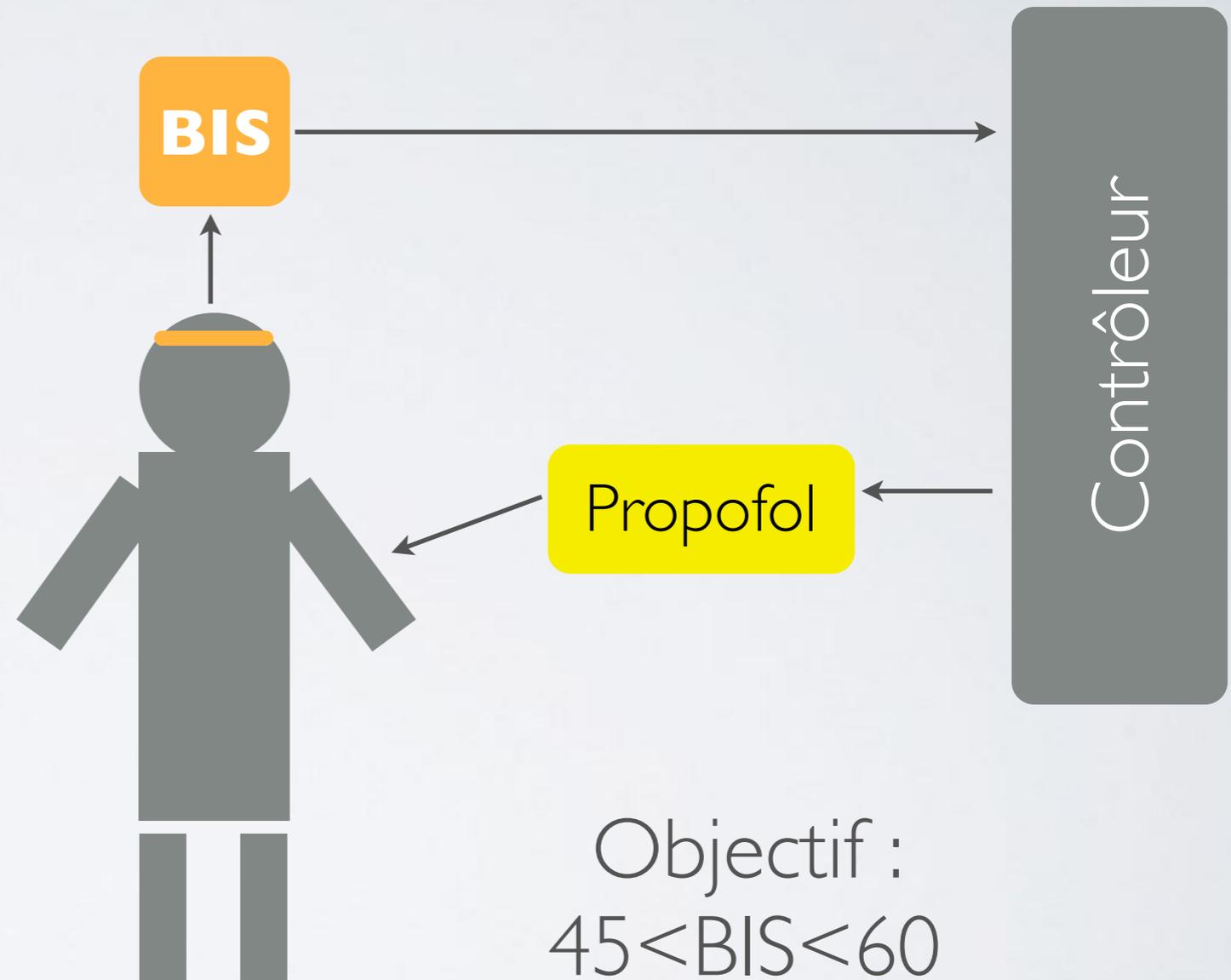


Schnider TW, Minto CF, Gambus PL, Andresen C, Goodale DB, Shafer SL, et al. The influence of method of administration and covariates on the pharmacokinetics of propofol in adult volunteers. *Anesthesiology*. 1998;88(5):1170-82.

