NeuroWave
HARNESSING THE POWER OF EEG

AutoTIVA™ System

an autopilot for Total IntraVenous Anesthesia (TIVA)

enabling safe **TIVA**
for *improved* outcomes

The first fully automated

total intravenous anesthesia delivery system

Product highlights

NeuroWave is proud to introduce the **AutoTIVA™** System – a portable closed-loop IV anesthesia system capable of automatically controlling the administration of intravenous anesthetic and analgesic drugs.

The **AutoTIVA** combines a brain monitor with an infusion system. The device acts as an "autopilot" for anesthesia, thereby allowing anesthesiologists or military physicians to concentrate on higher-level tasks, while leaving the minutiae of maintaining the patient at a proper anesthesia level to the **AutoTIVA**. It is also inherently capable of managing patients with severe hemorrhagic shock or organ failure. The **AutoTIVA** is intended to be a significant factor in improving patient safety and outcome.

- Dual anesthetic/analgesic administration for automatic control of anesthesia and sedation
- Per-second adjustments of infusion rates based on patient's state
- Automatic adaptation to changes in volemia and drug metabolism
- Robust controller design for enhanced patient safety [10, 11]
- Tested and validated concept in thousands of cases [6, 7, 9]
- Small logistical footprint: ideal for battalion aid stations and higher echelons of care
- Simple and easy-to-use
- Reduced care provider workload [7]

Why TIVA?

Improved Outcomes

- Enables the use of fast acting agents with rapid elimination
- Allows for better intra-operative hemodynamic control [15]
- Not prone to malignant hyperthermia
- Fast recovery and orientation [15]
- Does not induce seizures
- Lower incidence of post-operative pain [3] and nausea and vomiting [2]
- Associated with lower incidence of post-operative delirium [3]
- Associated with lower incidence of pulmonary complications [19]
- Associated with longer survival in cancer surgery patients [4]

Convenience of Use

- Small logistical footprint
- Uses only simple, cost-effective and low-maintenance equipment
- Non-toxic for care providers

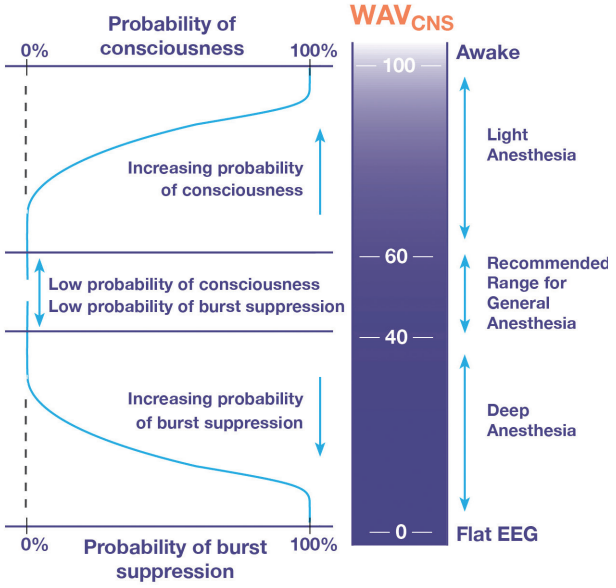
Theory of Operation

The **AutoTIVA** is a fully automated anesthesia delivery system, based on the closed-loop delivery of intravenous drugs Propofol (a potent anesthetic) and Remifentanil (a fast acting opioid). The device is designed to automatically regulate the infusion rates of the two drugs, to reach and maintain the patient at a desired depth of anesthesia.

The adjustments in drug infusion are based on a quantifiable measurement of patient's brain activity under the effect of anesthesia – the WAV_{CNS} (Wavelet Anesthetic Value for Central Nervous System) [12]. This proprietary variable is calculated from a non-invasive physiological EEG signal. Due to the fact that the brain is end-target organ of anesthetic drugs, brain activity derived variables such as the WAV_{CNS} can provide a direct measure of depth of anesthesia.

The WAV_{CNS} index takes values between 100 (an awake state) and 0 (deep coma). As anesthetic drug effect deepens, the WAV_{CNS} index decreases. The recommended WAV_{CNS} range for general anesthesia is between 40 and 60. Within this range, there is a very low probability of a patient being either conscious or in a too deep anesthetic depth.

The WAV_{CNS} is used as feedback by the **AutoTIVA** closed-loop control algorithm to calculate the infusion rates of intravenous drugs needed to deliver prescribed anesthesia. The anesthesiologist sets a WAV_{CNS} target for the patient's brain activity level indicative of the desired depth of anesthesia. The **AutoTIVA** device then continuously compares the target set by the user with the measured brain activity level, to automatically adjust the infusion of the device's pumps to attain the target. This above concept has been clinically confirmed in both adult and pediatric patients [5, 6, 13, 14, 17].



Why Closed-loop?

- Simplifies anesthesia management
- Leverages the benefits of both brain monitoring and TIVA
- Reduces anesthesia provider's workload
- Outperforms manual control
- Continuous vigilance
- Has been associated with reduced sedative and vasopressor use

Technology highlights

Simulation #1

The **AutoTIVA** enables care providers to achieve the desired anesthetic depth in a patient by setting a target range for the WAV_{CNS} index. The closed-loop controller then automatically adjusts TIVA infusion to reach and maintain the targeted depth.

A deeper depth typically leads to a significant increase in Propofol delivery, followed minutes later by a progressive decline in its infusion rate. Conversely, a shallower depth is achieved by stopping momentarily the pumps and resuming their operation at a lower infusion rate once the brain activity level is close to the targeted range.

The constant adaptation of the infusion rates is handled automatically by the **AutoTIVA** closed-loop controller, thereby freeing valuable time for the care provider.

