Acta Anaesth. Bel., 2026, 77 (2): *127-133*

Review

From Bolus of propofol to Automation in Intravenous Anaesthesia: A Historical Perspective with Key Contributions from Belgian Research

Barvais L.[1], Schmartz D.[1], Joosten A.[2], Coeckelenbergh S.[3], Struys M.[4,5]

[1]H.U.B – Hôpital Erasme, Department of Anesthesiology, Reanimation, Perioperative medicine and Algology; [2]School of Medicine at UCLA. Department of Anesthesiology and Perioperative Medicine, University of California, Los Angeles, USA; [3]Clinical Research in Anesthesiology. Department of Anesthesiology and Perioperative Medicine. University of California, Irvine, USA; [4]Department of Anesthesiology, University of Groningen, University Medical Center Groningen; [5]Department of Basic and Applied Medical Sciences, Ghent University, Gent, Belgium.

Corresponding author: Denis Schmartz, H.U.B – Hôpital Erasme, Department of Anesthesiology, Reanimation, Perioperative medicine and Algology, 808 route de Lennik, 1070 Bruxelles, Belgium.
Email: denis.schmartz@hubruxelles.be

Abstract

Intravenous anaesthesia has undergone a profound transformation over the past five decades, evolving from intermittent bolus administration to highly sophisticated automated delivery systems. Propofol, introduced in the 1980s, enabled continuous infusion techniques and later the development of target-controlled infusion (TCI), fundamentally changing anaesthetic practice. Advances in pharmacokinetic–pharmacodynamic modelling, many of which involved key contributions from Belgian research groups, facilitated increasingly precise drug delivery. More recently, closed-loop systems (CLS) integrating physiological feedback such as electroencephalographic or hemodynamic variables have demonstrated improved control of anaesthetic depth and cardiovascular stability compared with manual titration. Despite these advances and the wide clinical use of TCI nowadays, widespread clinical adoption of full closed-loop systems remains limited, and robust evidence demonstrating improved patient-centred outcomes is still lacking. This review traces the evolution of intravenous anaesthesia, highlights key scientific contributions, including those from Belgian teams, and critically appraises the current evidence supporting automation and artificial intelligence in perioperative medicine. While automation offers clear advantages in standardization and workload reduction, its future integration will depend on demonstration of clinical benefit, usability, and regulatory acceptance.

Introduction

The administration of modern intravenous anaesthesia has evolved from a simple, clinician-driven process based on bolus dosing to a complex, technology-assisted practice integrating pharmacological modelling, physiological monitoring, and automation. This evolution has been driven by the pursuit of more stable anaesthesia, improved recovery profiles, and enhanced patient safety.

This review will only briefly describe the fantastic contribution of the Belgian Baron Paul Janssen before turning to focus more specially on TIVA contributions of Belgian research. In 1958, Janssen synthesised haloperidol, a revolution in psychopharmacology. He also was the pioneer in the development of potent synthetic opioids like fentanyl, which he discovered in 1959, followed by sufentanil and alfentanil with their specific pharmacologic properties. These 3 phenylpiperidine derivative compounds became integral to modern anaesthetic regimens and are still used today in operating rooms worldwide. Janssen's lab has also developed etomidate, a general anaesthetic that gained widespread use due to its minimal cardiovascular and respiratory depression. The work of Paul Janssen bridging chemistry and clinical anaesthesia continues to benefit our patients.

Propofol, arguably one of the safest and most used anaesthetics, was developed in the United Kingdom and extensively tested in Belgium. Propofol has played a central role in the transformation of Total IntraVenous Anesthesia (TIVA), enabling continuous infusion techniques and, subsequently, the development of target-controlled infusion (TCI). Over time, advances in pharmacokinetic–pharmacodynamic (PK–PD) modelling and monitoring technologies paved the way for closed-loop systems (CLS) capable of automatically adjusting drug delivery based on real-time physiological feedback.