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

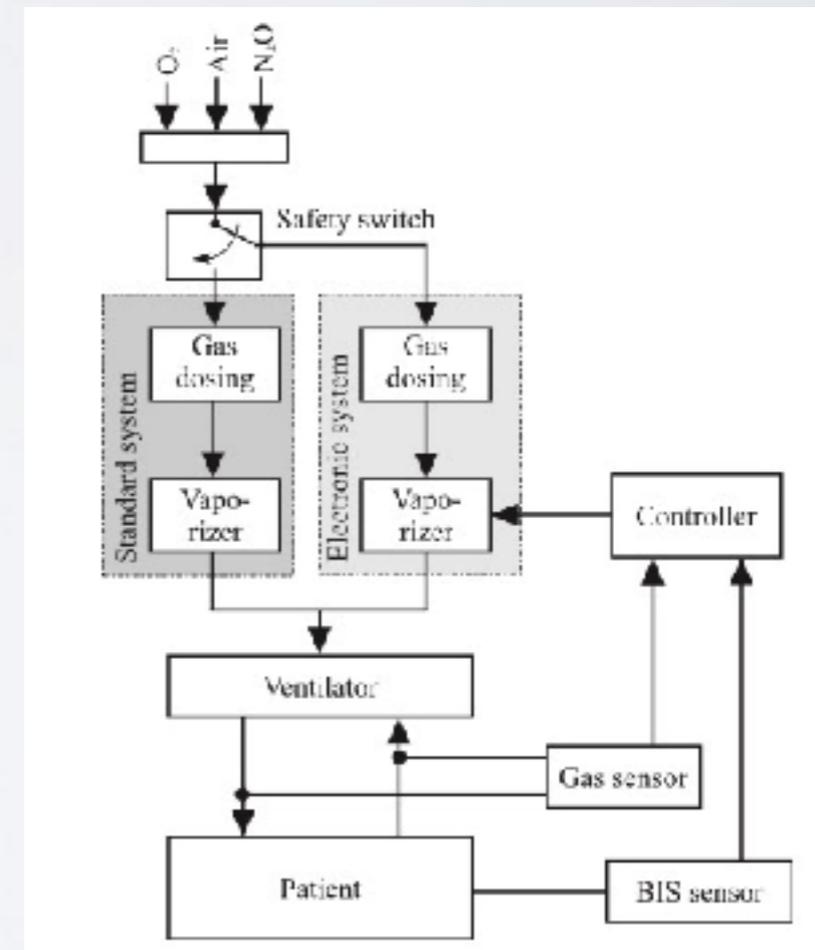
Anesthesiology 2004; 101:591-602

© 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 |

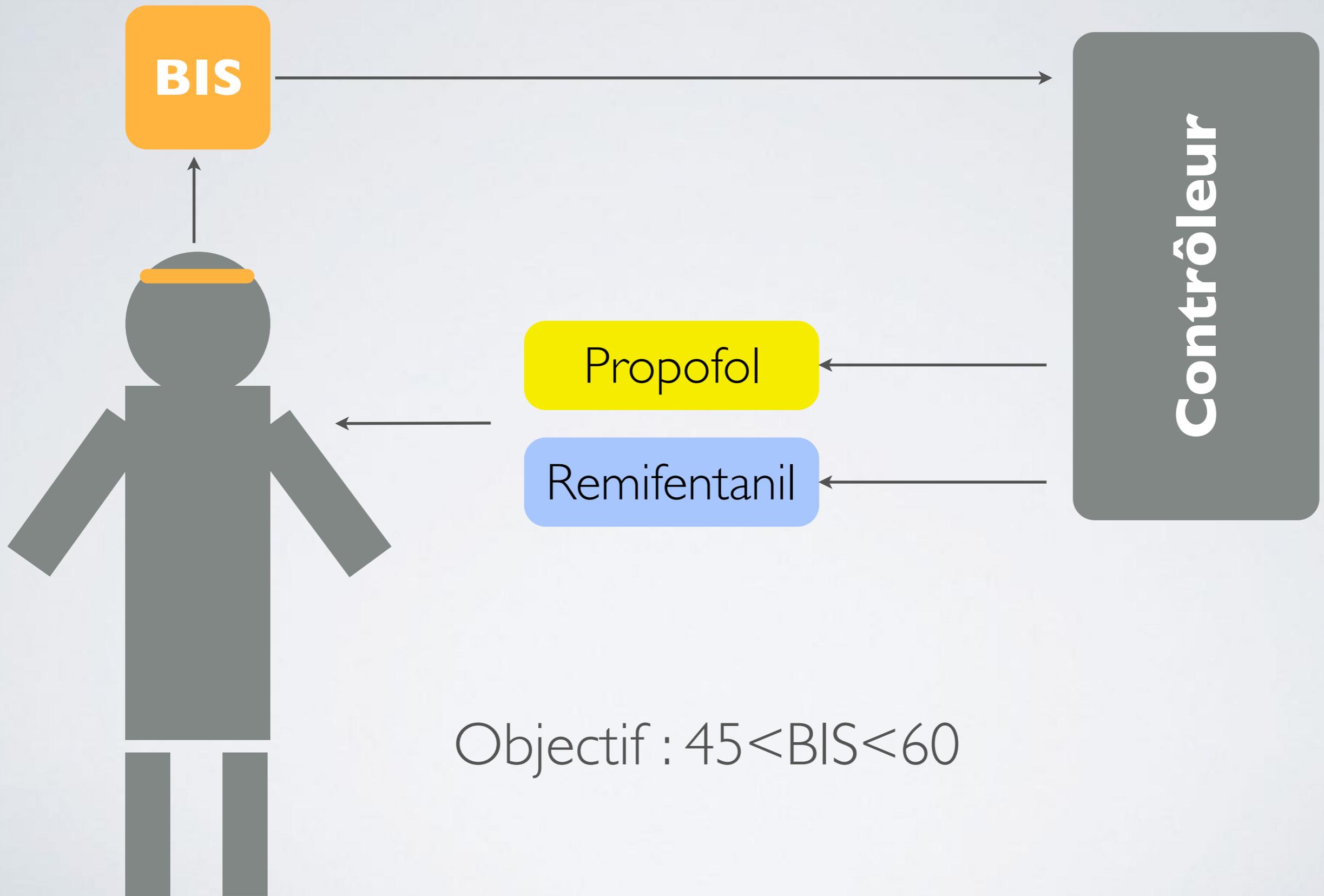
Boucles complexes : Hypnotique / Morphinique / Curare

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





Medical software interface on a laptop screen. The interface is divided into several panels:

- Top Left:** A grid of control buttons and numerical values, including 'Active Target' and 'Plasma'.
- Top Right:** A panel titled 'Steps of Catheterization' with a list of steps and 'Cancel'/'Exit' buttons.
- Middle:** Two line graphs showing data trends over time.
- Bottom Left:** A panel with 'Forward' and 'STOP' buttons, and a 'Duration' field.
- Bottom Right:** A panel titled 'Markers' with a list of markers and 'Cancel'/'Exit'/'Other' buttons.

Medical monitor on a stand. The screen displays a graph with the number '56' and the text 'The Highgate'. The monitor is part of a larger piece of equipment with various buttons and ports.







ANESTHÉSIE DU BRÛLÉ

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

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 ⁻¹ · min ⁻¹ | 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



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| Propofol target, µg/ml | 3.8 ± 1.2 | 3.2 ± 1.0 | < 0.0001 |
| Remifentanil induction dose, µg/kg | 2.5 ± 1.2 | 2.7 ± 1.1 | NS |
| Remifentanil target, µg · kg ⁻¹ · min ⁻¹ | 6.0 ± 2.2 | 6.1 ± 2.2 | NS |
| Ephedrine bolus, % | 16 | 12 | NS |
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RÉVEIL PLUS RAPIDE

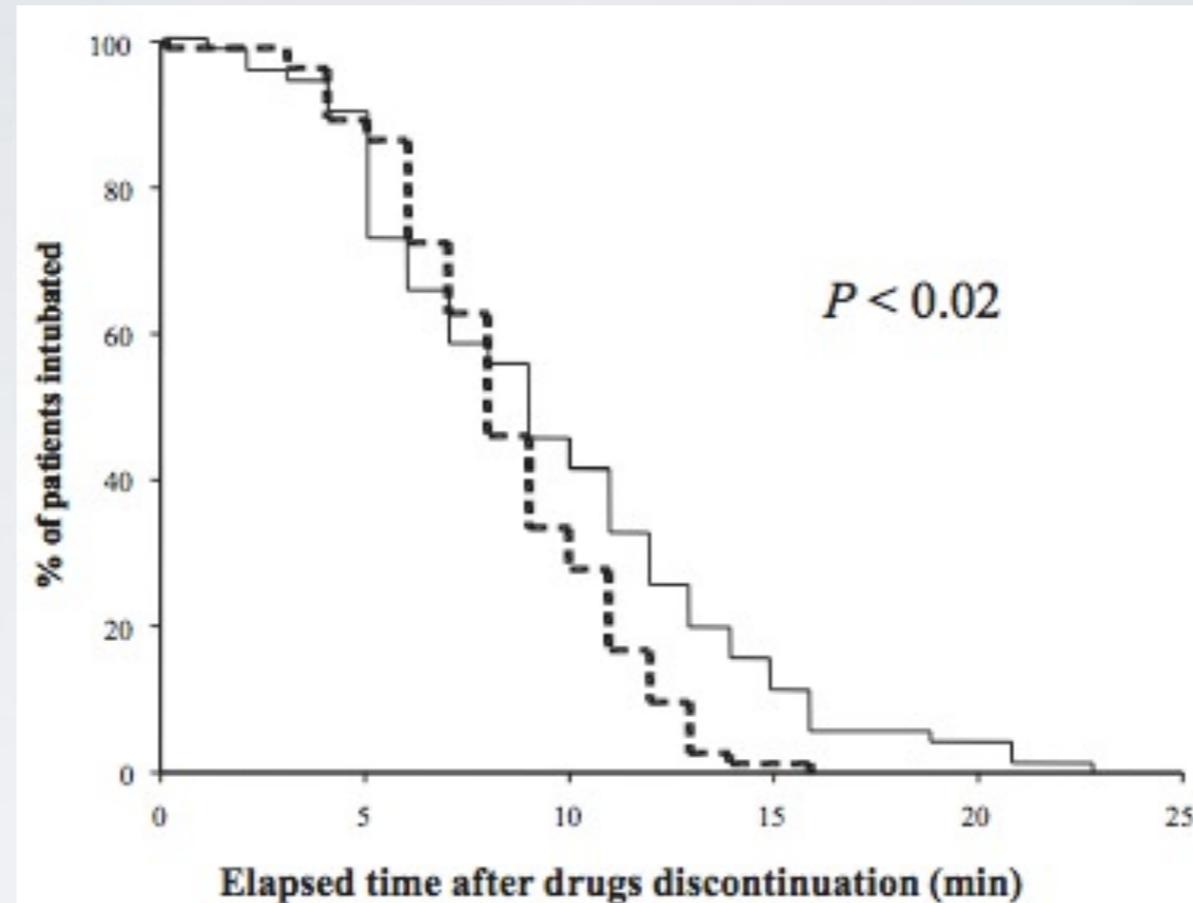


Figure 7. Kaplan-Meier analysis of remaining intubated patients after the discontinuation of propofol and remifentanyl in dual-loop (dashed line) and manual (solid line) groups.

