



The University of Vermont
LARNER COLLEGE OF MEDICINE

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MEDICAL CENTER

Analgesia Monitors

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Disclosures

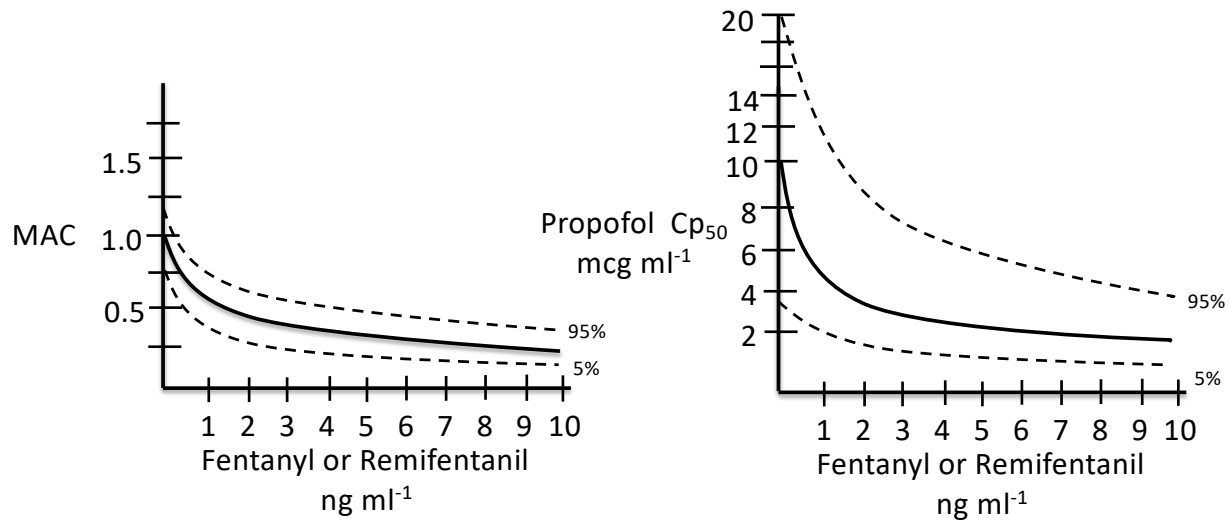
- Masimo Inc.: Consultancy, Advisory Board
- This talk will discuss several non-FDA approved monitors.

Learning Objectives

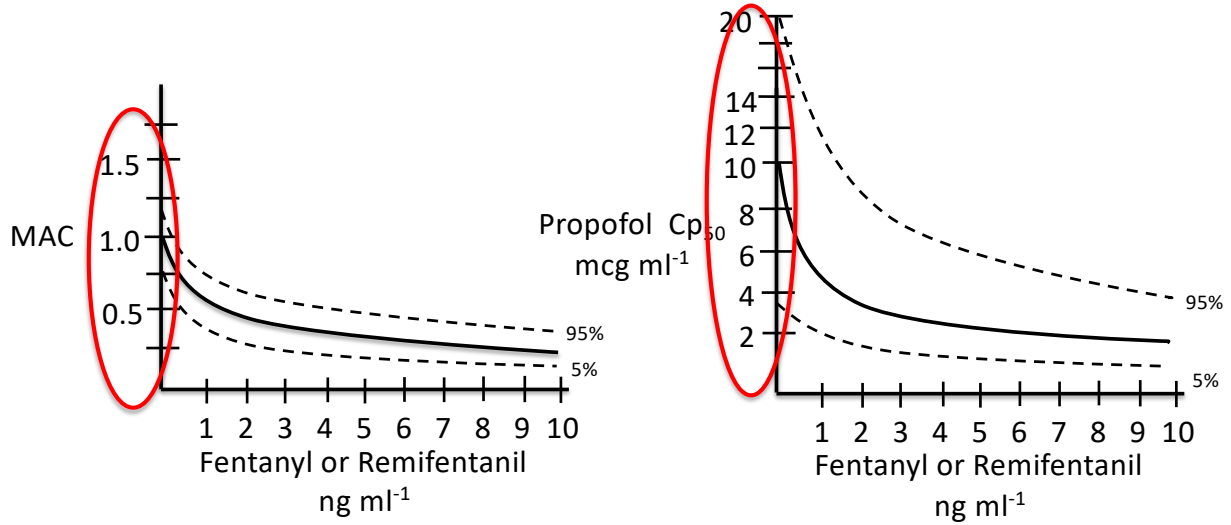
At the conclusion of this activity, participants should be able to:

- Understand how a “pain” monitor could be used in clinical practice.
- Describe the attributes of an ideal “pain” monitor.
- Discuss several approaches to developing a functional “pain” monitor.

