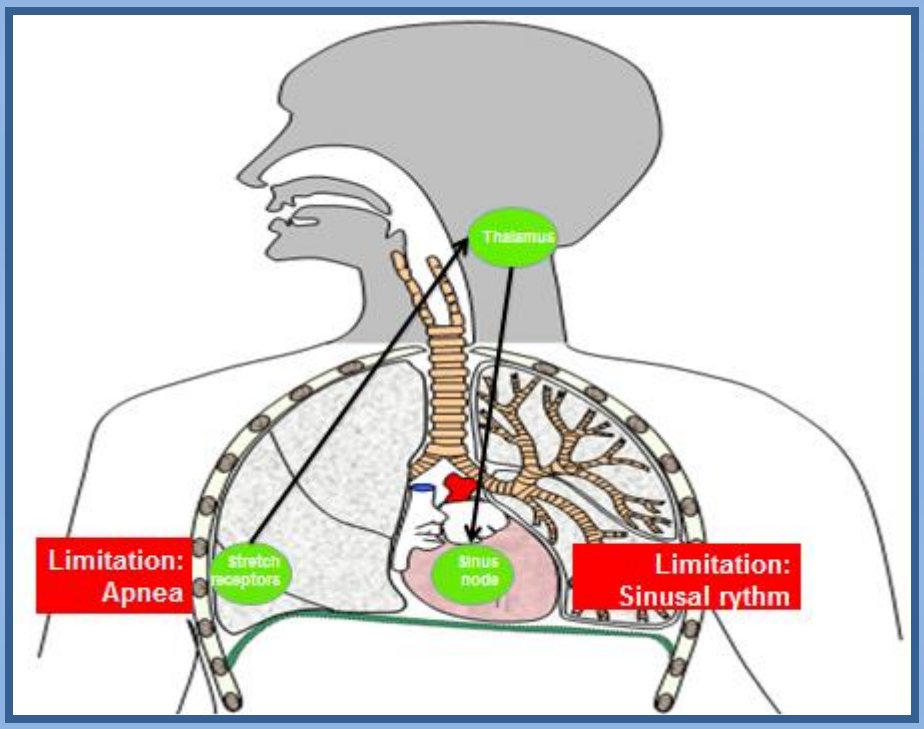
INTERPRETATION OF THE ANI PARAMETER,

THE EVOLVING ROLE OF ANALGESIC MONITORS.

MetroDoloris, SAS
Parc Eurasanté, 154 rue du docteur A. Yersin 59120 Loos.
Tel +33 (0)960117272 Fax +33(0)970065703
www.metrodoloris.com

The ANI technology calculates the power of the parasympathetic reflex loop as represented below:



A pain free patient will have a prevailing parasympathetic tone. The result will be a powerful parasympathetic reflex loop which will increase the heart rate during the inspiration and will decrease the heart rate during the exhalation. So the ANI parameter will be high.

A patient experiencing pain (noxious stimuli) will react by activating their sympathetic tone. The result will be a deactivation (like a reflection in a mirror) of the parasympathetic tone thus a light parasympathetic tone even non-existent. The power of the parasympathetic reflex loop will be light or non-existent as well. Thus heart rate variability remains unchanged during breath, reflected in a low ANI index*.

LIMITS:

- **The ANI parameter is explicable only when the stretch receptors within the lungs record a pulmonary dilatation (with positive ventilation or negative ventilation as well). So it is impossible to get a reliable ANI parameter during an apnoea (for the intubation for example)**
- **The ANI is measurable only if the parasympathetic reflex loop leads the heart rate via the sinus node. Any drug that affects the sinus node could influence the reliability of the ANI parameter (e.g.: atropine, ephedrine, catecholamines).**

*Jeanne M., Logier R., De Jonckheere J. and Tavernier B., Heart rate variability during total intravenous anesthesia: effects of nociception and analgesia. Auton Neurosci, 2009. 147(1-2): 91-6.