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

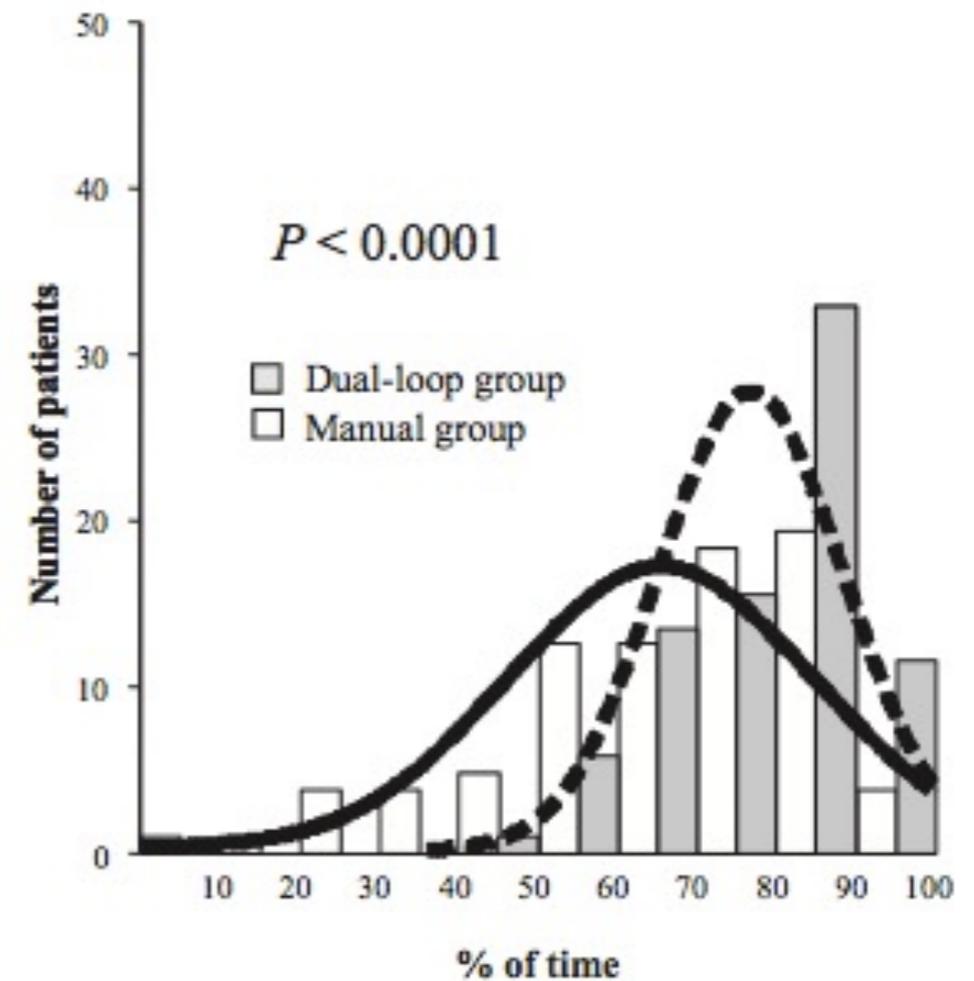
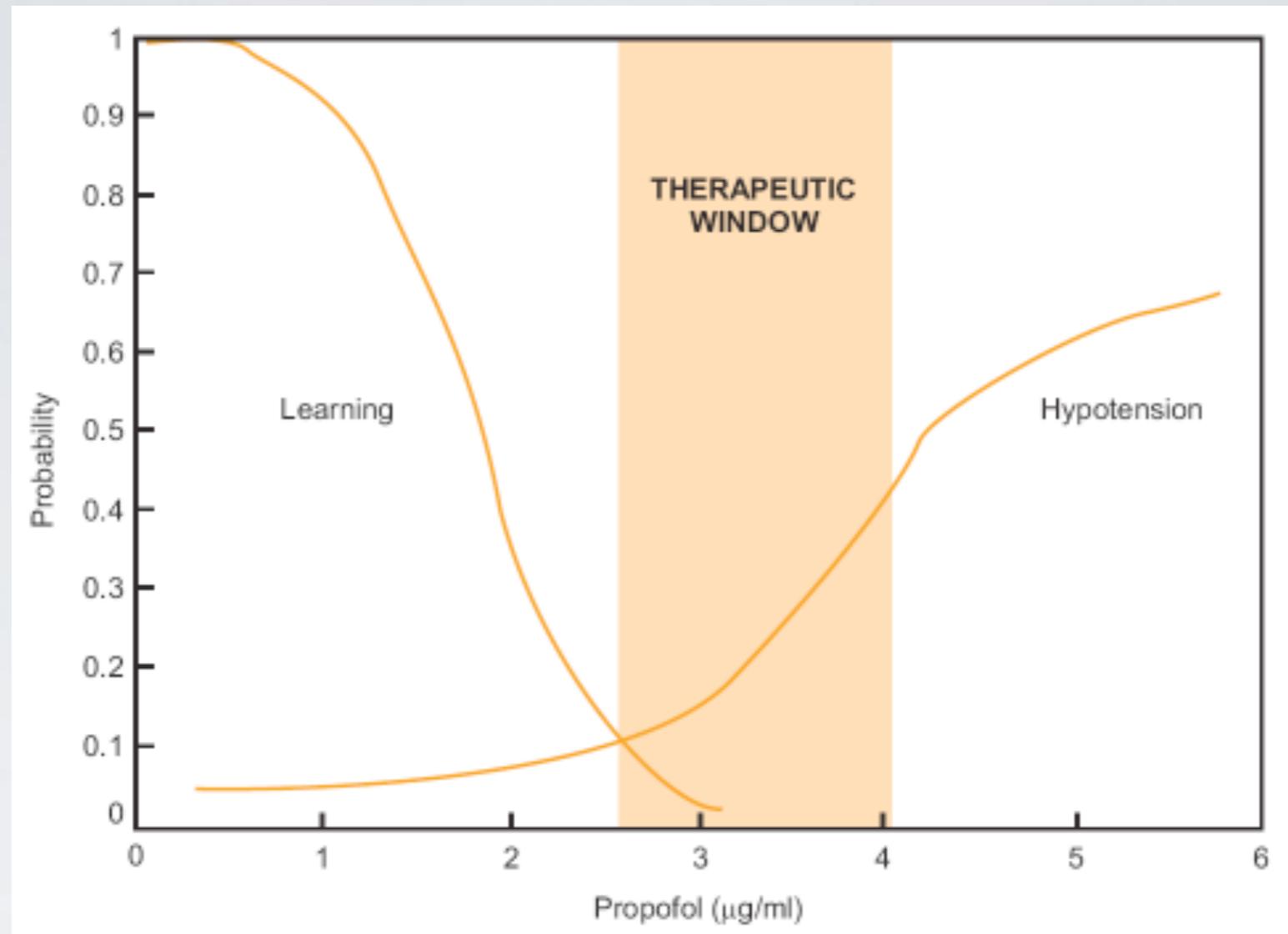


Figure 5. Histogram of percentage of time that the Bispectral Index value was between 40 and 60, which is defined as adequate maintenance control. Normal distribution curve for dual-loop (dashed line) and manual (solid line) groups.

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...

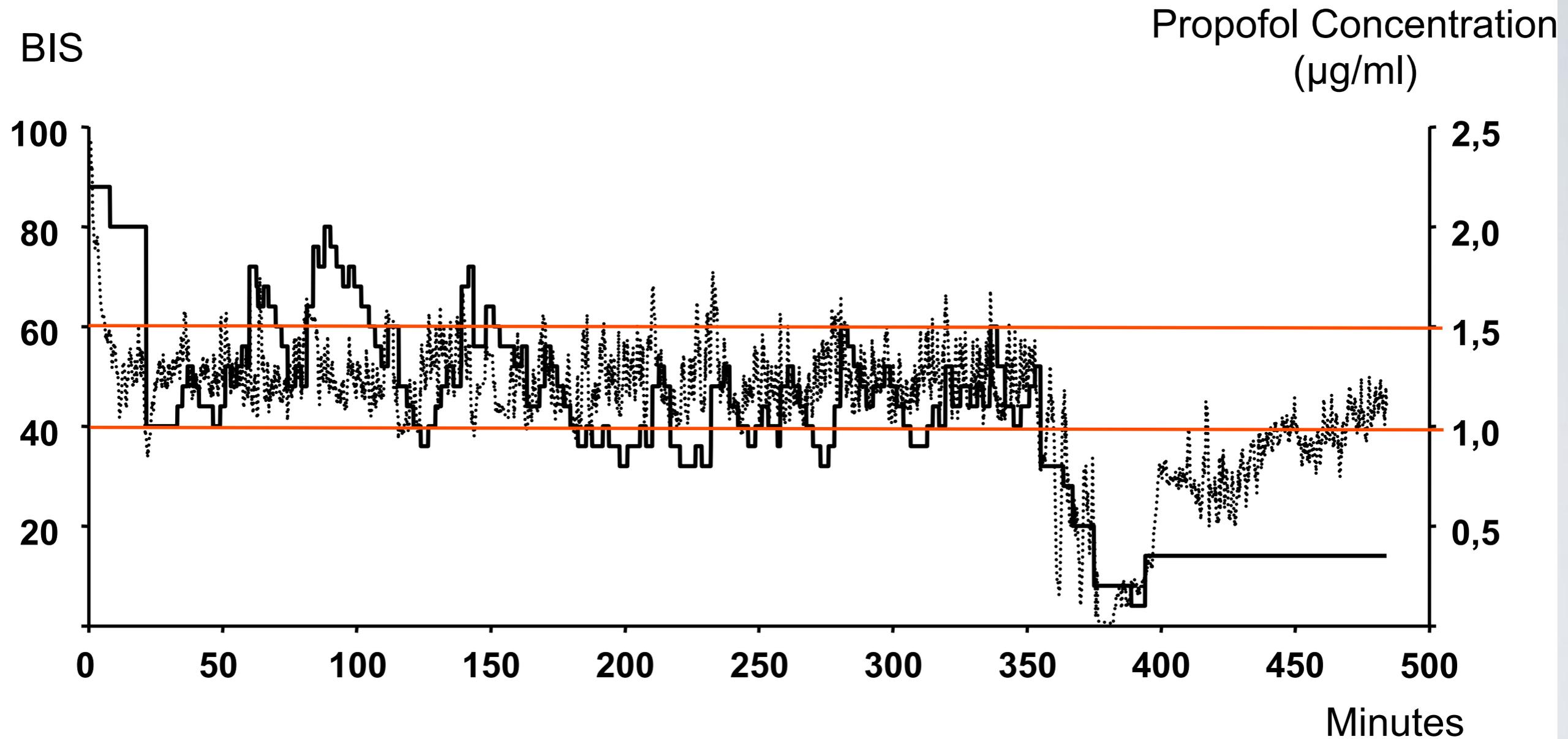
➔ Adaptation fine des doses grâce au rétrocontrôle