Modern Anesthesiology Practice



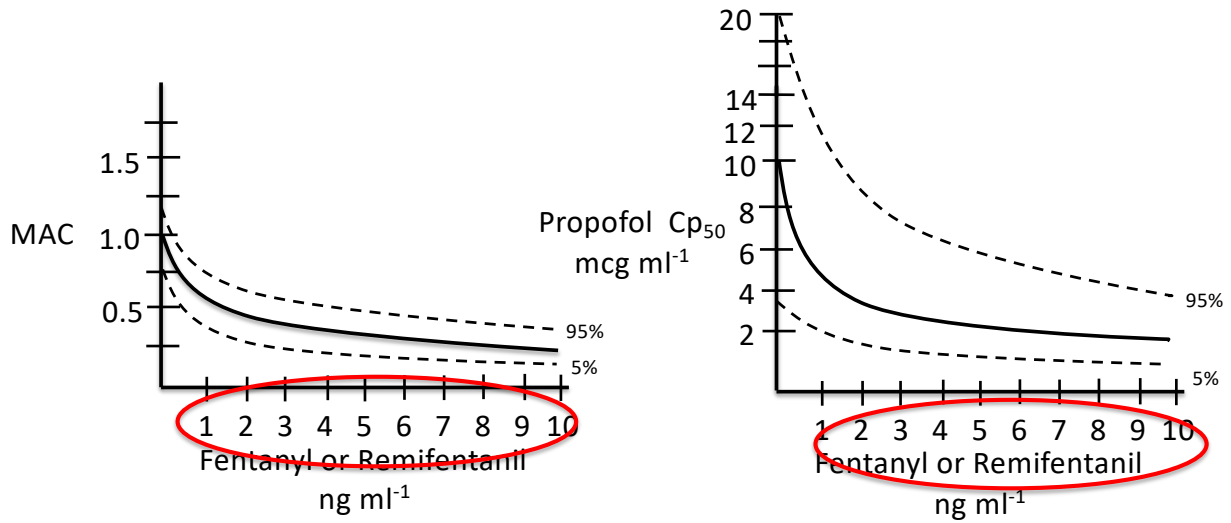
Modern Anesthesiology Practice



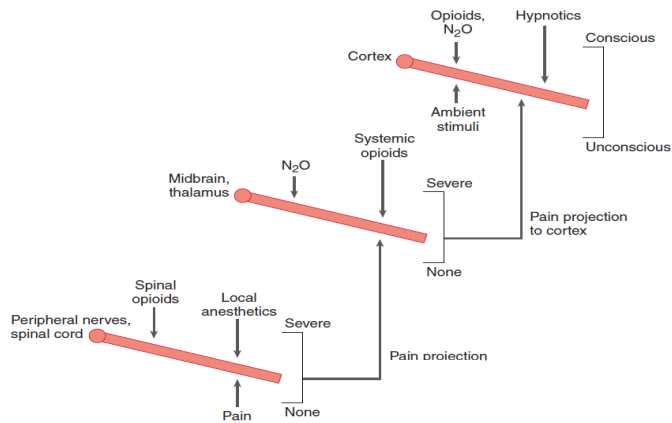
Brain activity monitors



Modern Anesthesiology Practice



Pain: “Hierarchical Model”



Stanski Shafer; Miller's Anesthesia, 2007

Why should we care when Remifentanil is so easy to use?

British Journal of Anaesthesia 112 (6): 991–1004 (2014)
doi:10.1093/bja/aeu137

BJA

Opioid-induced hyperalgesia in patients after surgery: a systematic review and a meta-analysis

D. Fletcher^{1,2,3*} and V. Martinez^{1,2,3}

First quantitative review on OIH in surgical patients

Our review clearly confirms that high intraoperative doses of remifentanil results in hyperalgesia in patients after surgery;

This is the first systematic review and meta-analysis of OIH in patients after surgery. It reveals that high intraoperative doses of remifentanil may slightly increase pain intensity at rest during the first postoperative 24 h, and moderately increase morphine use after surgery with no increase in

 THE OPEN MIND

Surgery-Induced Opioid Dependence: Adding Fuel to the Fire?