Jeanne M., Logier R., De Jonckheere J. and Tavernier B., Validation of a graphic measurement of heart rate variability to assess analgesia/nociception balance during general anesthesia. Conf proc IEEE Med Biol Soc, 2009.1:1840-3.

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1 – How to interpret the ANI?

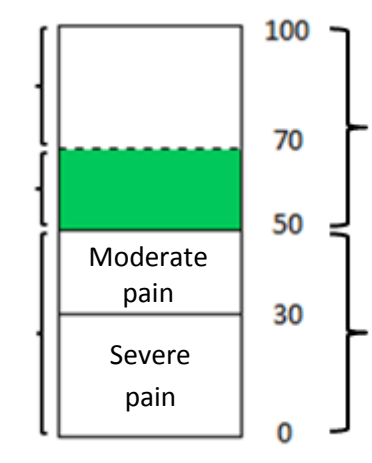
The ANI is represented as an index on a scale from 0 to 100. This index reflects the parasympathetic nervous system activity.

Unconscious patient	Conscious patient
ANI = tonus pΣ = Nociception + ~~psychological stress~~	ANI = tonus pΣ = Nociception + psychological stress
The clinical trials have shown that ANI between 50 and 70 represents adequate analgesia under general anesthesia. Studies have also shown that ANI under 30 predicts the occurrence of hemodynamic reactivity.	**With a conscious patient, the higher the ANI reading, the more predictive this is of the patient's pain free state. Thus it is possible that ANI reaches high values like 90 or 100 without any analgesic introduced. However, an ANI under the adequate analgesic level is not necessarily a pain indicator but could reflect psychological stress state as well.**
Jeanne M., Logier R., De Jonckheere J. and Tavernier B., Heart rate variability during total intravenous anesthesia: effects of nociception and analgesia. Auton Neurosci, 2009. 147(1-2): 91-6.	B. Champigneulle , B. Schweitzer , E. O. Domagni , P. Carli , G. Orliaguet, O. Gall, Variabilité sinusale du rythme cardiaque au cours de la titration morphinique chez l'enfant, hôpital Necker - enfants malades, PARIS, France Faye PM., De jonckheere J., Logier R., Kuissi E., Jeanne M., Rakza T., Storme L. – *Newborn infant pain assessment using heart rate variability analysis* – Accepted for publication, Clinical journal of pain, 2010.