Although these developments have been international, several key advances, particularly in PK modelling and early automation, have involved important contributions from Belgian research groups. While automation offers clear advantages in standardization and workload reduction, its future integration will depend on demonstration of clinical benefit, usability, and regulatory acceptance.

Propofol: from bolus administration to continuous infusion

Propofol was synthesized by Dr. John (Iain) Glen at ICI, (later AstraZeneca) in the early 1970[1]. Owing to its high lipid solubility and rapid hepatic metabolism, propofol exhibits pharmacokinetic properties that allow not only bolus administration for induction of anaesthesia, but also continuous infusion for maintenance, an important distinction from earlier intravenous hypnotic agents. Initially formulated with Cremophor, propofol was associated with allergic reactions. In 1983, a lipid emulsion formulation was introduced, which remains the standard today. The first clinical trial evaluating bolus administration of propofol in humans was conducted in Belgium, in Ghent, by the team of Professor Georges Rolly and published in 1985[2]. In this randomized study of 30 premedicated ASA I–II patients undergoing minor gynaecological surgery, patients received either propofol (1.5 or 2 $mg \cdot kg^{-1}$) or thiopentone (4 $mg \cdot kg^{-1}$). Induction times and duration of apnoea were comparable across groups, and no major adverse events were observed. Importantly, recovery following propofol was faster than with thiopentone.

Subsequently, in 1988, Herregods and colleagues demonstrated that maintenance of anaesthesia using continuous propofol infusion was associated with improved quality of recovery compared with isoflurane-based anaesthesia[3]. In this study of 60 adult patients undergoing arthroscopy, no major differences in cardiovascular parameters were observed between groups. However, early recovery was less smooth in the group receiving propofol combined with repeated boluses of alfentanil. These early studies established propofol as a versatile agent suitable for both induction and maintenance of anaesthesia and laid the foundation for total intravenous anaesthesia (TIVA).

Target-controlled infusion (TCI) anesthesia

A major breakthrough in intravenous anaesthesia came with the development of target-controlled infusion, which enables drug administration based on predicted plasma or effect-site concentrations rather than fixed infusion rates. In 1987, Gepts and Camu, from the Vrije Universiteit Brussel, published the first pharmacokinetic parameters for propofol[4]. Their work involved arterial blood sampling during and after propofol infusions at different rates, demonstrating that propofol pharmacokinetics could be accurately described using a three-compartment model with rapid distribution and high clearance. The Marsh model, developed in 1991 by Kenny and colleagues, was derived from these earlier data and became the foundation for the first commercial TCI system[5]. TCI allows automated adjustment of infusion rates to achieve a user-defined target concentration, based on pharmacokinetic modelling rather than empirical dosing. Early TCI systems incorporated microprocessors capable of continuously recalculating infusion rates. The initial prototypes featured user interfaces similar to vaporizers with a rotating black knob (Fig. 1), allowing clinicians to adjust target concentrations in real time according to the parameters of the Marsh pharmacokinetic model[6]. In 1997, the first 2 syringe pumps dedicated to propofol in TCI mode were marketed. These automatic syringes, called Diprifusor® were put on the market by the Alaris and Graseby companies in collaboration with AstraZeneca. They had an automatic TAG system allowing recognition of the concentration of 1 or 2% of propofol prepared in a glass syringe.

In 2000, Struys and colleagues demonstrated that TCI targeting the effect-site concentration—rather than plasma concentration—improved prediction of drug effect, as assessed by electroencephalographic monitoring[7]. Effect-site targeting resulted in faster induction without increasing the risk of hypotension. One-hundred twenty healthy women patients received propofol via TCI for 12 min at a target of 5.4 µg/ml[6]. In Group I, propofol TCI controlled the plasma concentration using the Marsh model whereas in groups II and III, TCI controlled the effect-site concentration using the Marsh model as

Fig. 1 — Prototype of the Diprifusor® allowing the delivery of propofol TCI using the Marsh pharmacokinetic set.

pharmacokinetic model enlarged with an effect-site compartment connected to the plasma compartment using a half-life for plasma effect-site equilibration of 3.5 min in group II and 1.6 min in group III. The time course of propofol drug effect, as measured by the bispectral index, was best predicted in group III. Targeting the effect-site concentration shortened the time to loss of consciousness without causing hypotension. The conclusion of this study was that effect compartment-controlled TCI can be safely applied in clinical practice.