Lauren K. Dunn, MD, PhD, Marcel E. Durieux, MD, PhD, Edward C. Nemergut, MD,
and Bhiken I. Naik, MBCh

Dunn LK, et al. *Anesth Analg* 2017;125:1806-9

For 150 Years:

- Heart Rate
- Blood Pressure
- Lacrimation
- Patient Movement



Ideal Qualities of a Nociception Monitor

- Uses currently available data
- Responsive
- Reliable
- Robust
- Well correlated (good P_k) with:
 - Changes in opioid levels
 - Changes in degree of stimulation
- Demonstrated Clinical Utility
- Reasonable Price

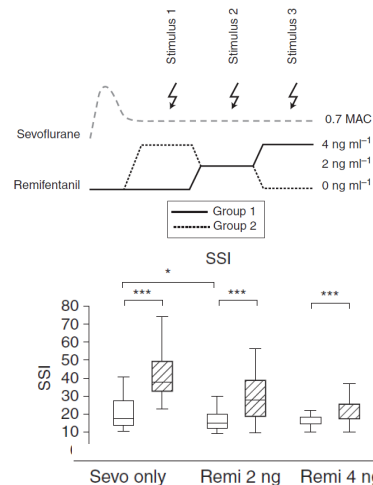
Approach #1: Surgical Pleth Index

- Surgical Pleth Index (SPI, GE Healthcare, Helsinki, Finland) combined metric based on photoplethysmographic pulse wave amplitude (PPGA) and the normalized heart beat interval (HBI).
- Scaled between 0-100, higher value-less likelihood of adequate anti-nociception.



Approach #1: Surgical Pleth Index

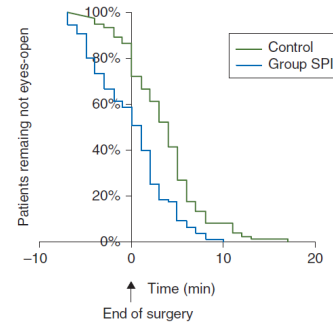
- Volunteer studies: SPI tracks with changes in opioids and degree of stimulation.
- Investigated with propofol and inhalational agents.



Gruenewald et al, BJA 2009;103:586-93

Approach #1: Surgical Pleth Index

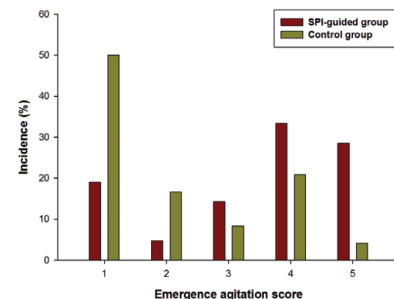
- 170 outpatients received TIVA with propofol and remifentanyl.
- Randomized to have the remifentanyl dose either adjusted according to the SPI or to clinical parameters (control group).
- Adjusting the remifentanyl dosage according to the SPI reduced the consumption of both remifentanyl and propofol and resulted in faster recovery.



Bergmann et al, BJA 2013; 110:622-8

Approach #1: Surgical Pleth Index

- 45 children elective adenotonsillectomy randomly allocated to SPI-guided group (n = 21) or control group (n = 24).
- Intraoperative fentanyl requirement was lower in SPI-guided group.
- The proportion of patients with high emergence agitation scores was greater in SPI-guided group.
- The postoperative pain score and rescue fentanyl consumption were higher in SPI-guided group.