Over administration range
Risk of postoperative hyperalgesia

Adequate analgesia

Inadequate analgesia



Patient's comfort

Patient's discomfort

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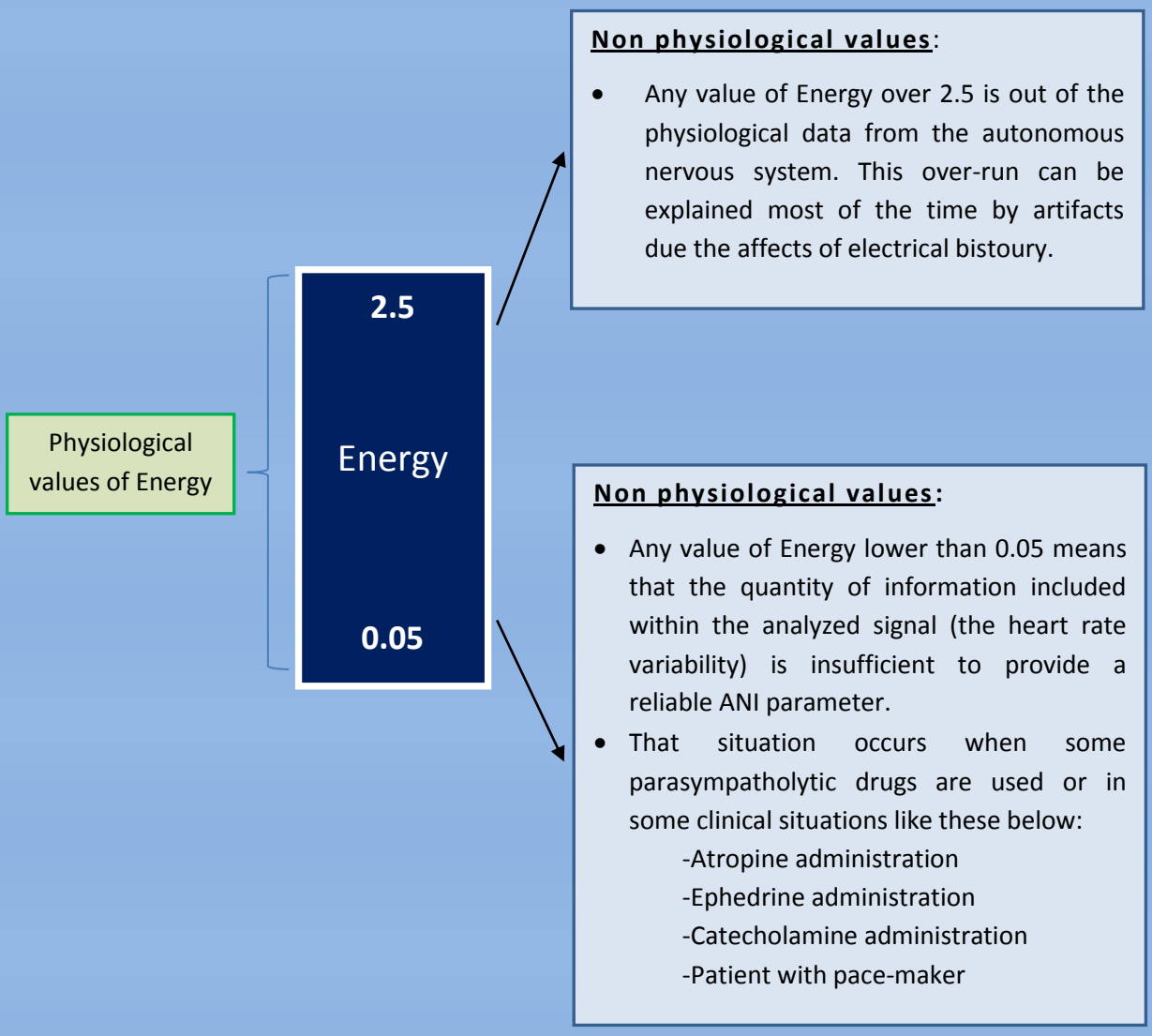
2 – How to interpret the Energy?

Scientific explanations: the Energy represents the total spectrum power of high frequencies (HF) and low frequencies (LF), thus the autonomous nervous system power (parasympathetic and sympathetic).

Clinical explanations: the Energy parameter represents the quantity of information included in the signal of heart rate variability or the signal respiratory sinus arrhythmia. Under some values, we consider that the quantity of information included in the analyzed signal is insufficient to provide a reliable ANI parameter.

The Energy parameter is used in order to confirm the reliability of the ANI index calculated:

We consider that the ANI parameter calculation is reliable between the values: 0.05<Energy<2.5



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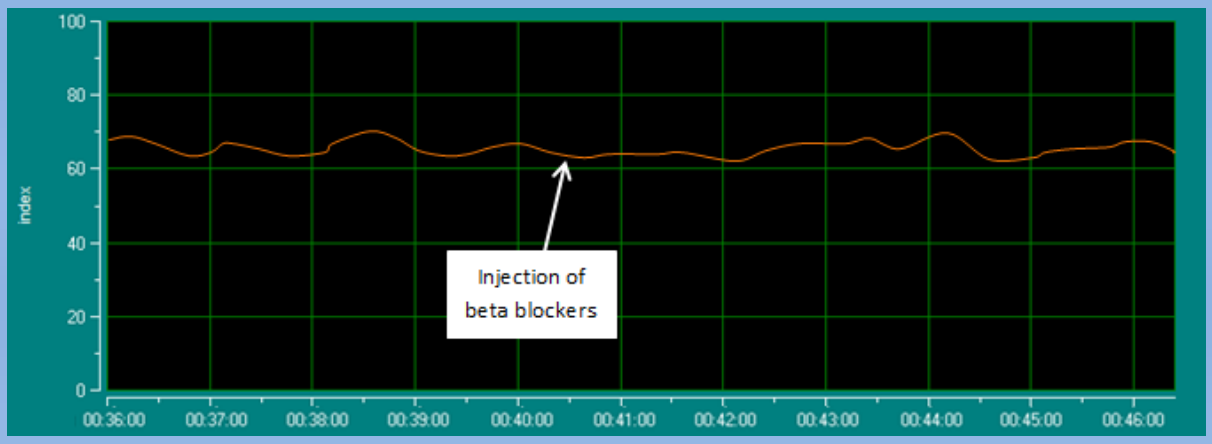
The information below is reproductions of examples based on clinical results and on experiences from the use of ANI technology.

