



MEASURE THE ANS  
CONTROL NOCICEPTION  
IMPROVE OUTCOMES

## ANI and NIPE in the PICU

Analgesia  
Nociception Index

New born Infant  
Parasympathetic Evaluation

# The problem

In the pediatric intensive care unit (PICU) there are patients that require mechanical ventilation and sedation, where analgesia is key to supporting patients with a high respiratory drive to synchronize with the ventilator, preventing patient-ventilator asynchrony (PVA).

To achieve good patient-ventilator synchrony, optimal balance between sedation and analgesia is needed. The latter can be obtained more effectively by monitoring the effect of each procedure with:

### An EEG monitor

To control the desired level of consciousness.

### The ANI monitor

To detect noxious stimulation. ANI may help to guide analgesia [13]



ANI Monitor V2



NIPE Monitor V1



ANI MOC-9 Module



ANI-MR Module



Several publications have proven that, in mechanically ventilated patients, a protocol based on analgesia more than sedatives (analgo-sedation) will improve pain scores, reduce sedatives (54%) and related consequences of delirium, decrease length of stay (50.8 h), time on ventilation (45.5h) and associated medication costs [1]. However, overuse of analgesia, especially opioids, must also be avoided as 20% to 70% of patients receiving opioids during ARDS will experience side effects: respiratory depression (27%), gastrointestinal problems (41%), delayed emergence (28%) and tachyphylaxis (37%) [2]. Hence, it is of great value to be able to specifically titrate the analgesic needs of each patient with a monitor dedicated to guiding analgesia.

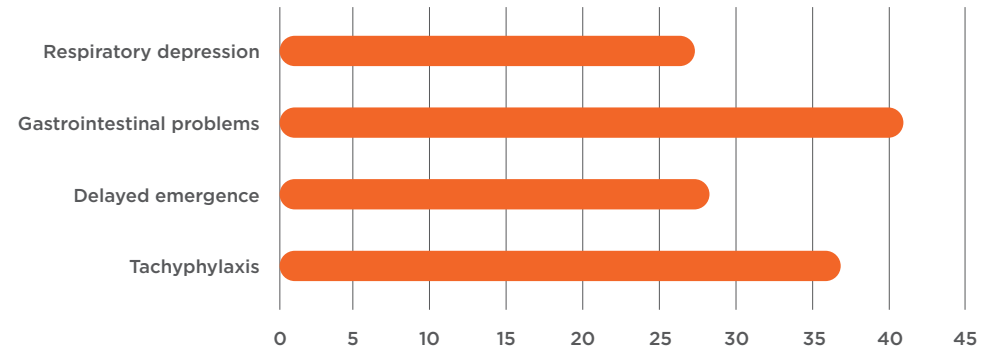
## The benefits of an analgo-sedation protocol

**54%**  
reduction  
of sedatives

**50,8h**  
decrease length  
of stay

**45,5h**  
decrease time  
on ventilation

## % of opioid-overdosing side effects

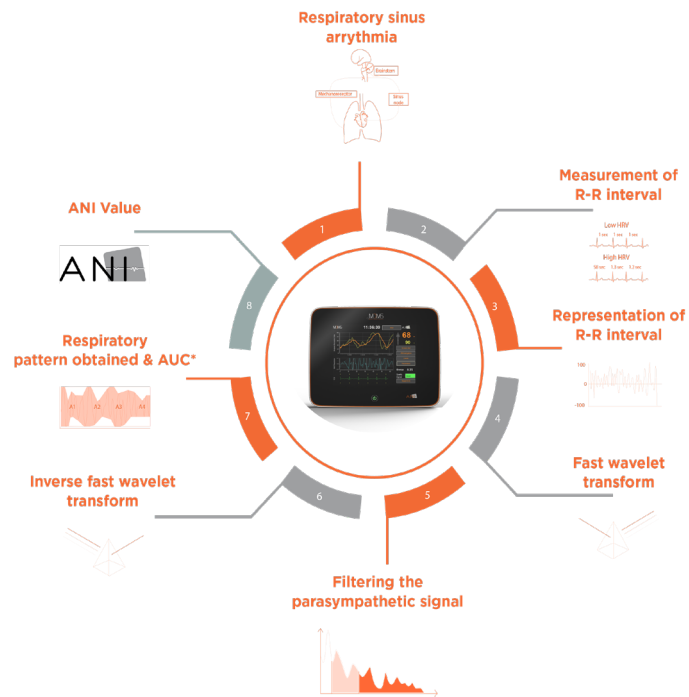


# Our solution

## Measure the autonomic nervous system (ANS)

Heart rate variability (HRV) is a well-known phenomenon that controls the regulation of the cardiovascular system via the ANS. By analyzing the HRV oscillations we can measure the activity of the sympathetic and parasympathetic nervous systems [3].