Park JH et al, Anesthesiology 2015;122:1280-7

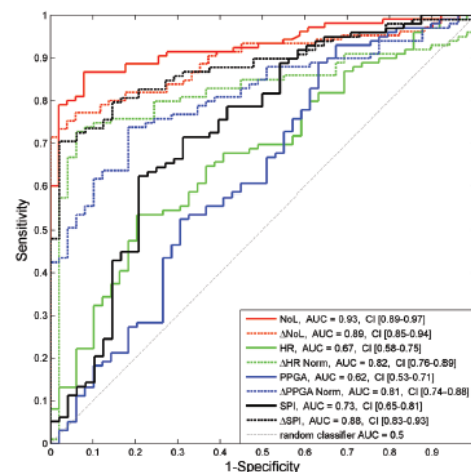
Approach #2: Multi-parameter

- NoL (Nociception Level Index, (Medasense Biometrics Ltd, Ramat Gan, Israel)
- Non-linear combination of:
 - Heart rate
 - HRV
 - Plethysmographic wave amplitude
 - Skin conductance
 - Skin conductance fluctuations
 - Time derivatives
- PMD-200™ Monitor – CE Mark, not FDA approved.



Approach #2: Multi-parameter

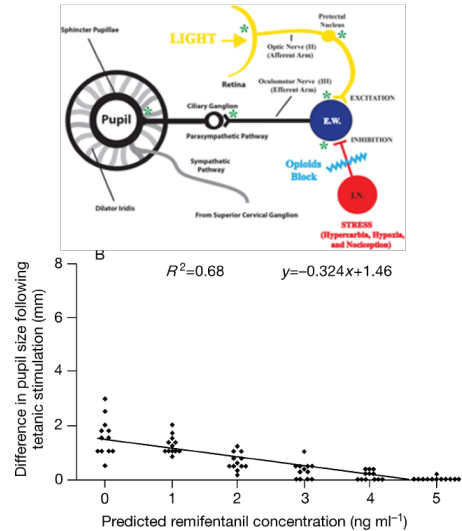
- Index 0-100
- Validated via study of 68 patients.
 - NM Tetanus before and after 2 mcg kg⁻¹ fentanyl.
 - Intubation
 - 2 or 4 ng ml remifentanyl
 - Skin incision



Edry R et al, Anesthesiology 2016;125:193-203

Approach #3: Pupillometry

- In anesthetized patients, noxious stimulation causes pupillary dilation (inhibition of parasympathetic pupilloconstrictor muscle).
- Nociceptive pupillary dilation blunted by opioids.



Rollins MD et al. Anesthesiology 2014;121:1037-1044

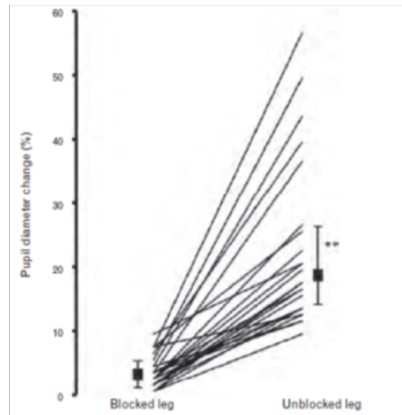
Barvais L et al, Br J Anaesth 2003;91:347-52

Approach #3: Pupillometry

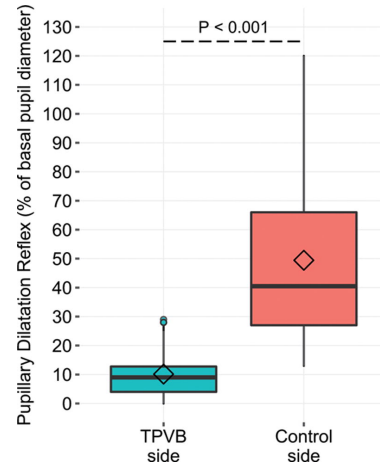
- AlgiScan® (IDMed, Marseille, France) measures pupillary dilatation reflex (PDR) to electrical stimulation.
- Can also measure comparative pupillary diameter.