Simulation #2

In this example, an abrupt loss of hepatic function is simulated (marker #1). Propofol is no longer metabolized and accumulates quickly in the blood stream leading to a deepening of the anesthetic effect. Based on this change, the **AutoTIVA** closed loop controller slows down the rate of delivery to prevent exceeding its targeted depth-of-anesthesia range.

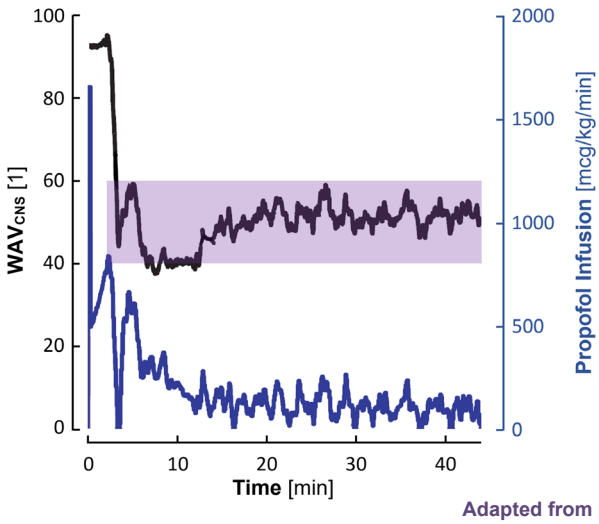
Once the hepatic function returns to its baseline value (marker #2), Propofol metabolism is resumed, and the subsequent reduction of the drug concentration in the blood plasma is automatically compensated by the **AutoTIVA**. This example shows how a change in the patient's physiological response to anesthesia is automatically corrected by the **AutoTIVA** system.

Clinical Experience

Dual Propofol and Remifentanil closed-loop delivery based on brain activity monitoring has been the subject of intense clinical research. Clinical evidence has demonstrated the technical and clinical feasibility of this method [17]. Clinical studies, in particular, have demonstrated that closed-loop TIVA delivery outperforms manual delivery in maintaining a pre-defined target range [6, 9, 16], while significantly reducing the care provider workload [7]. Reports in the literature have also pointed to improved patient safety [18].

In multi-centric studies, performance of the closed-loop delivery system was shown to be identical between centers, in contrast to the performance of the care providers delivering TIVA manually [16]. Thus, closed-loop delivery can provide institutions with the means to develop and implement goal-directed anesthesia protocols. This would also allow junior anesthesia providers to perform at the same level as experienced care providers.

Finally, trials in deep sedation have shown the association between closed-loop delivery and a significant reduction in sedative and vasopressor use [8].



Adapted from [6]

Example case from a pediatric study showing the measured WAV_{CNS} (black line), the targeted range (purple background) and the Propofol infusion rate (blue line). In this case, the closed-loop controller was used to induce and maintain the patient in an adequate anesthesia range defined as a WAV_{CNS} value of 50 (+/-10 units).

Product Specifications

Infusion Pumps	Pump #1: For *Remifentanil*	Pump #2: For *Propofol*
Indications	• Volumetric pump for intravenous drug delivery. • Intended for therapies requiring a continuous rate of infusion or clinician-controlled boluses. • The infusion rate for each drug can be set manually by the user, or automatically by the AutoTIVA controller to drive and maintain patients at the desired depth-of-anesthesia range selected by the user. • Intended to be used under the supervision and interpretation of a medical professional licensed to provide anesthesia.	
Drug Reservoirs	20 mL or 50 mL drug vial	100 mL drug vial
Delivery Methods	Continuous infusion, clinician-initiated bolus	
Mechanism	• Rotary peristaltic with epicyclical gears • Single use pump head integrated with the administration set	
Continuous Rate	1-1,200 mL/h	
KVO Rate	1 mL/hr (user selectable)	
Bolus Rate	600 or 1,200 mL/h (user selectable)	
Bolus Dose	User defined	
Flow Accuracy (per IEC 60601-2-24)	• +/- 2.5% for continuous infusion rates • +/- 5.0% for boluses	
Downstream Occlusion Thresholds	300 mmHg, 600 mmHg or 900 mmHg (user selectable)	
Max Oper. Pressure	750 mmHg	
Max Bolus after Occlusion	< 1.0 mL	
Patient Safety Features	• Free-flow protection • Downstream occlusion detection • Retrograde flow prevention • Air-in-line detection • Incorrect cartridge & cartridge placement detection • High visibility alarm	
Set Change Interval	24 hrs	
Standard	IEC 60601-2-24:2012	

Brain Monitor	
Indications	• Acquires and displays bilateral electroencephalographic (EEG) signals to monitor brain function in clinical settings. • The WAV_{CNS} index, a processed EEG variable calculated by the AutoTIVA, may be used as an aid in monitoring the effects of certain anesthetic agents on adult patients. • Intended to be used under the supervision and interpretation of a medical professional licensed to provide anesthesia.
Processed Variables (per hemisphere)	• Depth-of-Anesthesia Index: **WAV_{CNS}** (Wavelet Anesthetic Value for Central Nervous System) • Electromyographic (EMG) power (70-110 Hz) • Suppression Ratio (SR) • Continuous measurement of electrode-skin contact impedances • Signal Quality Indicators: Artifacts & 50/60 Hz Noise
Number of Channels	2 bilateral EEG channels
Bandwidth	0 - 200 Hz
Noise	< 2 μVpp (0.125 - 100 Hz)
Sampling Frequency	896 S/s per channel
CMRR	> 110 dB @ 60 Hz
Electrodes Change Interval	24 hrs
Standard	IEC 60601-2-26:2012

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ISO International Organization for Standardization

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