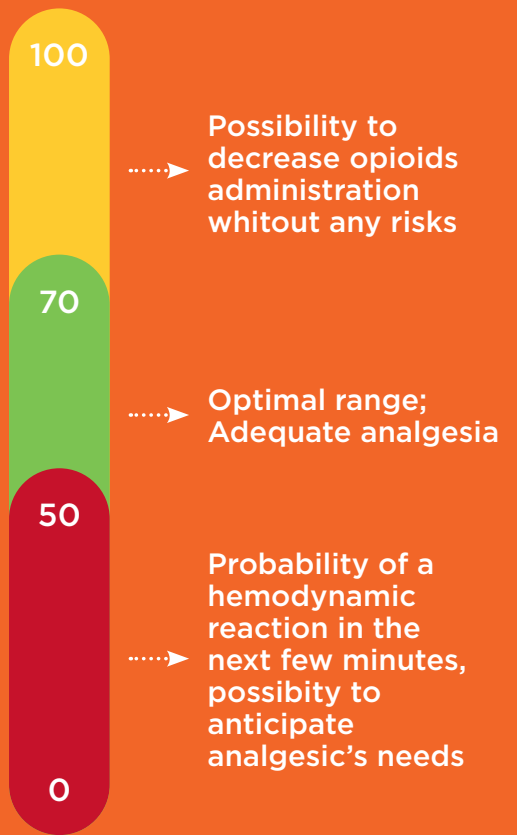
All mammals exhibit what is known as respiratory sinus arrhythmia. The latter process is controlled by the sympathetic and the parasympathetic branch of the nucleus accumbens and nucleus ambiguus, causing the heart to beat slower during expiration due to vagal activation and faster in inspiration because of sympathetic innervation [4].



The ANI and NIPE values express the relative parasympathetic activity of the patient.

The total energy of the ANS is shown in the screen of the monitor. An ANI or NIPE range between 50-70 relates to adequate analgesia, meaning that antinociception is adequate and parasympathetic activity is mildly predominant over sympathetic activity. When the ANI (or NIPE) value falls below 50, the occurrence of a hemodynamic response within the following 5 minutes is very likely [5]. This information can be used to predict and avoid a hemodynamic response by increasing the analgesia.

## Interpretation of ANI



nb : the energy must be between 0,05 and 2,5 for an interpretable ANI.

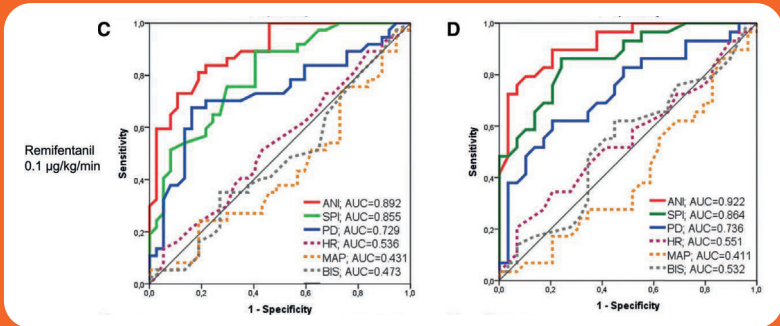
\*AUC : calculation of area under the curve of the respiratory pattern



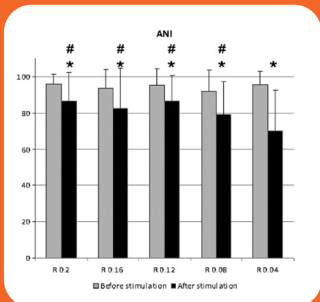
# The result

**ANI can detect nociception <sup>(6,7)</sup> and may help to take the decisions <sup>(8)</sup> to control the autonomic response improving patient outcomes <sup>(17)</sup>**

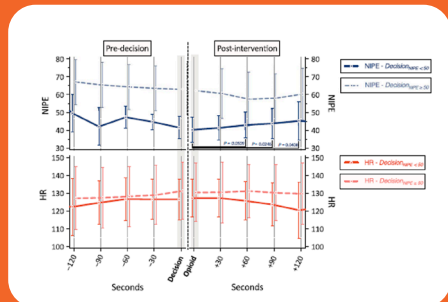
In Anesthesiology 2017, Funcke et al. showed that the ANI is the best in its class for detecting nociception versus other parameters, especially under opioid conditions [6]. Intensivists titrate analgesics based on heart rate (HR) and blood pressure, but Funcke et al., demonstrated that ANI is more sensible and specific than haemodynamics to detect nociception for adults [6] and children [7]. NIPE is able to show the effect of the analgesic provided and detect nociception better than HR [8].



Picture modified from Funcke et al. [6]



Picture modified from Sabourdin N. [7]



Picture modified from Weber et al. [8]

Detecting nociception would allow improved titration of analgesics.