Approach #3: Pupillometry

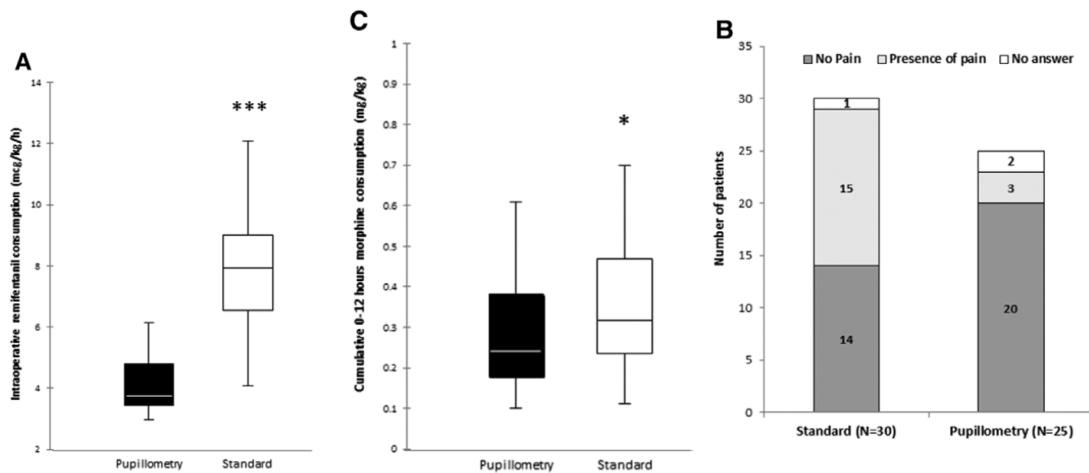


Isnardon S et al, Eur J Anaesthesiol 2013;30:429-34



Duceau B et al, Anesth Analg 2017;125:1342-7

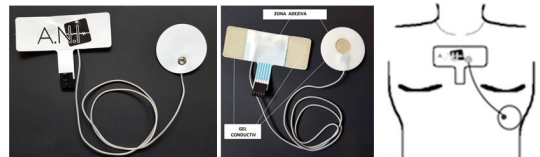
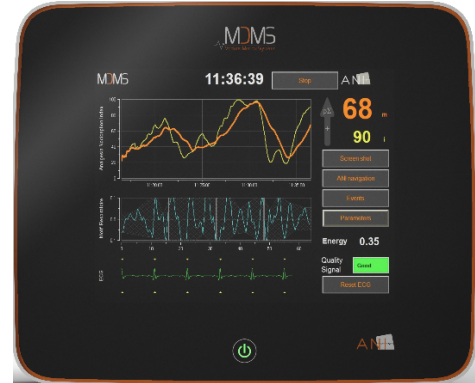
Approach #3: Pupillometry



Sabourdin N et al, Anesthesiology 2017;127:284-92

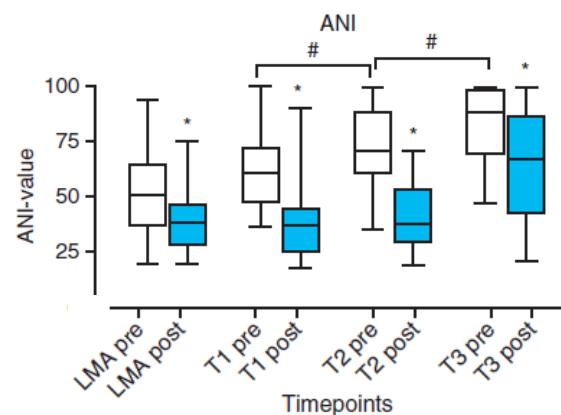
Approach #4: Parasympathetic Nervous System

- Analgesia Nociception Index (ANI, Mdoloras, Lille, France)
- Analyzes high frequency modulations (0.15-0.4 HZ) of heart rate variability.
- Highly specific measurement of parasympathetic tone.
- Requires sinus rhythm.
- CE Mark, FDA 501K pending.



Approach #4: Parasympathetic Nervous System

- Decrease in index indicates loss of parasympathetic tone.
- Seen with nociception, ameliorated with opioid.



Gruenewald M et al, BJA 2013;110:1024-8

Approach #4: Parasympathetic Nervous System

- Outcome studies:
 - Significantly less remifentanyl used during breast surgery with paravertebral block when remi titrated to ANI between 50-70.
 - Dundar et al, J Clin Monit Comput. 2017 Epub ahead of print
 - ANI-guided morphine administration in elective laparoscopic cholecystectomy failed to show any advantage over the current standard of care.
 - Scental JA et al, Br J Anaesth. 2015;114:640-5