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 opératoire



EN OPEX

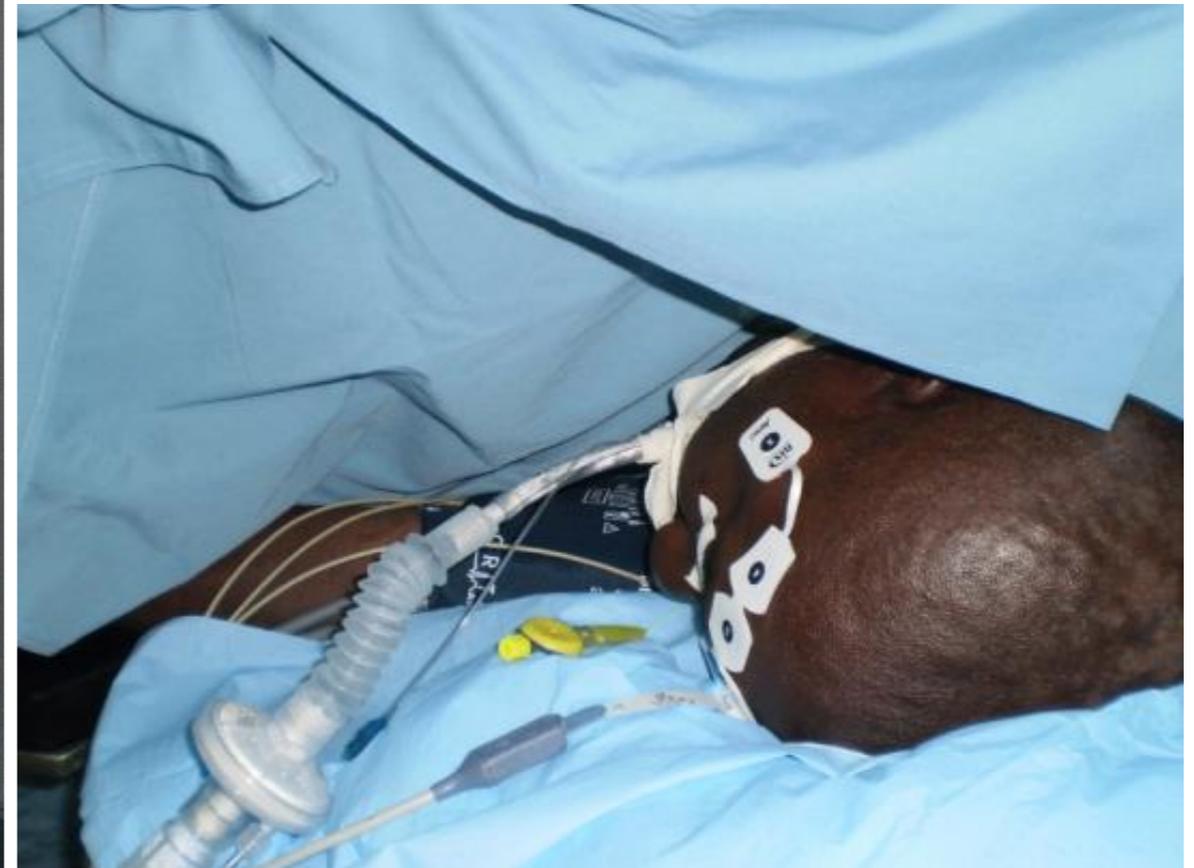
Tchad : 21 patients

| | Durée (min) | 40<BIS<60 (%) | BIS<40 (%) | BIS>60 (%) |
|---------------------------------|-------------------------|--------------------------------|--------------------------|--------------------------|
| Moyenne (écart type) | 124,1 (42,1) | 82 (11,1) | 14,1 (9,3) | 3,8 (2,8) |

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 ²⁰ | 2009 | CLADS | 22/18 | BIS |
| Biswas et al ²¹ | 2013 | CLADS | 20/20 | BIS |
| Breton et al ²² | 2012 | Glucose control (sCTR) | 26/26 | BG |
| | | Glucose control (eCTR) | 12/12 | |
| Cavalcanti et al ²³ | 2009 | CAIP | 56/58 | BG |
| Claire et al ²⁴ | 2001 | cFiO ₂ system | 14/14 | SpO ₂ |
| Claire et al ²⁵ | 2011 | cFiO ₂ system | 32/32 | SpO ₂ |
| Dauber et al ²⁶ | 2013 | Insulin therapy | 10/10 | BG |
| De Smet et al ²⁷ | 2008 | Propofol administration | 20/20 | BIS |
| Dojat et al ²⁸ | 2000 | PSV control | 10/10 | RR, Vt, EtCO ₂ |
| Dussaussoy et al ¹⁰ | 2014 | Dual loop | 18/18 | BIS |
| Elleri et al ²⁹ | 2013 | Insulin delivery | 12/12 | BG |
| Hallenberg et al ³⁰ | 2014 | CLAC | 34/34 | SpO ₂ |
| Hemmerling et al ³¹ | 2010 | Propofol administration | 20/20 | BIS |
| Hemmerling et al ⁸ | 2013 | McSleepy | 93/93 | BIS Analgoscore TOF |
| Hovorka et al ³² | 2010 | Insulin delivery | 12/12 | BG |
| Johannigman et al ³³ | 2009 | FiO ₂ control | 15/15 | SpO ₂ |
| Kee et al ³⁴ | 2012 | AP control | 108/103 | AP |
| Le Guen et al ³⁵ | 2013 | Dual loop | 15/14 | BIS |
| Leelarathna et al ³⁶ | 2013 | Glucose control | 12/12 | BG |
| Lellouche et al ³⁷ | 2013 | Intelli-Vent system | 30/30 | EtCO ₂ , SpO ₂ |
| Liu et al ³⁸ | 2006 | Propofol administration | 83/81 | BIS |
| Liu et al ³⁹ | 2011 | Dual loop | 83/84 | BIS |
| Liu et al ⁴⁰ | 2012 | Dual loop | 30/31 | SE, RE |
| Locher et al ⁴¹ | 2004 | Isoflurane | 10/10 | BIS |
| Ly et al ⁴² | 2014 | USS | 20/29 | BG |
| Nimri et al ⁴³ | 2013 | MDLAP | 12/12 | BG |
| Nimri et al ⁴⁴ | 2014 | MDLAP | 19/19 | BG |
| Plank et al ⁴⁵ | 2006 | MPC control | 30/30 | BG |
| Puri et al ⁹ | 2007 | CLADS | 20/20 | BIS |
| Renard et al ⁴⁶ | 2010 | Intraperitoneal pump | 8/8 | BG |
| Schädler et al ⁴⁷ | 2012 | SmartCare/PS | 150/150 | RR Vt EtCO ₂ |
| Madhavan et al ⁴⁸ | 2011 | IAADS | 20/20 | BIS |
| Sng et al ⁴⁹ | 2014 | Dual loop | 106/107 | AP |
| Solanki et al ⁵⁰ | 2010 | CLADS | 20/20 | BIS |
| Struys et al ⁵¹ | 2001 | Propofol administration | 10/10 | BIS |
| Urschitz et al ⁵² | 2004 | FiO ₂ control | 12/12 | SpO ₂ |