This approach was further refined with the introduction of the Schnider model, which incorporates a more accurate description of the delay between plasma and brain concentrations[8]. Thereafter, in 2003, new types of automatic syringes were marketed which allowed the administration of propofol targeted at the effect site using the Schnider set which incorporates a rapid constant transfer of propofol from the blood to the brain[8].

Then Michel Struys' team built a population Pharmacokinetic model with a variable effect compartment based on age which allows propofol to be administered to children, obese adults and elderly patients[9]. The Eleveld pharmacokinetic model is derived from a group of nearly 1000 patients. This model should replace definitively all the older sets of Marsh or Schnider. Recently, it has been finally incorporated into the new automatic syringes available on the market.

In parallel, several Belgian research groups contributed to the clinical[6] understanding of propofol-based anaesthesia. For example, Hans and colleagues demonstrated a lower incidence of coughing during extubation with propofol compared with sevoflurane anaesthesia[10]. Ickx and colleagues showed that renal failure does not significantly alter propofol pharmacokinetics[11]. Vermeyen and colleagues described the hemodynamic effects of propofol–fentanyl anaesthesia during cardiac surgery, noting reductions in arterial pressure without evidence of myocardial ischemia[12].

Closed loop systems (CLS) for intravenous anesthetic drugs

Closed-loop systems represent the next stage in the evolution of intravenous anaesthesia, enabling automated drug delivery based on continuous feedback from physiological variables. A CLS typically includes a sensor (e.g. electroencephalography or hemodynamic monitoring), a controller (algorithm), and an actuator (infusion pump). The system continuously compares measured values with predefined targets and adjusts drug delivery in real time using control algorithms such as proportional–integral–derivative (PID) or model-based controllers. The use in clinical practice of CLS aims to improve the stability of the controlled variables while reducing the practitioner's workload by performing simple and repetitive tasks, without increasing the risks for patients.

There are many domains in anaesthesia where CLS can be applied but the most common application of closed-loop anaesthesia is the control of propofol TCI based on EEG monitoring

The introduction of the bispectral index (BIS) monitor in the 1990s provided a practical measure of anaesthetic depth, facilitating the development of CLS for propofol administration. In 2001, Mortier and colleagues reported the first clinical application of a propofol CLS guided by BIS. In this study, sedation was achieved and maintained without episodes of apnoea or significant oxygen desaturation, demonstrating the feasibility and safety of such systems[13]. The target of sedation was an Observer Assessment of Alertness and Sedation scale rating of 1, which corresponds to a patient who does not respond to mild prodding and shaking. The 10 patients were allowed to breathe spontaneously. The propofol plasma target concentration was initially set at 2 $\mu g.ml^{-1}$ and increased by 0.5 $\mu g.ml^{-1}$ every minute. Once the sedation target was reached, the increase of propofol TCI was stopped. At that moment, the corresponding individual BIS value was 63.9±6.2 and used as the target BIS to steer the closed loop. Recovery time after stopping propofol administration was 8.3±3.1 minutes. During maintenance, no episode of apnoea was observed. SpO_2 never decreased below 90%. This Belgian study was the first paper published on propofol CLS applied in human patients. It has proven that such a propofol TCI feedback control system, coupled with BIS as the controlled variable could be adequate and safe. This Belgian article was the start of automation in the domain of TCI anaesthesia.