Approach #4: Parasympathetic Nervous System

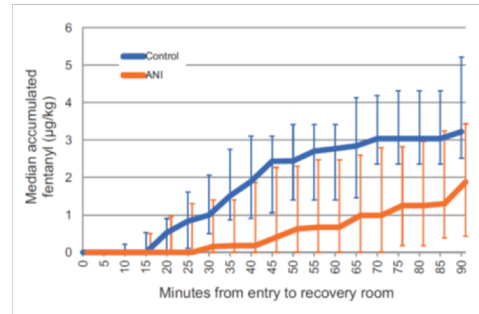
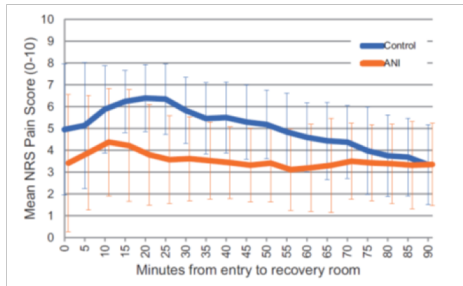
- 50 Discectomy patients fentanyl titrated by traditional practice or when ANI < 50.

Table 3. Comparison of Intraoperative Measurements

	ANI Group (n = 24)	Control Group (n = 26)	P
Intubation to first incision (min)	23 ± 7	25 ± 8	–
Total operative time: first incision to final suture (min)	85 ± 28 ^a	100 ± 51 ^a	>.99 ^b
Emergence time: final suture to awake time (min)	14 ± 6 ^a	15 ± 6 ^a	>.99 ^b
Total intraoperative fentanyl administration (µg)	416 ± 191 ^a	426 ± 247 ^a	>.99 ^b
Fentanyl bolus per hour	5.1 ± 3	2.4 ± 1.2	.0001
Fentanyl bolus size (µg) ^c	41 ± 12	82 ± 49	.0002
Fentanyl bolus size for <50 yo (µg) ^c	50 ± 0	93 ± 53	–
Fentanyl bolus size for ≥50 yo (µg) ^c	25 ± 0	64 ± 42	–
Intraoperative movement	4 (17%)	5 (19%)	>.99 ^b
BIS ^c	40 ± 6	40 ± 5	>.99
ANI ^c	68 ± 11	64 ± 12	.23
Time (%) good-quality ANI readings	97 ± 2	98 ± 2	.25
Time (%) ANI <50	20 ± 15	25 ± 23	.39

Upton HS et al. Anesth Analg 2017;125:81-90

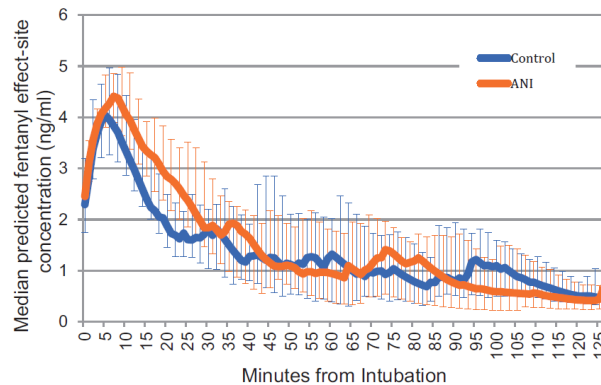
Approach #4: Parasympathetic Nervous System



Upton HS et al. Anesth Analg 2017;125:81-90

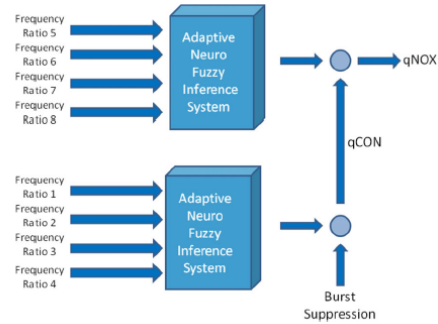
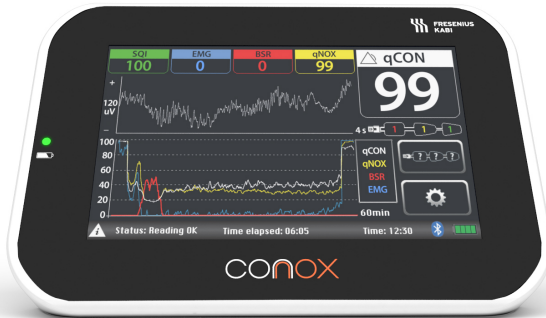
Approach #4: Parasympathetic Nervous System