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

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

SYSTEMATIC REVIEW ARTICLE

Clinical Systematic Review

| 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

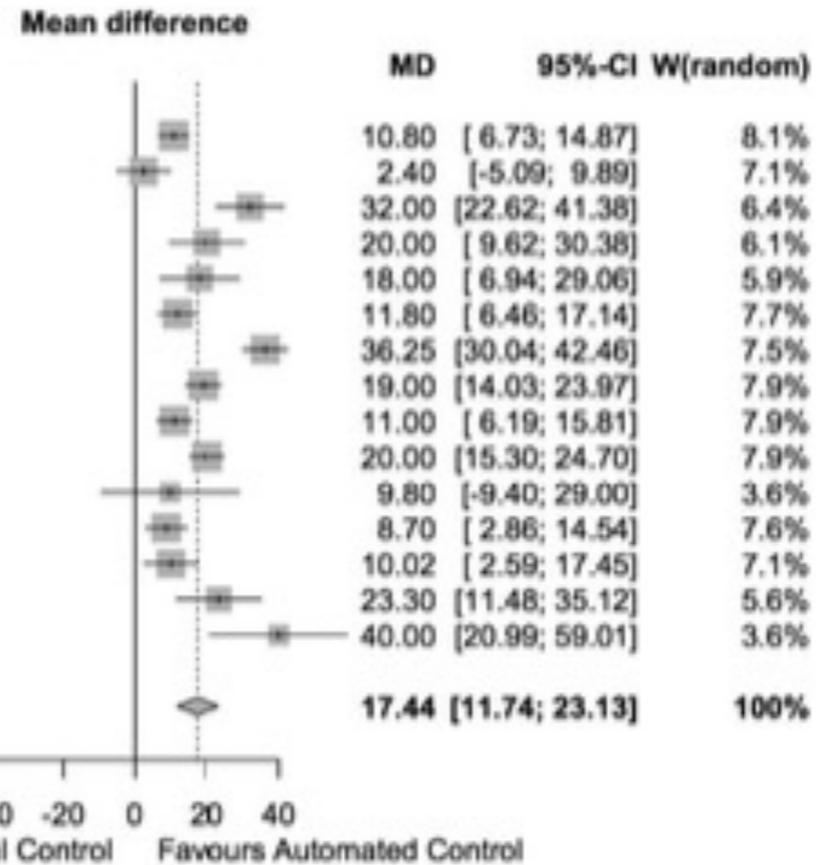


Figure 2. Forest plot presenting the percentage of time a given target (bispectral index or SE) was maintained within the desired range in closed-loop delivery systems (automated control) in comparison with manual control. The diamond represents the pooled results while the horizontal line represents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

| | | | | |
|------------------------------|------|--------------------------|-------|------------------|
| Solanki et al ²⁹ | 2010 | CLADS | 20/20 | BIS |
| Struys et al ³¹ | 2001 | Propofol administration | 10/10 | BIS |
| Urschitz et al ³² | 2004 | FiO ₂ control | 12/12 | SpO ₂ |

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 ¹⁰ | 2009 | Acta Anaesthesiol Scand | Elective cardiac surgery requiring cardiopulmonary bypass | 1 | CLADS™ |
| De Smet ¹¹ | 2008 | Anesth Analg | Ambulatory ovocytes retrieval | 1 | RUGLOOP II™ |
| Dussaussy ¹² | 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 ¹³ | 2010 | Can J Anaesth | Elective abdominal, thoracic, urologic, and spine or upper extremity orthopedic surgery | 1 | Self-designed interface |
| Hemmerling ¹⁴ | 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 ¹⁵ | 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 ¹⁶ | 2006 | Anesthesiology | Elective surgical procedures requiring general anesthesia of at least 30 min | 3 | Infusion Toolbox 95™ |
| Liu ¹⁷ | 2006 | Eur J Anesthesiol | Elective general, gynecologic, urologic, orthopedic, or lung surgery | 1 | Infusion Toolbox 95™ |
| Liu ¹⁸ | 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 ¹⁹ | 2000 | Anesthesia | Gynecologic or general surgery | 1 | Monitor™ |
| Puri ²⁰ | 2007 | Anesth Intensive Care | Elective cholecystectomy, upper and lower abdominal surgery, hernia surgery under general anesthesia | 1 | CLADS™ |
| Puri ²¹ | 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.

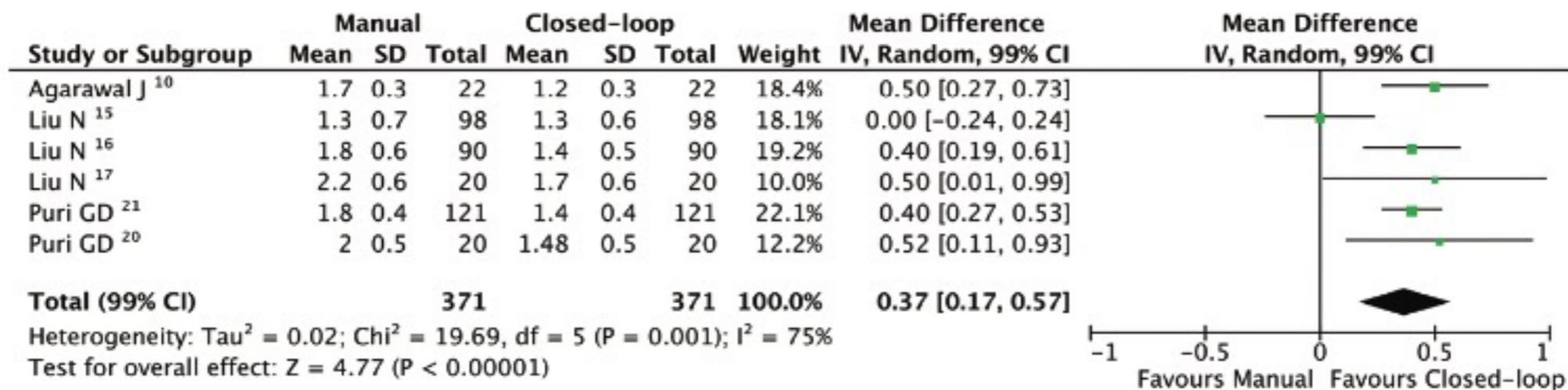


Figure 3. Forest plot of dose of propofol for anesthesia induction (milligram per kilogram). CI indicates confidence interval.

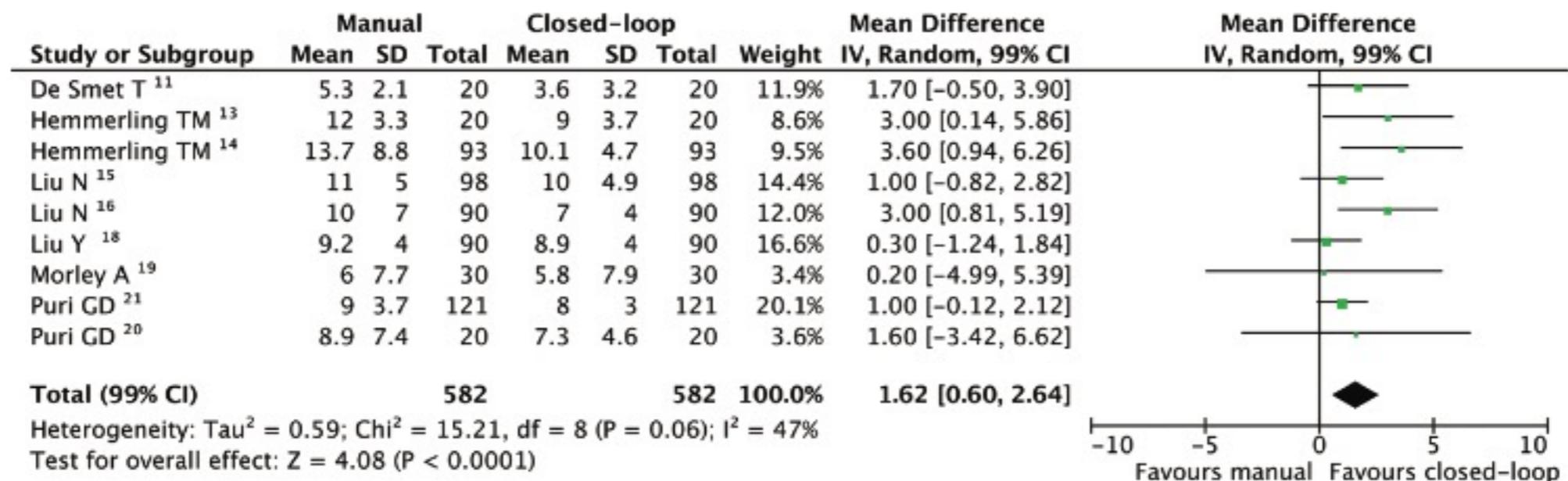


Figure 2. Forest plot of recovery times (minutes). CI indicates confidence interval.