Thereafter, Struys and colleagues have studied twenty female patients, ASA I or II, who were scheduled for gynaecologic laparotomy under propofol remifentanil anaesthesia[14]. In group 1, 10 patients were anesthetized with propofol TCI using a model-based CLS with a BIS targeted at 50. In group II, 10 patients received propofol infusion titration based on classical hemodynamic signs of (in)adequate anaesthesia. The patients of group II undergoing manual induction of anaesthesia at 300 ml/h reached a BIS level of 50 faster than patients but with a more pronounced initial overshoot of the BIS target and a more pronounced decrease in blood pressure. During the maintenance phase, better control of BIS and systolic blood pressure was found in the CLS group compared with the manual propofol group. Recovery was also faster in the CLS group. They concluded that a CLS for propofol using the BIS as a controlled variable together with a model-based controller is clinically acceptable during general anaesthesia. The article was accompanied by an editorial: Automatic anaesthesia: reality or fantasy?[15]. Later, this group enlarged their CLS model-based controller with a Bayesian-based adaptive system continuously adapting the patient-individual pharmacodynamic relation and tested this system successfully during moderate to deep sedation and general anaesthesia[16-18].

In 1989, Cantraine and Coussaert from the computer science department of the Université libre de Bruxelles in collaboration with the Anaesthesia department of the Erasmus hospital, have developed software capable of controlling multiple infusion pumps simultaneously, integrating hypnotic, opioid, neuromuscular blocking, and vasodilator agents[19]. The later system, called TOOLBOX, enabled both TCI and closed-loop control and was widely used in European centres. Using this platform, Liu and colleagues conducted a multicentre prospective randomized study demonstrating that a propofol Proportional Integral Derivative closed-loop controller using the Schnider effect site pharmacokinetic model and the BIS as the EEG parameter, maintained BIS within target ranges more effectively than manual control during the 3 phases of anaesthesia: induction, maintenance and recovery[20]. Waking up was also faster in the CLS group. Meta-analyses have confirmed the better maintenance of an EEG target with an CLS controller compared to the anaesthesiologist's manual control[21].

Automated control of opioid delivery or analgesic drugs is more complex because there is no universally accepted real-time marker of nociception. Various signs of the autonomic system such as plethysmogram waves, heart rate variability, pupillary reflexes, and skin conductance have been explored. Their combination is probably the better approach but it is very complex to find the most appropriate algorithm, especially when antinociceptive drugs are combined. CLS of neuromuscular blocking agents (e.g., atracurium, rocuronium) based on train-of-four (TOF) monitoring are easy to implement and ensure that muscle relaxation is maintained within a defined range, reducing the risk of under- or overdosing. Unfortunately, up to now, no system has been commercialized on a large scale because it is more expensive than the use of antagonists.

Hemodynamic CLS

While most developments in closed-loop anaesthesia have focused on hypnotic control using propofol and electroencephalographic monitoring, similar principles have been explored in other domains of perioperative management. In particular, CLS for fluid administration and vasopressor delivery have been developed to maintain hemodynamic targets using variables such as stroke volume variation or arterial pressure. Rinehart and Joosten demonstrated that there was less total volume given compared when an automatic fluid management system was used compared with a group of patients in whom the

anaesthesiologist was responsible of the fluid delivery[22]. The interest of a norepinephrine CLS to outperform clinicians in maintaining a blood pressure target, during major abdominal surgery has also been demonstrated in Belgium[23]. In parallel, the Belgian Coeckelenbergh with colleagues from the Bicêtre hospital in Paris have demonstrated that decision support tools and emerging artificial intelligence–based approaches aim to assist clinicians by predicting hemodynamic instability and optimizing therapeutic interventions[24,25]. Although promising, these technologies remain conceptually distinct from propofol-based closed-loop anaesthesia and are still undergoing clinical evaluation. A detailed discussion of these systems is beyond the scope of the present review, which focuses on the evolution of intravenous hypnotic delivery and its automation.