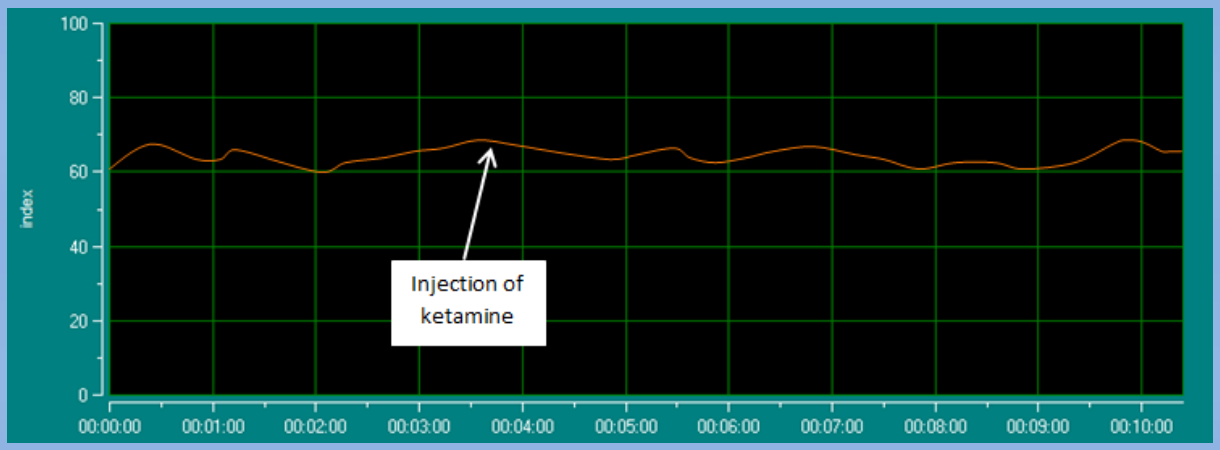
Example 1: Injection of Beta blockers



The injection of beta blockers has only limited impact on the ANI calculation.

The value of the Energy is not subjected to significant variations and stays in normal range values (0.05 < Energy < 2.5).

Example 2: Injection of ketamine (with anti NMDA dose)



The injection of ketamine doesn't cause any impact on the ANI calculation. There is no significant modification on the ANI calculation.