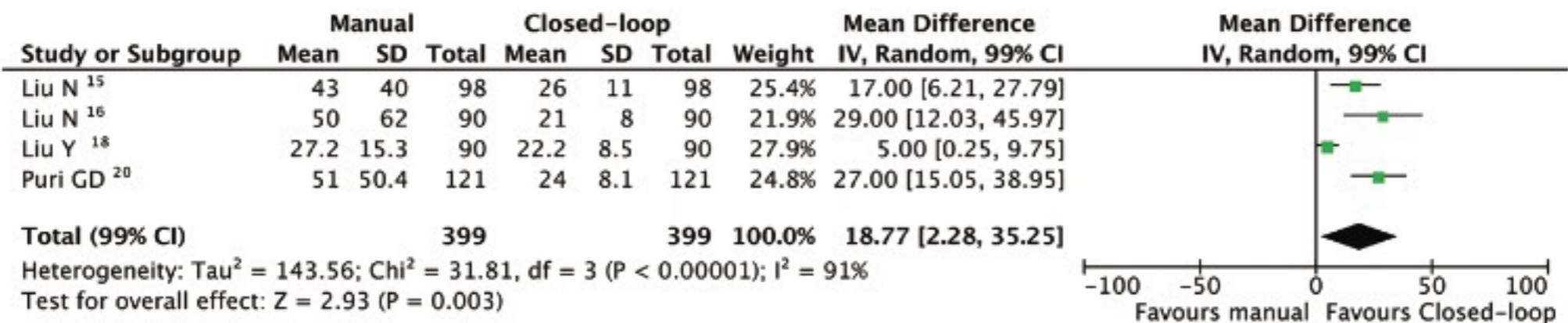


Figure 5. Forest plot of the Global Scores. CI indicates confidence interval.

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

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

CONCLUSION

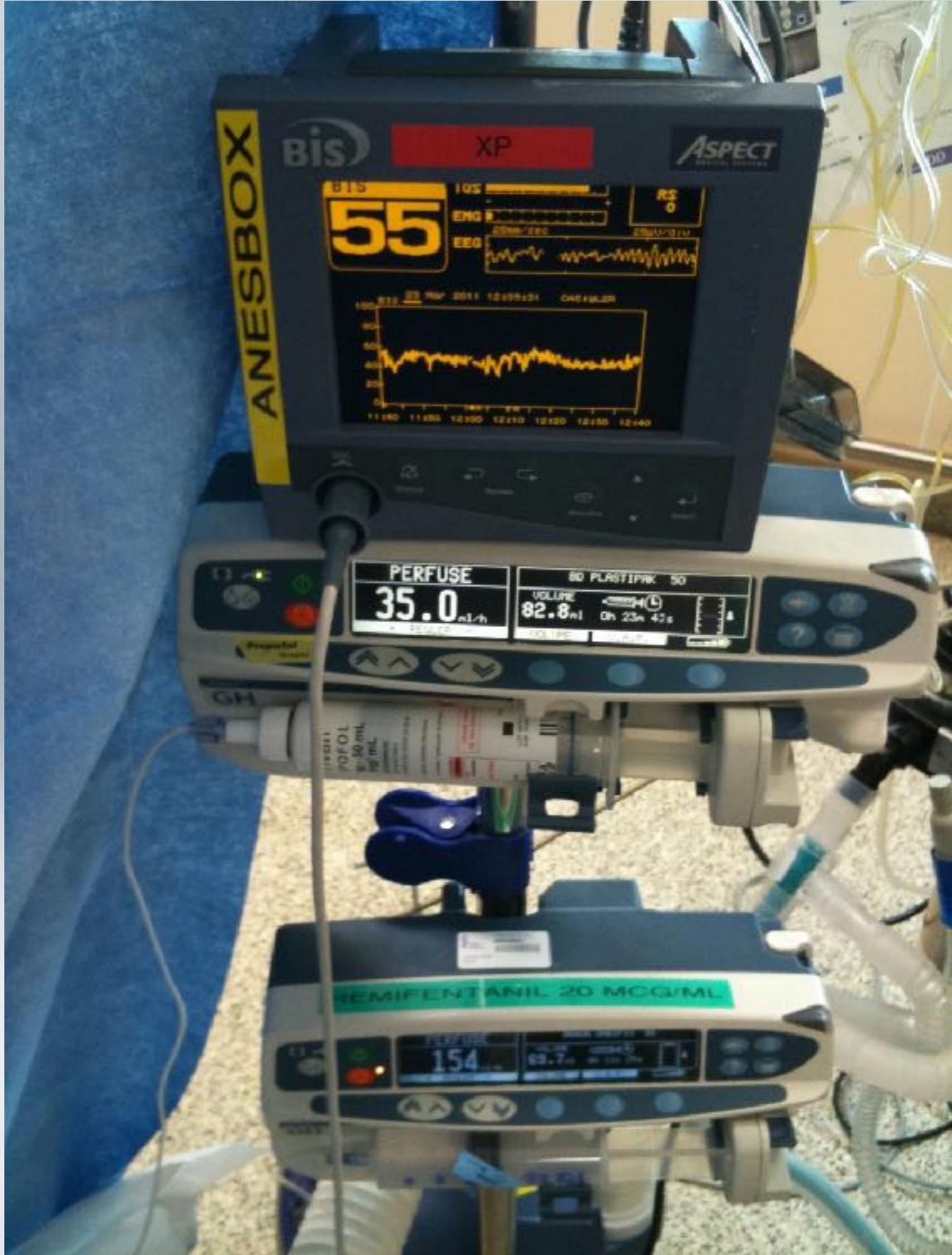
- La délivrance automatisée des produits de l'anesthésie est une réalité
- Avantages reconnus et recul satisfaisant