Multiple CLS

In 2016, Joosten and colleagues published the first case report of a combination of 2 independent closed loops: Propofol-BIS CLS associated with a loop combining variations in the stroke volume of the heart with the administration of fluid boluses (Fig. 2)[26]. This case report was followed by a study of the same team, demonstrating the clinical ability to maintain BIS and hemodynamic parameters within their target range in a group of 13 patients undergoing major vascular surgery[27]. The 2 loops operated continuously for 4700 minutes with more than 3000 changes in the target concentration at the site of action of propofol. The CLS were not overridden by the supervising anaesthesiologist in any case with no degradation of the stability of both systems due to the presence of the other. The anaesthesiologist never stopped a fluid bolus and never changed the controller from the standard SVV target of 11%.

Finally, in 2020, Joosten and colleagues in Brussels, have studied the impact of 3 CLS working simultaneously (Propofol BIS, SVV - fluid and $ETCO_2$-Ventilation) on postoperative cognitive function measured by the Montreal psychological cognitive test[28]. Patients in the 3 CLS group spent less time during surgery with a BIS <40, had less episodes of hypocapnia, and a lower fluid balance compared to the control group. Regarding the primary outcome, there was a significant decrease in the cognition score compared to baseline in the control group at one-week post-surgery. This effect persisted at 3 months post-surgery. This article was associated with an editorial in Anesthesiology[29]. The message was that there was no doubt that closed loop anaesthesia was at least as good as the best human anaesthesia. However, the biggest challenges of anaesthesia CLS remains the anticipation of events. Only trained specialists are capable of providing valuable information (bleeding, surgical progress, …) to collaborate with robots. The question was: "when will robotic anaesthesia become a daily reality"?

Conclusions

Intravenous anaesthesia has evolved from empirical bolus administration to increasingly