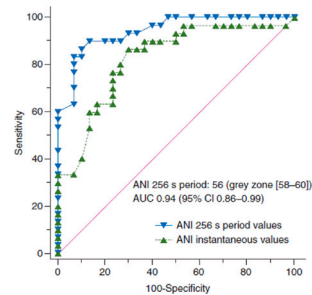




There are several publications indicating that ANI and NIPE can detect nociception and can be safely used in the PICU setting for guiding analgesia in deeply sedated patients [9][10][11].

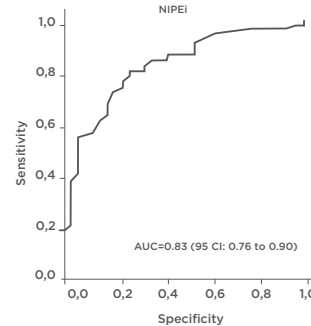
## Analgesia nociception index for the assessment of pain in critically ill patients: A diagnostic accuracy study

Postoperative pain assessment in children: a pilot study of the usefulness of the analgesia nociception index



Picture modified from Gall O. et al. [9]

Assessment of Procedural Distress in Sedated/Intubated Children Under 3 Years Old Using the Newborn Infant Parasympathetic Evaluation: A Diagnostic Accuracy Pilot Study



Picture modified from Recher M. et al. [10]

Newborn Infant Parasympathetic Evaluation Index for the Assessment of Procedural Pain in Nonanesthetized Infants: A Multicenter Pilot Study

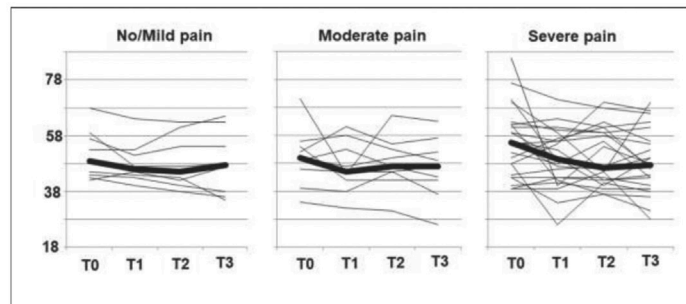


Fig. 2 Plots of individual time courses (thin lines) and median time courses (thick lines) of NIPE for no/mild pain, moderate pain and severe pain subgroups. NIPE values 1 minute before (T0), 1 (T1), 2 (T2), and 3 (T3) minutes after a painful stimulus. NIPE, Newborn Infant Parasympathetic Evaluation Index.

Picture modified from Wallas et al. [11]

In this context, ANI can differentiate the pain, and correlates with FLACC scores, in postsurgical patients [9]. A NIPE of 53 or higher correlates with adequate analgesia in children below 3 years [10]. NIPE is able to differentiate between different stimulation intensities in babies below 1 year [1].

### Clinical Guidelines

ANI has been mentioned as an interesting technology for nociception detection in the 2018 Society of Critical Care Medicine clinical guidelines for sedoanalgesia in ICU [15], in the sedoanalgesia and ventilation protocol for Covid-19 from Hospital Puerta de Hierro de Madrid [16] by the SEMICYUC (Spanish Society of Intensive Care Medicine) [17] and in the guidelines from the Society for Pediatric Anesthesia recommendations for the use of opioids in children during the preoperative period [18]. MDoloris technology is being increasingly used worldwide for the detection and management of nociception.





## The main benefits of using ANI/NIPE technology



Predictivity of hemodynamic reactivity [5]



Helpful to diagnose the etiology of a haemodynamic event [12]



Refine opioids titration [13]



Predict post-extubation pain [14]





## Testimonials



*“Using ANI and NIPE in my daily practice, I am able to titrate the analgesics more efficiently in my pediatric patients.”*

**Dr. David Lozano Diaz MD**

**Pediatrician in Neonatal and Pediatric ICU. Pediatric Pulmonology at Hospital General La Mancha Centro, Ciudad Real**



*“I found the ANI and NIPE monitor in PICU extraordinarily useful in the following situations:  
a) to monitor easily and continuously the comfort/distress balance in children  
b) to detect nociception in those patients without any alternative with scales like in deep sedated patients and neuromuscular blocked patients. I recommend its use to the PICU professionals to improve their patients care.”*

**Dr. Rocio Tapia**

**Pediatrician in Pediatric ICU. Hospital Ramón y Cajal, Madrid**

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The Society for Pediatric Anesthesia recommendations for the use of opioids in children during the perioperative period  
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ANI Monitor V2, ANI MOC-9, NIPE Monitor V1 and the ANI-MR are class IIa medical device, manufactured by MDoloris Medical Systems. CE evaluation was performed by Bureau Veritas Italy (1370) for the ANI Monitor V2, NIPE Monitor V1 and the ANI MOC-9. CE evaluation was performed by BSI (2797) for the ANI-MR. © 2021 MDoloris Medical Systems. All rights reserved. MD/QUA/EN14.1 v.03