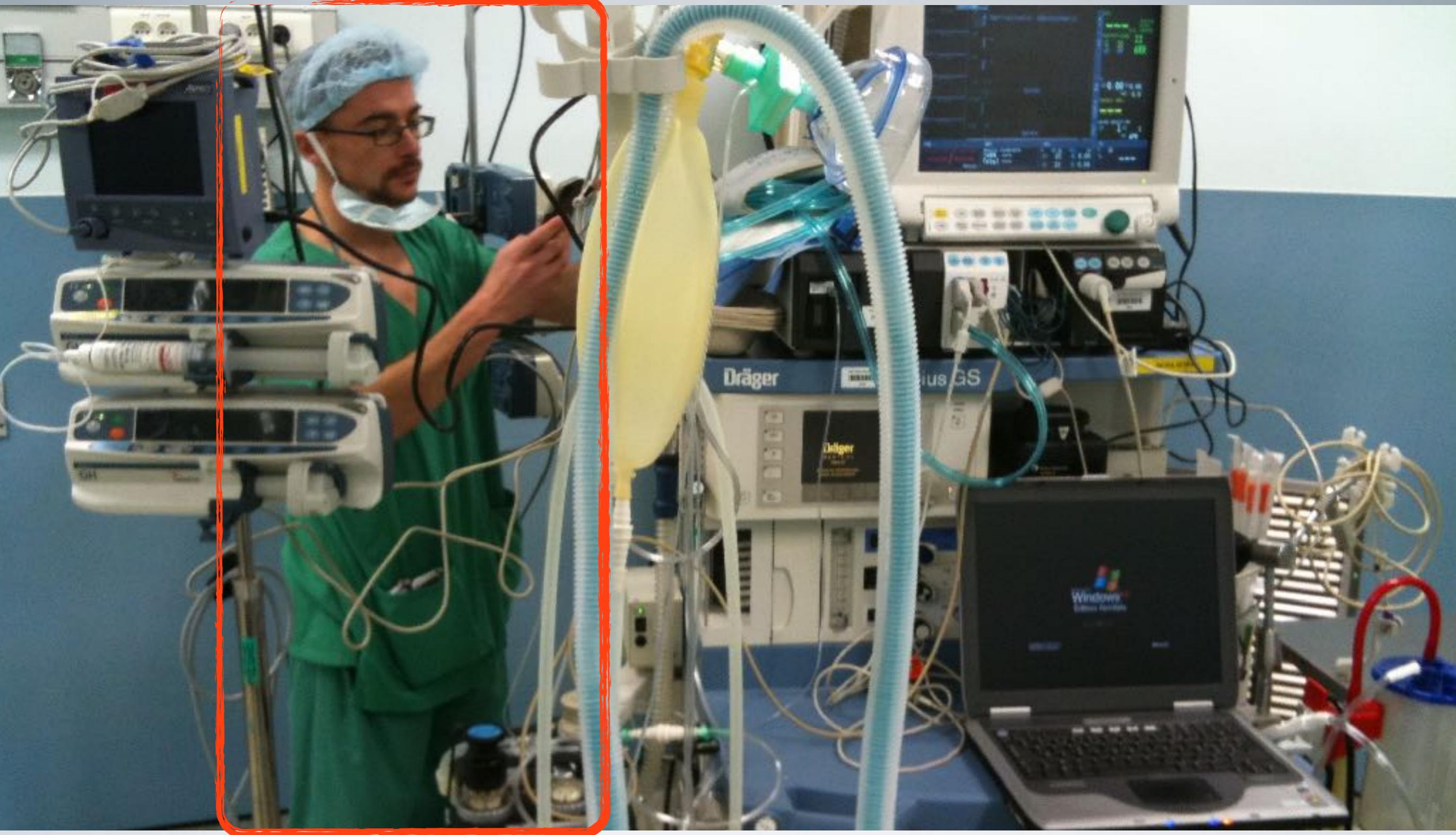
CONCLUSION

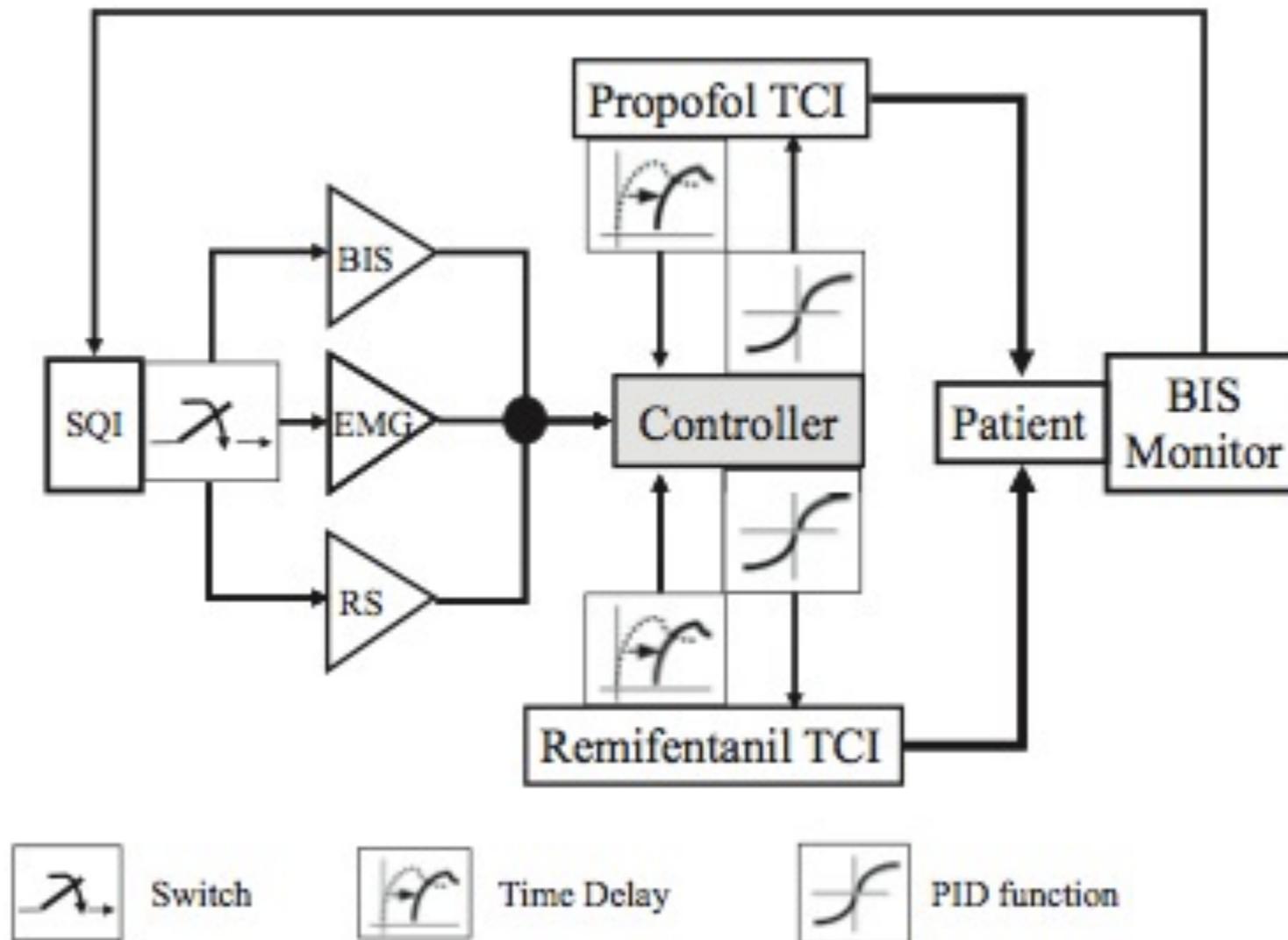
- La délivrance automatisée des produits de l'anesthésie est une réalité
- Avantages reconnus et recul satisfaisant
- Hétérogénéité des systèmes

CONCLUSION

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



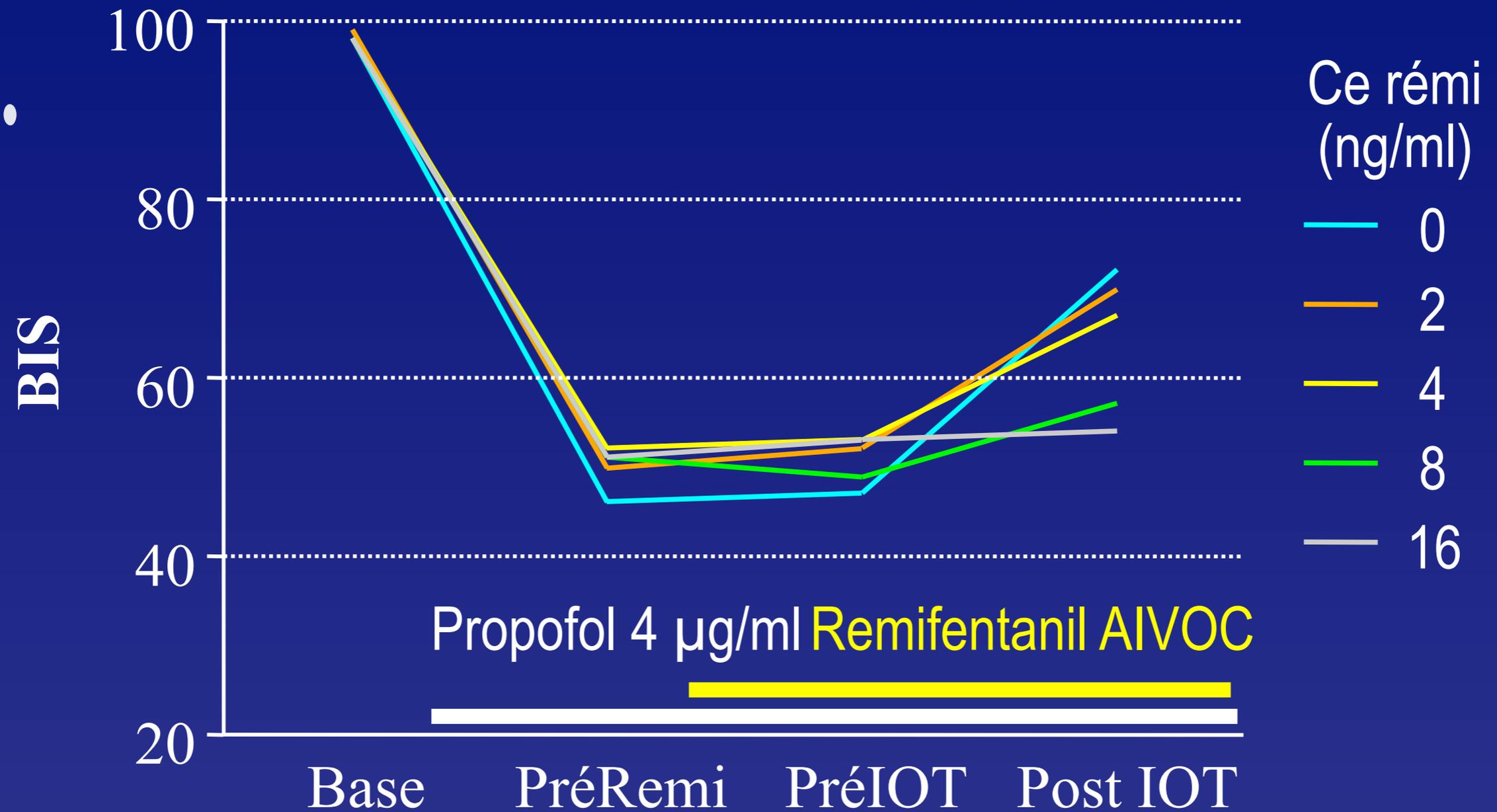




ALGORITHME PID

- 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”