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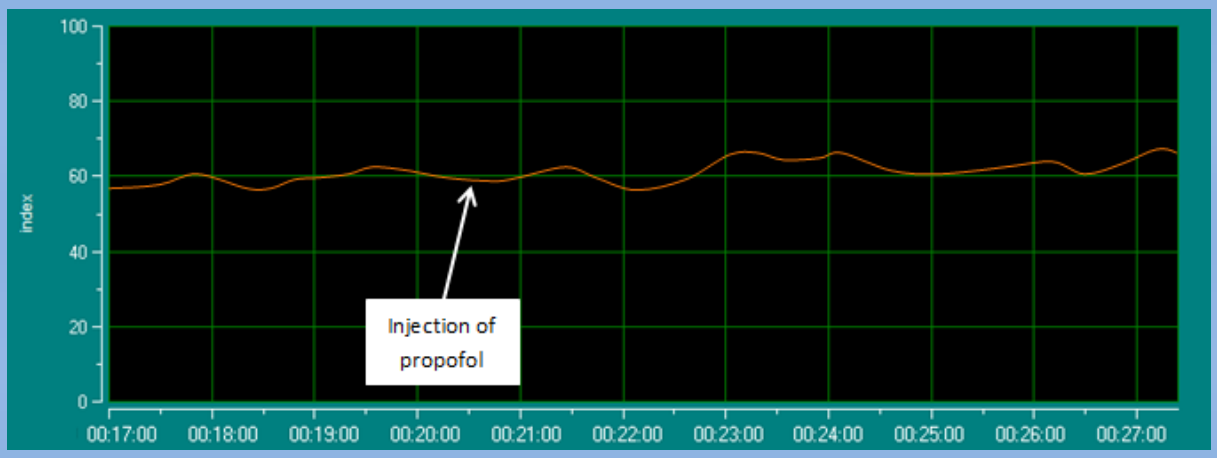
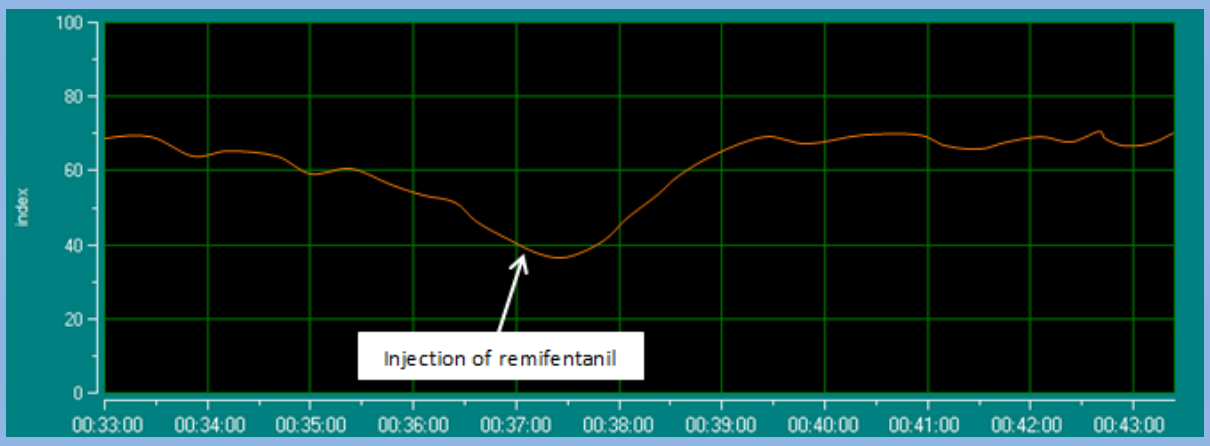
Example 3: Injection of propofol



The injection of propofol or the rise of halogenated gases level for the support of anesthesia doesn't cause any impact on the ANI calculation. In the example above, the subsequent variations of ANI values are not significant during the administration of the drug. It is necessary to always make the connection of the ANI values with the context of cares given to the patient.

Example 4: Injection of remifentanil



The injection of remifentanil causes a rise of the curve back towards normal values in line with the surgical setting. The time interval of the action of analgesia (or opioid) used, added to the ANI calculation explains the gap between the injection and the rise if the curve.