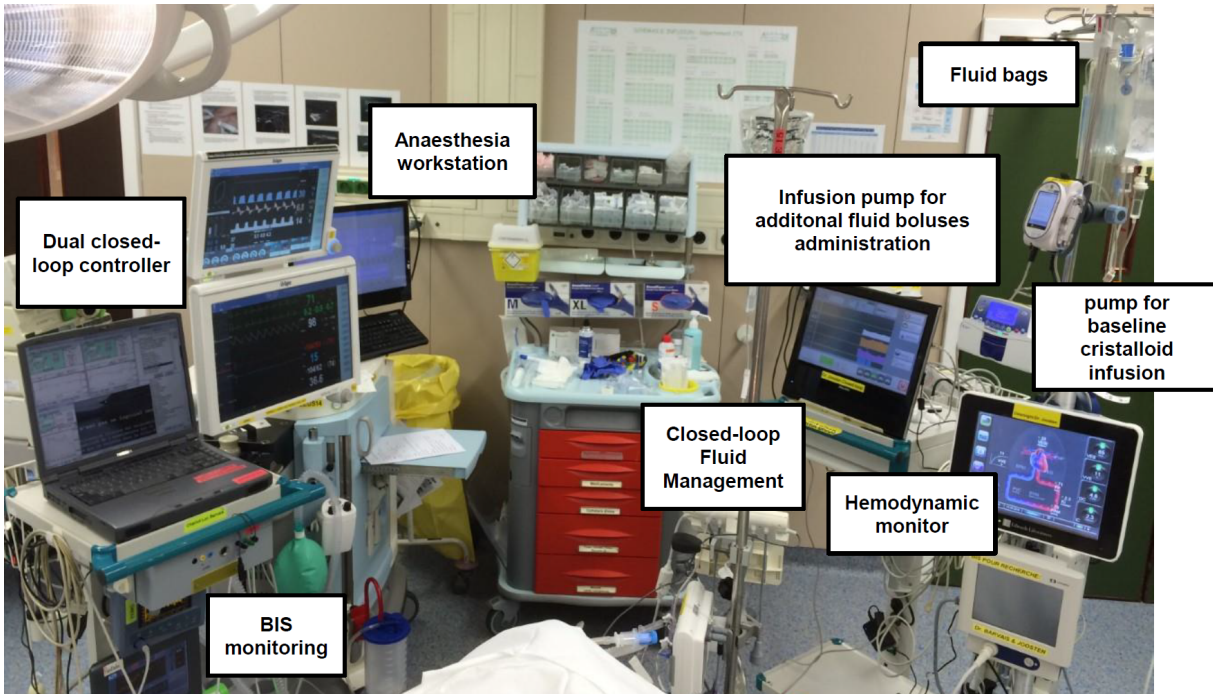

Fig. 2 — The Operating Room installation with 2 independent closed loop systems for Propofol-BIS and Stroke volume variations combined with fluid bolus delivery.

sophisticated, model-based and automated delivery systems. Propofol has been central to this transformation, enabling continuous infusion techniques and the development of target-controlled anaesthesia, which fundamentally re-shaped anaesthetic practice. Subsequent advances in pharmacokinetic–pharmacodynamic modelling and electroencephalographic monitoring have paved the way for CLS capable of maintaining anaesthetic depth with greater precision and reduced variability compared with manual titration. CLS reduce the workload of the anaesthesia team and the errors due to distraction and fatigue. However, despite these technological advances, the clinical impact of full closed-loop automation on a large scale remains incompletely established. The robust evidence demonstrating improvements in patient-centred outcomes is still lacking. In addition, challenges related to system robustness, usability, and integration into routine clinical workflows continue to limit widespread adoption. Additionally, new regulation on medical devices has created a higher barrier for industry to introduce closed-loop automated systems into clinical practice. The future of intravenous anaesthesia will likely rely on a balanced integration of pharmacological modelling, real-time monitoring, and intelligent automation, combined with clinical expertise. Further large-scale studies focusing on meaningful clinical outcomes will be essential to define the true value of these technologies in perioperative care. Don't be afraid, the anaesthesiologists will never be replaced by a robot, but they must climb on the bandwagons of the development towards the Intelligent Anaesthesia of the future.