- In PACU, ANI group:
 - 64% less fentanyl
 - 82% lower nausea score
 - 4% shivering vs. 27%



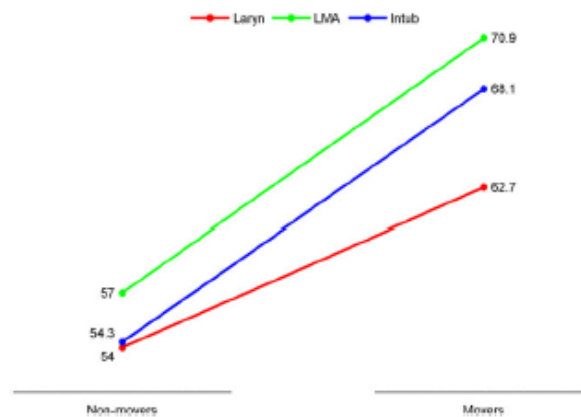
Upton HS et al. Anesth Analg 2017;125:81-90

Approach #5: EEG Parameters



Approach #5: EEG Parameters

- qNOX able to predict whether or not patients would move to noxious stimulation.



Jensen EW et al. Acta Anaesthesiol Scand 2014;58:933-941

Probability of Response to Stimulation

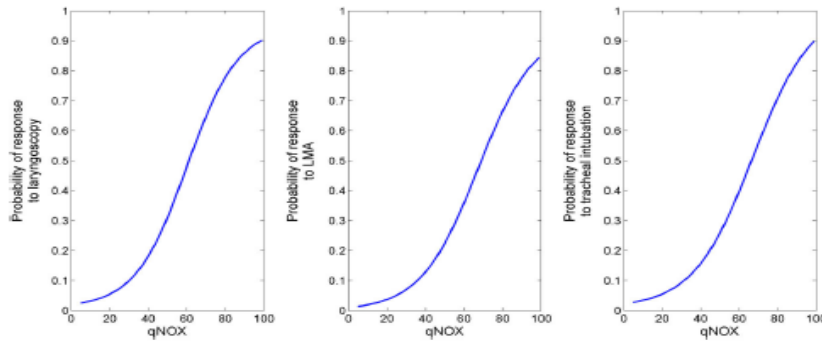
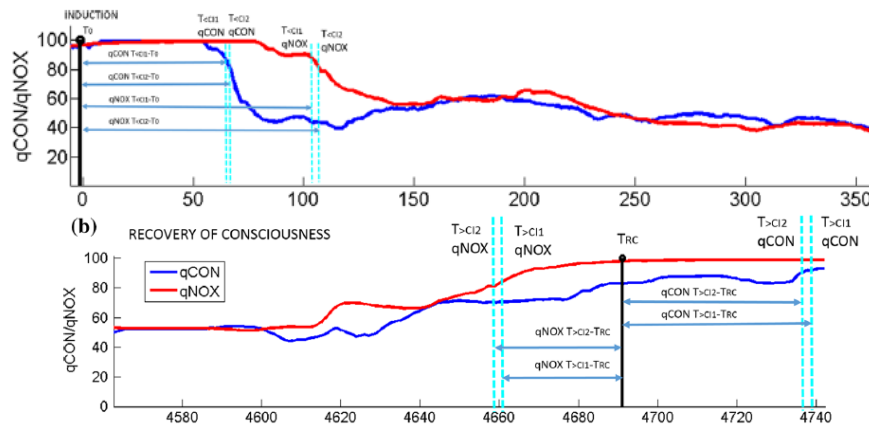


Fig. 3. Logistical regression of the probability of response to laryngoscopy, laryngeal mask airway (LMA) and tracheal intubation.

Jensen EW, Acta Anaesth, 2014

Approach #5: EEG Parameters

- qNOX lags behind qCON at LOC, but increases before qCON at ROC.



Melia et al. J Clin Monit Comput 2017; 31:1273-1281

Conclusions

- Multiple approaches being developed to improve information about nociceptive/anti-nociceptive balance during surgery.
- Utility may extend to post-op pain assessment.
- Utility studies not yet done or do not yet show convincing clinical benefit.