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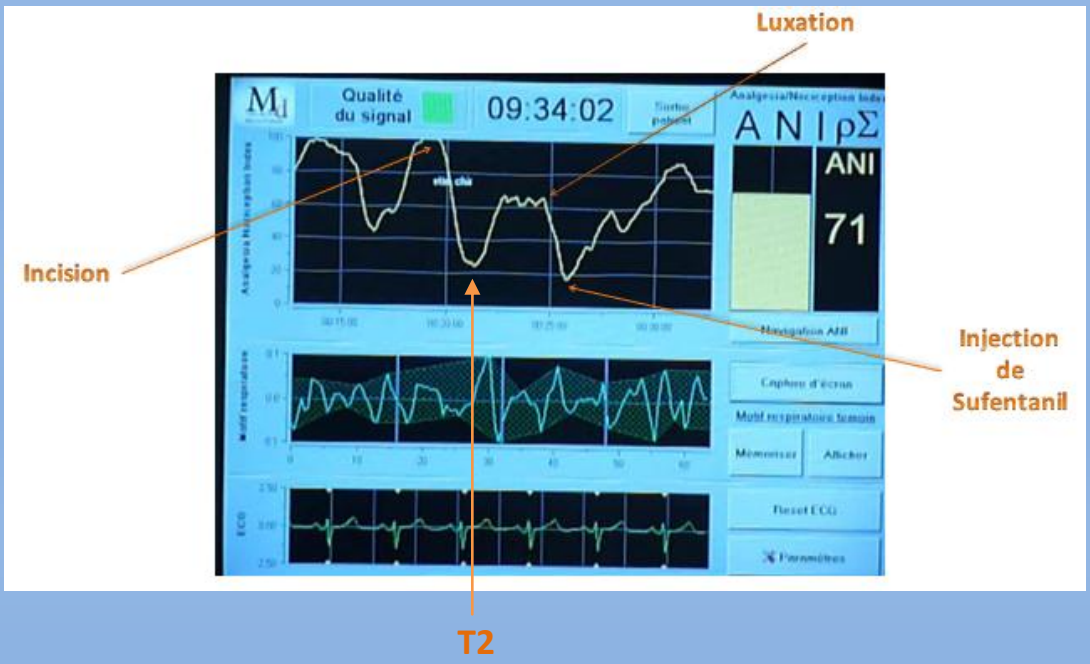
Example 5: Implementation of complete hip prosthesis



This is an example of total hip replacement surgery. It demonstrates that the incision is a noxious stimulus due the curves significant downward gradient.

At the T2 time, the patient was supplemented with an additional injection of sufentanil in order to achieve normal ANI values again.

As the dislocation of the hip represents a painful event greater than the average of previous events. The consequence is the concentration of analgesia (or opioid) is insufficient to compensate for this new event.

So the bolus of sufentanil provides enough analgesic properties to allow the curve to return to normal values.

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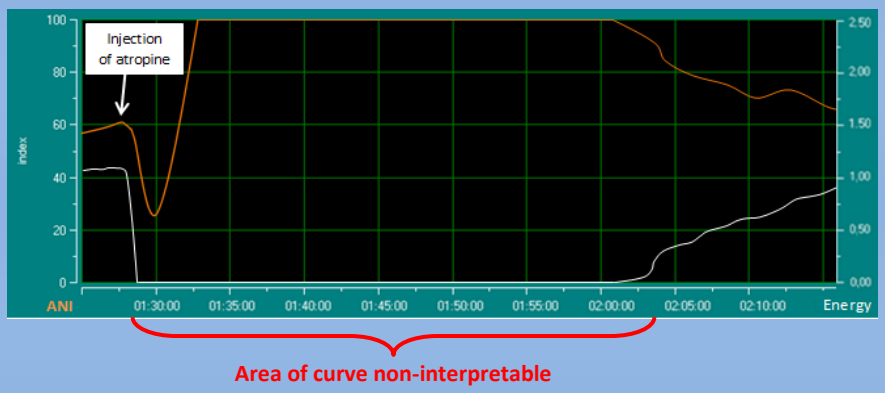
LIMITATIONS