References

1. Glen JB, Hunter SC. Pharmacology of an emulsion formulation of ICI 35 868. Br J Anaesth. juin 1984;56(6):617-26. doi:10.1093/bja/56.6.617 PubMed PMID: 6202310.
2. Rolly G, Versichelen L. Comparison of propofol and thiopentone for induction of anaesthesia in premedicated patients. Anaesthesia. oct 1985;40(10):945-8. doi:10.1111/j.1365-2044.1985.tb10547.x PubMed PMID: 3877474.
3. Herregods L, Capiau P, Rolly G, De Sommer M, Donadoni R. Propofol for arthroscopy in outpatients. Comparison of three anaesthetic techniques. Br J Anaesth. avr 1988;60(5):565-9. doi:10.1093/bja/60.5.565 PubMed PMID: 3259889.
4. Gepts E, Camu F, Cockshott ID, Douglas EJ. Disposition of propofol administered as constant rate intravenous infusions in humans. Anesth Analg. déc 1987;66(12):1256-63. PubMed PMID: 3500657.
5. Marsh B, White M, Morton N, Kenny GN. Pharmacokinetic model driven infusion of propofol in children. Br J Anaesth. juill 1991;67(1):41-8. doi:10.1093/bja/67.1.41 PubMed PMID: 1859758.
6. Gray JM, Kenny GN. Development of the technology for « Diprifusor » TCI systems. Anaesthesia. avr 1998;53 Suppl 1:22-7. doi:10.1111/j.1365-2044.1998.53s114.x PubMed PMID: 9640111.
7. Struys MM, De Smet T, Depoorter B, Versichelen LF, Mortier EP, Dumortier FJ, et al. Comparison of plasma compartment versus two methods for effect compartment--controlled target-controlled infusion for propofol. Anesthesiology. févr 2000;92(2):399-406. doi:10.1097/00000542-200002000-00021 PubMed PMID: 10691226.
8. 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. mai 1998;88(5):1170-82. doi:10.1097/00000542-199805000-00006 PubMed PMID: 9605675.
9. Eleveld DJ, Colin P, Absalom AR, Struys MMRF. Pharmacokinetic-pharmacodynamic model for propofol for broad application in anaesthesia and sedation. Br J Anaesth. mai 2018;120(5):942-59. doi:10.1016/j.bja.2018.01.018 PubMed PMID: 29661412.
10. Hans P, Marechal H, Bonhomme V. Effect of propofol and sevoflurane on coughing in smokers and non-smokers awakening from general anaesthesia at the end of a cervical spine surgery. Br J Anaesth. nov 2008;101(5):731-7. doi:10.1093/bja/aen271 PubMed PMID: 18818191.
11. Ickx B, Cockshott ID, Barvais L, Byttebier G, De Pauw L, Vandesteene A, et al. Propofol infusion for induction and maintenance of anaesthesia in patients with end-stage renal disease. Br J Anaesth. déc 1998;81(6):854-60. doi:10.1093/bja/81.6.854 PubMed PMID: 10211008.
12. Vermeyen KM, Erpels FA, Janssen LA, Beeckman CP, Hanegreefs GH. Propofol-fentanyl anaesthesia for coronary bypass surgery in patients with good left ventricular function. Br J Anaesth. sept 1987;59(9):1115-20. doi:10.1093/bja/59.9.1115 PubMed PMID: 3499162.
13. Mortier E, Struys M, De Smet T, Versichelen L, Rolly G. Closed-loop controlled administration of propofol using bispectral analysis. Anaesthesia. août 1998;53(8):749-54. doi:10.1046/j.1365-2044.1998.00467.x PubMed PMID: 9797518.
14. Struys MM, De Smet T, Versichelen LF, Van De Velde S, Van den Broecke R, Mortier EP. Comparison of closed-loop controlled administration of propofol using Bispectral Index as the controlled variable versus « standard practice » controlled administration. Anesthesiology. juill 2001;95(1):6-17. doi:10.1097/00000542-200107000-00007 PubMed PMID: 11465585.
15. Glass PS, Rampil IJ. Automated anesthesia: fact or fantasy? Anesthesiology. juill 2001;95(1):1-2. doi:10.1097/00000542-200107000-00005 PubMed PMID: 11465546.
16. De Smet T, Struys MMRF, Greenwald S, Mortier EP, Shafer SL. Estimation of optimal modeling weights for a Bayesian-based closed-loop system for propofol administration using the bispectral index as a controlled variable: a simulation study. Anesth Analg. déc 2007;105(6):1629-38, table of contents. doi:10.1213/01.ane.0000287269.06170.0f PubMed PMID: 18042860.
17. De Smet T, Struys MMRF, Neckebroek MM, Van den Hauwe K, Bonte S, Mortier EP. The accuracy and clinical feasibility of a new bayesian-based closed-loop control system for propofol administration using the bispectral index as a controlled variable. Anesth Analg. oct 2008;107(4):1200-10. doi:10.1213/ane.0b013e31817bd1a6 PubMed PMID: 18806028.
18. Neckebroek M, Ionescu CM, van Amsterdam K, De Smet T, De Baets P, Decruyenaere J, et al. A comparison of propofol-to-BIS post-operative intensive care sedation by means of target controlled infusion, Bayesian-based and predictive control methods: an observational,