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)

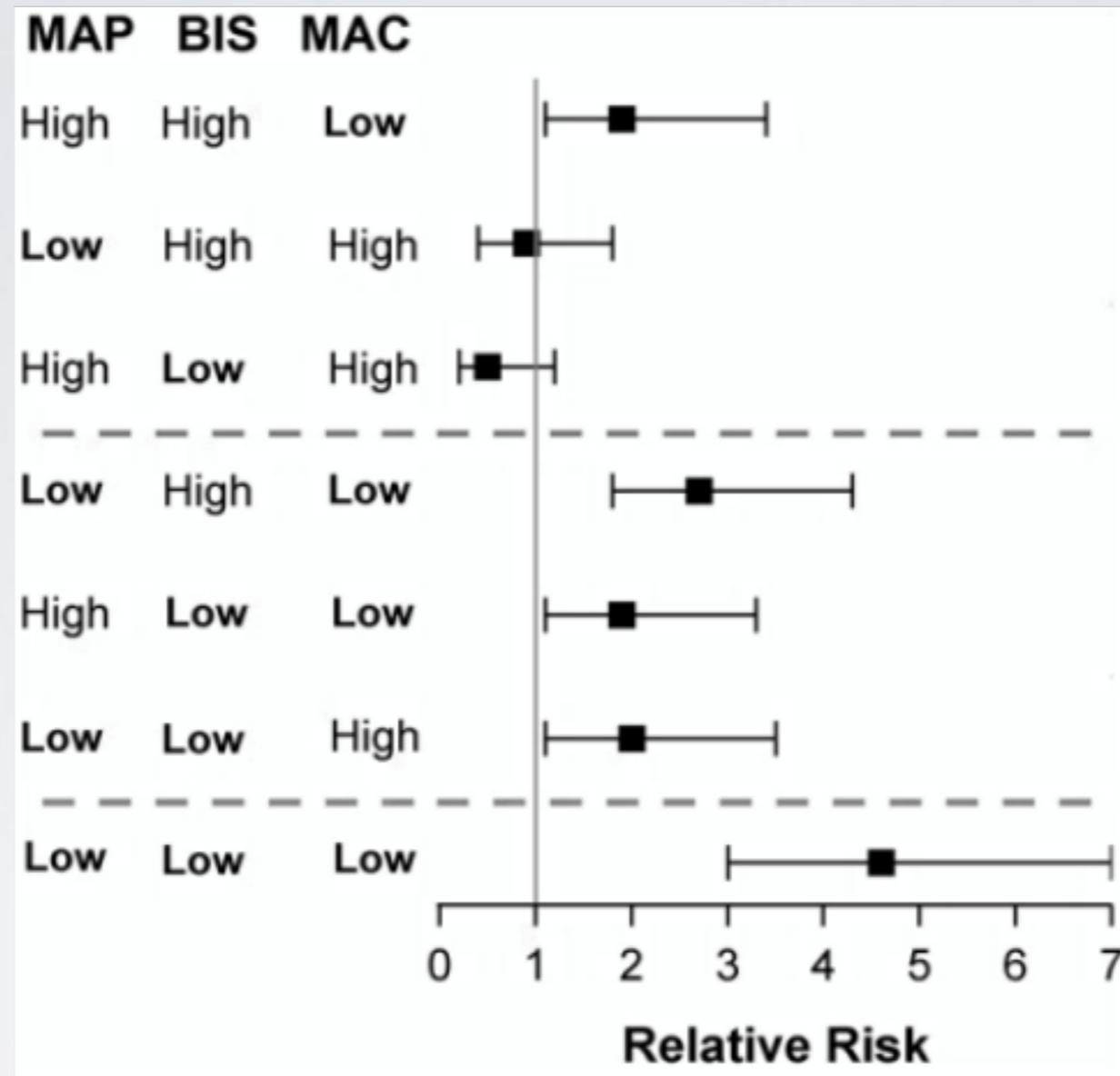
- “Presence of EEG suppression in critically ill patients is associated with increased mortality” CCM In Press
- **Hazard ratio (HR) 2.04** (1.12-3.70) for 6-month endpoint

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

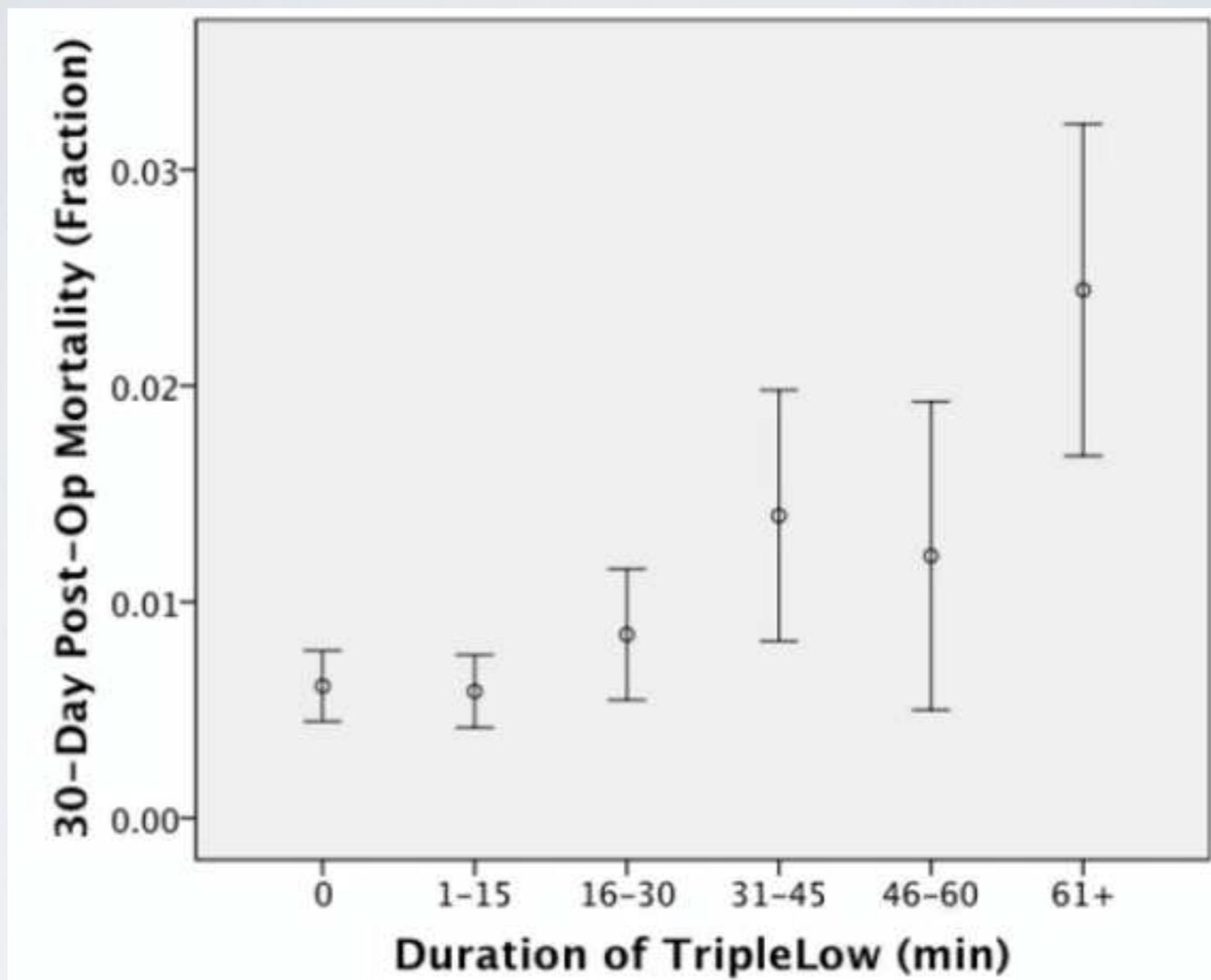
Leslie et al (TIVA/TCI Congress 2009)

- 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