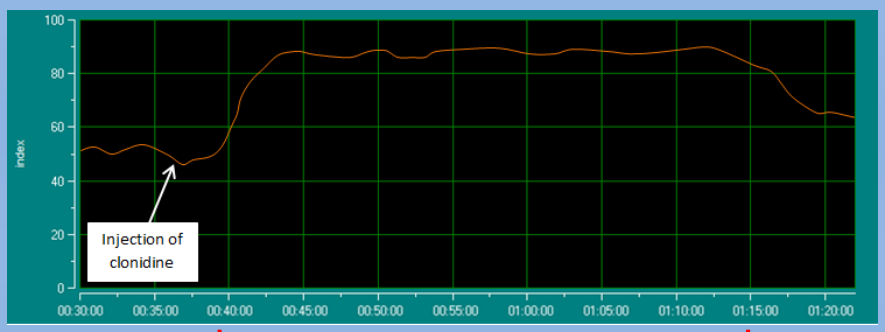
The atropine



Area of curve non-interpretable

The effect of atropine is parasympatholytic, results in artificial regularity and the ANI calculation principle becomes misguided. The curve rises to ANI value of 100 for the time of atropine effect, around 20 min. If you check the window of "Energy", you'll notice the value lower than 0.05. This parameter confirms the non-interpretable characteristic of the ANI value during that interval of time.

Injection of alpha-2 agonists (clonidine)

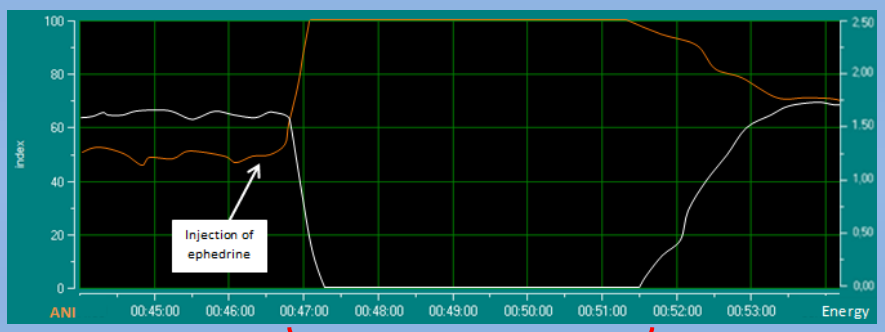


Area of curve non-interpretable

The literature highlights the sympatholytic effect of the alpha-2 agonists (e.g.: clonidine) by release of catecholamine. The result is an artificial rise of the parasympathetic tone thus of the ANI.

In that case, the sympatholytic effect induces a significant rise of the ANI to a threshold between 80 and 100 and will remain for 30 to 45 min, the time of clonidine effect.

Injection of ephedrine



Area of curve non-interpretable

The effect of ephedrine is parasympatholytic which results artificial regularity and the ANI calculation principle becomes misguided. The ANI curve rises to a value of 100 during the time of atropine effect, from 5 to 6 min. This reaction will be accompanied by a fall of the Energy value under 0.05 during the time of ephedrine effect.

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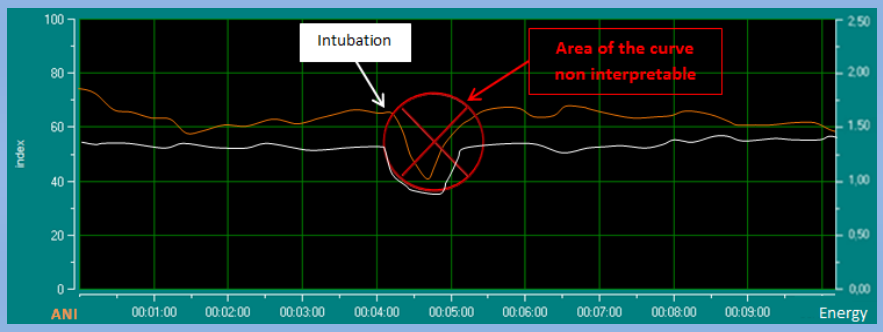
The intubation



The intubation process causes apnoea. The stimulation of stretch receptors responsive to mechanical stress during the breathing is interrupted and the parasympathetic reflex loop is stopped.

Return to breathing: the assisted respiration returns to "mechanical respiratory" then finding the respiratory sinus arrhythmia phenomenon which determines the ANI calculation. The ANI value is also reestablished.

If you check the window of "Energy", you'll notice the value falls in non-physiological values (lower than 0.05) during the intubation process. This parameter confirms the lack of relevance of the ANI parameter.

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