open-label pilot study. J Clin Monit Comput. août 2019;33(4):675-86. doi:10.1007/s10877-018-0208-2 PubMed PMID: 30311073; PubMed Central PMCID: PMC6602998.
19. Cantraine F, Coussaert E, d'Hollander A, Barvais L. MINA: monitoring of intravenous anaesthesia. A system to monitor the infusion of 4 intravenous drugs under the control of a personal computer. Int J Clin Monit Comput. avr 1989;6(2):109-17. doi:10.1007/BF01720421 PubMed PMID: 2794738.
20. 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. avr 2006;104(4):686-95. doi:10.1097/00000542-200604000-00012 PubMed PMID: 16571963.
21. 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. févr 2017;124(2):446-55. doi:10.1213/ANE.0000000000001372 PubMed PMID: 27482773.
22. Rinehart J, Lilot M, Lee C, Joosten A, Huynh T, Canales C, et al. Closed-loop assisted versus manual goal-directed fluid therapy during high-risk abdominal surgery: a case-control study with propensity matching. Crit Care. 19 mars 2015;19(1):94. doi:10.1186/s13054-015-0827-7 PubMed PMID: 25888403; PubMed Central PMCID: PMC4372998.
23. Joosten A, Chirnoaga D, Van der Linden P, Barvais L, Alexander B, Duranteau J, et al. Automated closed-loop versus manually controlled norepinephrine infusion in patients undergoing intermediate- to high-risk abdominal surgery: a randomised controlled trial. Br J Anaesth. janv 2021;126(1):210-8. doi:10.1016/j.bja.2020.08.051 PubMed PMID: 33041014; PubMed Central PMCID: PMC8489152.
24. Coeckelenbergh S, Entzeroth M, Van der Linden P, Flick M, Soucy-Proulx M, Alexander B, et al. Assisted Fluid Management and Sublingual Microvascular Flow During High-Risk Abdominal Surgery: A Randomized Controlled Trial. Anesth Analg. 1 mai 2025;140(5):1149-58. doi:10.1213/ANE.0000000000007097 PubMed PMID: 39116013; PubMed Central PMCID: PMC12621645.
25. Coeckelenbergh S, Soucy-Proulx M, Van der Linden P, Roullet S, Moussa M, Kato H, et al. Restrictive versus Decision Support Guided Fluid Therapy during Major Hepatic Resection Surgery: A Randomized Controlled Trial. Anesthesiology. 1 nov 2024;141(5):881-90. doi:10.1097/ALN.0000000000005175 PubMed PMID: 39052844; PubMed Central PMCID: PMC12713225.
26. Joosten A, Delaporte A, Cannesson M, Rinehart J, Dewilde JP, Van Obbergh L, et al. Fully Automated Anesthesia and Fluid Management Using Multiple Physiologic Closed-Loop Systems in a Patient Undergoing High-Risk Surgery. Case Rep. 15 déc 2016;7(12):260-5. doi:10.1213/XAA.0000000000000405 PubMed PMID: 27669030.
27. Joosten A, Jame V, Alexander B, Chazot T, Liu N, Cannesson M, et al. Feasibility of Fully Automated Hypnosis, Analgesia, and Fluid Management Using 2 Independent Closed-Loop Systems During Major Vascular Surgery: A Pilot Study. Anesth Analg. juin 2019;128(6):e88-92. doi:10.1213/ANE.0000000000003433 PubMed PMID: 31094779.
28. Joosten A, Rinehart J, Bardaji A, Van der Linden P, Jame V, Van Obbergh L, et al. Anesthetic Management Using Multiple Closed-loop Systems and Delayed Neurocognitive Recovery: A Randomized Controlled Trial. Anesthesiology. févr 2020;132(2):253-66. doi:10.1097/ALN.0000000000003014 PubMed PMID: 31939839; PubMed Central PMCID: PMC7517610.
29. Hemmerling TM. Robots Will Perform Anesthesia in the Near Future. Anesthesiology. 2020;132(2):219-20. doi:10.1097/ALN.0000000000003088 PubMed PMID: 31939836.

doi.org/10.56126/77.2.14